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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, DOI/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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Annals of Geriatric Medicine and Research receives the First Impact Factor of 3.6 by Journal Citation Reports

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Annals of Geriatric Medicine and Research (AGMR) has grown into an academic platform offering future perspectives on the research needs related to geriatrics and gerontology.[1] The journal's comprehensive aim and scope cover not only clinical research of geriatric medicine, but aging-related basic research, pre-clinical, and translational studies in the field of gerontology. Policy and health system research related to senior health and welfare are also considered for publication. As the official journal of the Korean Geriatrics Society and the Korean Society for Gerontology, the journal provides a non-profit, open-access platform supported by the Korean Geriatrics Society and the Korean Federation of Science and Technology Societies Grant funded by the Korean government. Our journal was listed in the Emerging Sources Citation Index database, one of the Web of Science Core Collections in 2018, and indexed in Scopus, a comprehensive abstract and citation database in 2019. The contents of AGMR published since 2018 are now available in PubMed ensuring greater visibility of the research published in AGMR.[2]

AGMR has captured the seminal research findings from various researchers worldwide and the readership has expanded widely around the world. Noting the challenge of addressing the tremendous research gaps in Asian countries experiencing the rapid aging of their populations, AGMR sought to become a high-profile journal to first serve and support this region with evidence-based materials and to embrace a dualistic outlook of harnessing the eclectic richness of international and regional perspectives.[3] During the pandemic and at the beginning of the post-pandemic era, the journal has contributed to delivering critical information related to coronavirus disease 2019 and highlighting the challenge of geriatric care in the unprecedented global health crisis.[4,5]

As a result, AGMR could release innovative research results for the professional geriatric community. As a fast-growing journal in the multidisciplinary aging research field, the visibility of our scientific literature to researchers working in relevant fields continues to improve. From the 2023 release, Clarivate has included all Web of Science Core Collection journals for Journal Impact Factor (JIF). This year, AGMR gained the first JIF of 3.6 by Journal Citation Reports, which is the official source to find a journal's impact factor integrated with the Web of Science platform.[6] It means that the citable articles published during 2020 or 2021 in AGMR have been cited 3.6 times on average in 2022. This is a splendid achievement given that the impact factor of AGMR was comparable to some prestigious journals of the geriatric field such as European Geriatric Medicine (JIF = 3.8) and Geriatrics Gerontology International (JIF = 3.3). In addition to JIF, the CiteScore 2022 of AGMR was 4.2 which continues to rise every year (Fig. 1).[7] The CiteScore is an average of citations per document over the past 3 years and a useful journal evaluation metric released by Scopus to give a comprehensive and transparent view of a journal's impact. SCImago Journal & Country Rank (SJR) published by Scopus ranked AGMR 49 among 113 journals in Geriatric and Gerontology category, which is the second quartile (Q2) of indexed journals.[8] This achievement would not have been possible without the enthusiastic support and contributions of our editorial board members, reviewers, authors, and readers to develop a rigorous academic platform in the field of geriatric and gerontology.

In recent years, AGMR has been actively participating in the global call to action for the Decade of Healthy Ageing declared by the United Nations.[4] The Decade of Healthy Ageing is a concerted global action urgently needed to ensure that older adults enjoy dignity, equality, and a healthy environment. In 2022, the World Rehabilitation Alliance has been established in the World Health Organization Rehabilitation program to strengthen networks and partnerships for the integration of rehabilitation into health systems.[9] AGMR has endorsed the call to action from the research workstream of the World Rehabilitation Alliance to promote the

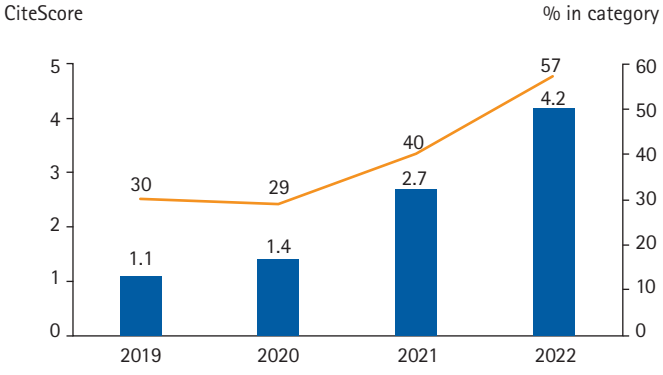

Fig. 1. The trend of CiteScore and percentile in category of Annals of Geriatric Medicine and Research by CiteScore tracker from 2019–2022.

health policy and systems research for strengthening rehabilitation ahead of global aging society. Furthermore, challenges and opportunities for our journal to serve the older population in global aging will be presented at the Research Symposium on publishing high-impact Asian research at the Asian Conference of Frailty and Sarcopenia to be held in Singapore in this October.

In order to increase its global influence beyond emerging countries in Asia, our journal continues to cover the new agenda to improve the health outcomes of older adults in post-pandemic future, and to drive the issues of geriatric care in developing countries heading towards a super-aging society, and to promote the health policy and systems research on geriatric care services in each country. It is our hope that the AGMR continue to serve an arena highlighting the importance of geriatric and gerontological research to address the unique needs of older adults in the globe.

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CONFLICT OF INTEREST

The other author claims no conflicts of interest.

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REFERENCES

1. Lim JY. Moving forward as a growing platform of geriatric medicine and gerontologic research. Ann Geriatr Med Res 2019;23:93-4.
2. Lim JY, Jung HW, Ga H. Annals of Geriatric Medicine and Research indexed in PubMed Central: an important milestone toward the leading journal. Ann Geriatr Med Res 2020;24:155-6.
3. Jung HW, Won CW, Lim JY. Annals of Geriatric Medicine and Research as a space of for developing research ideas into better clinical practices for older adults in emerging countries. Ann Geriatr Med Res 2019;23:157-9.
4. Lim JY. Challenges and opportunities toward the decade of healthy ageing in the post-pandemic era. Ann Geriatr Med Res 2021;25:63-4.
5. Noh JH, Arai H, Auyeung TW, Cesari M, Frontera WR, Ga H, et al. Bounce forward better: geriatric and gerontological research in the post-pandemic future. Ann Geriatr Med Res 2022;26:285-8.
6. Clarivate. 2022 Journal Citation Reports [Internet]. London, UK: Clarivate; c2023 [cited 2023 Sep 26]. Available from: https://jcr.clarivate.com/jcr/home.
7. Scopus. CiteScore of Annals of Geriatric Medicine and Research [Internet]. Amsterdam, Netherlands: Scopus; c2023 [cited 2023 Sep 26]. Available from: https://www.scopus.com/sourceid/21100943510.
8. SJR: SCImago Journal & Country Rank [Internet]. Amsterdam, Netherlands: Scopus; c2023 [cited 2023 Sep 26].Available from: https://www.scimagojr.com/.
9. Cieza A, Kwamie A, Magaqa Q, Paichadze N, Sabariego C, Blanchet K, et al. Framing rehabilitation through health policy and systems research: priorities for strengthening rehabilitation. Health Res Policy Syst 2022;20:101.

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Geriatric and Gerontology Research: A Scientometric Investigation of Open Access Journal Articles Indexed in the Scopus Database

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Background: Scientometric analyses of specific topics in geriatrics and gerontology have grown robustly in scientific literature. However, analyses using holistic and interdisciplinary approaches are scarce in this field of research. This article aimed to demonstrate research trends and provide an overview of bibliometric information on publications related to geriatrics and gerontology. **Methods:** We identified relevant articles on geriatrics and gerontology using the search terms "geriatrics," "gerontology," "older people," and "elderly." VOSviewer was used to perform bibliometric analysis. **Results:** A total of 858 analyzed articles were published in 340 journals. Among the 10 most contributory journals, five were in the United States, with the top journal being the *Journal of the American Geriatrics Society*. The United States was the leading country in research, followed by Japan, Canada, and the United Kingdom. A total of 5,278 keywords were analyzed. In the analysis of research hotspots, the main global research topics in geriatrics and gerontology were older adults (n=663), education and training (n=471), and adults aged 80 years (n=461). These were gradually expanded to include areas related to caring for older adults, such as geriatric assessments (n=395). **Conclusion:** These results provide direction for fellow researchers to conduct studies in geriatrics and gerontology. In addition, they provide government departments with guidance for formulating and implementing policies that affect older adults, not only in setting academic and professional priorities but also in understanding key topics related to them.

Key Words: Older adults, Geriatrics, Gerontology, Bibliometric analysis, Trends

INTRODUCTION

Due to the accelerated growth of older adult populations worldwide, there is an urgent need for the development of research and public health policy to understand and support healthy aging.[1)] A growing research consensus indicates that the characteristics of aging, once considered disparate, are likely interconnected. This scenario promotes a greater need for interdisciplinary research as this field of study is extremely complex. Interdisciplinary research enables a greater understanding of the extent of topics of interest to increase scientific productivity and provide theoretical and practical support for professional training.[2-4)] The exponential increase in interdisciplinary research in the field of geriatrics and gerontology results from the accelerated aging process worldwide and the financial investments of public and private institutions.[2)] Considerable progress has been made in understanding the aging process through multidisciplinary and/or interdisciplinary methods. However, despite these developments, many important issues require better understanding.

In an editorial on new perspectives in gerontology and geriat-

rics,[5] the authors highlighted the need to assess the cooperation and impact of studies in this area to identify trends and generate new topics, materials, and research methods. Thus, interdisciplinary research requires the exploration of a field of study using a more holistic approach. The quantitative increase in scientific publications in this area in different databases and newspapers underscores the urgent need for analyses to allow researchers to obtain information about the topic of interest. Among these approaches, bibliometric analyses reveal perspectives inherent to the main trends related to the geriatric population. Bibliometrics (or bibliometric analysis) is a statistical method that determines which topics are trending through a quantitative analysis of articles in a defined field of study.[6]

While some bibliometric investigations in geriatrics and gerontology have been published, these studies have investigated more specific areas, such as Alzheimer's dementia,[7] cardiovascular diseases,[8] psychological and physical activity,[9] multimorbidity,[10] sarcopenia,[11] falls, healthy aging,[2] coronavirus disease 2019 (COVID-19),[12] and social participation.[13] In addition to specific investigations, literature reviews on geriatrics and gerontology can provide researchers with a broader view of this field and clarify possible research directions. However, few literature reviews of geriatrics and gerontology have been conducted from a holistic perspective.[13]

Moreover, few studies have investigated the development and trends of research in geriatrics and gerontology, and the hotspots in this field remain unclear. Therefore, this study aimed to identify the research trends and hotspots to provide an overview of bibliometric information on publications related to geriatrics and gerontology using the Scopus database.

MATERIALS AND METHODS

Bibliometric methods are an integral part of research evaluation methodology within scientific fields and are increasingly used in the study of various aspects of science.[13] This study analyzed the Scopus database, an Elsevier product with a broad scope, which is the largest database, with citation data from peer-reviewed articles in various disciplines.[14] The Scopus database offers several features that facilitate bibliometric analysis. These operational functions include the journal name, document type, year of publication, authors and their affiliations, citation count, and h-index metrics for documents.[15,16] Screening of this database revealed 858 articles, which were included in the bibliometric analysis. Fig. 1 shows the schematic flowchart of the article selection process.

Search Strategy

The data for this study were acquired from the Scopus database without defining the analysis period. The search started on January 21, 2023, and contained all articles with terms using the Medical Subject Headings (MeSH) combination: (geriatrics AND gerontology AND elderly OR older AND adult) AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT-TO (DOCTYPE, "re")). This strategy enabled a broader and interdisciplinary analysis of geriatrics and gerontology. Therefore, these keywords were used such that the maximum number of relevant publications were incorporated into the extracted data.

Inclusion and Exclusion Criteria

All data from the Scopus database, including article information, such as author names, titles, journals, keywords, institutional affiliations, citations, and abstracts, were downloaded. All data were imported into a Microsoft Excel file (xls format) to check for data errors. Then, all downloaded data were filtered by the inclusion criteria, as follows: (1) open access (OA) publications (all OA publications were included); (2) papers published as articles; and (3) articles published in English. The corresponding authors of the present study, LSSN and NBO, reviewed the titles of all articles

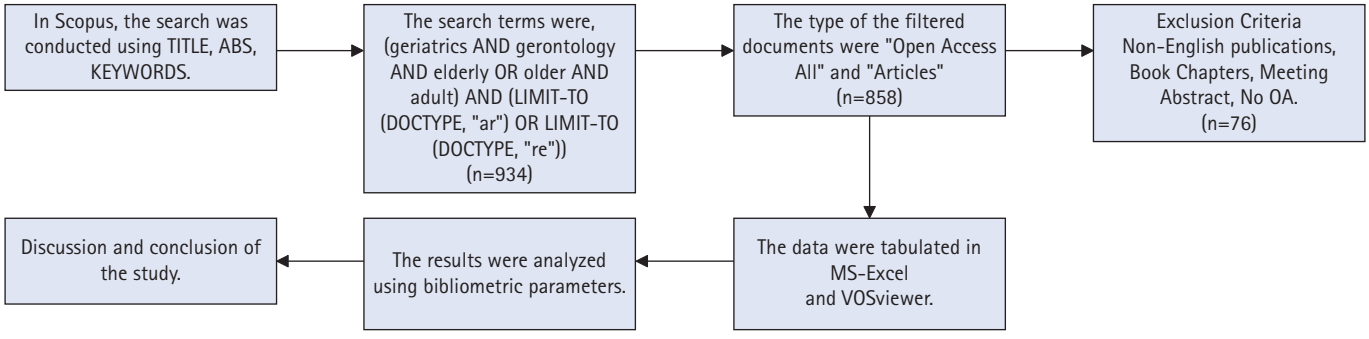

Fig. 1. Research flowchart.

for inclusion in the analysis. Any differences between them were discussed and resolved by a third author. Duplicate documents were defined as articles with the same title, authors, and year and were identified using Microsoft Excel software. In recent years, the importance of OA for authors has been heightened by the policies of major research funders in many countries, which have required that publications arising from funded work be freely available to all.

Statistical Analysis

Scientometrics is involved in productivity analysis and the measurement of scientific fields. The quantitative assessment of publication productivity through scientometric parameters is a reliable technique used to understand the impact of any research on a community.[16,17] We explored global publications related to geriatrics and gerontology through the quantitative metrics of scientometrics and bibliometrics. OA articles were analyzed. The large increase in subscription rates for conventional subscription-based journals and traditional publication editions led to the formation of the Open Access Academic Communication Movement. In this study, we used Microsoft Excel version 2019 (v16.0) and VOSviewer (v1.6.18; https://www.vosviewer.com/) to describe the basic characteristics of the publications, countries, institutions, keywords, and citations. VOSviewer uses text mining functions and advanced visual analysis to perform co-occurrence analyses.[18] Co-occurrence analysis helps quantify common information in various data, revealing the association between content and common information relations.[19] The types of co-occurrence analysis research are broad, including co-country, co-institution, co-keyword, and co-citation analyses. After searching the literature, we extracted publication dates, journals, countries, institutions, and keywords using Microsoft Excel. The analysis was then separated into three stages: (1) a descriptive statistical analysis of the growth patterns, numbers, years, institutions, countries, and main journals of the publications; (2) a co-occurrence analysis of keywords using VOSviewer; and (3) a co-citation analysis to rank the most influential articles in this field.

The results and discussion are presented together for clarity. The topics include survey status, hotspots and co-institutions, survey hotspots, and top topics.

Ethics Statement

This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[20]

RESULTS

Bibliometric analysis provides an idea of the progress of research and the contributions of researchers in a given field. In this study, we searched the Scopus database to analyze the current status and research development trends in geriatrics and gerontology to identify the contributions of different nations, institutions, and partnerships. Research hotspots were tracked using cluster keyword mapping and burst term analysis. Finally, co-citation analysis was used on the Scopus database, and global trends and the most-contributing articles in geriatrics and gerontology were compared to encourage further dialogue among scholars.

Research Status, Topics, and Co-institutions

The 858 articles analyzed from the Scopus database, published between 1965–2022 confirmed the trend of increasing research publications in geriatrics and gerontology (Fig. 2). Interdisciplinary research in geriatrics and gerontology has become more widespread, thus promoting a wide range of more in-depth research.[21] In the last 8 years (2014–2022), referred to as the "prosperity" period, global publications in this field have increased, indicating gradually increasing attention from scholars, a growth trend that is expected to continue. We consider this period to be the "perfect storm," in the sense that the aging of the population advances quickly and dynamically, together with the availability of new instruments, procedures, methods, and technologies to drive the development of research in geriatrics and gerontology. A bibliometric study by Ang et al.[22] reported that geriatrics and gerontology are new research areas, as no journals have published more than 10,000 articles. This reinforces the need for greater investments from public and private institutions and researchers to consolidate this field of study.

The articles were published in a total of 340 journals. The two journals with the largest contributions were from the clinical area of geriatrics; however, most journals had more interdisciplinary scopes, with contributions from various disciplines, especially in health and social and educational gerontology. Among the 10 journals with the highest contributions in this study (Table 1), five are from the United States, including the *Journal of the American Geriatrics Society* and the *Journal of the American Medical Directors Association* with the highest impact factors (IF), respectively. The bibliometric analysis by Ghamgosar et al.[1] on geriatric nursing also showed that these two journals published the most articles in that field. Our results showed that the listed journals are active and have high IFs based on Journal Citation Reports (JCR). In recent years, the importance of OA for authors has been heightened by the policies of major research funders in many countries, which require that publications arising from funded work be freely available.[2] Although the listed journals are traditional subscription-based periodicals, authors may choose to pay to have their articles published

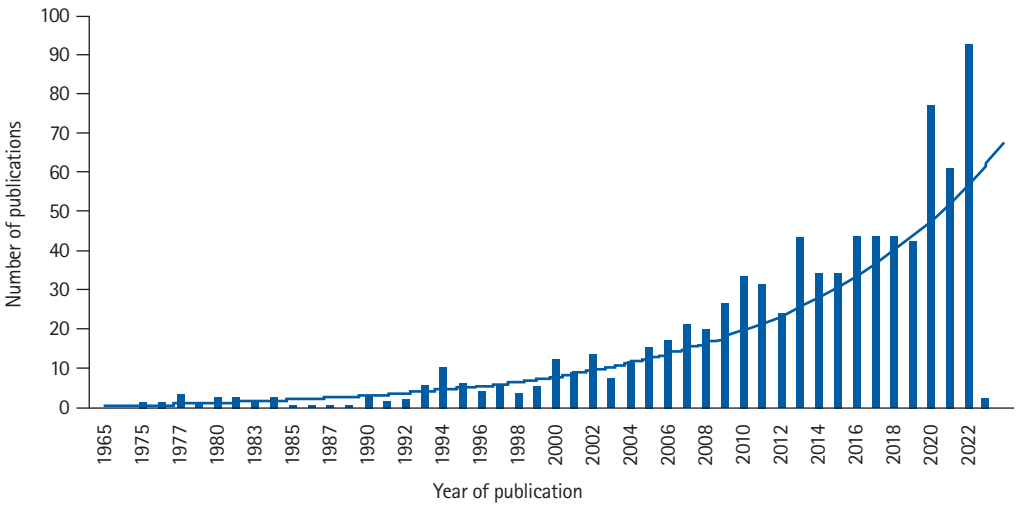

Fig. 2. Trends in publications of research on geriatrics and gerontology from 1965 to January 2023.

with OA, making them immediately and permanently available for everyone to read and download. Researchers can access most studies in geriatrics and gerontology by following the journals listed in Table 1.

The United States (n = 378) was the leading country in geriatrics and gerontology research, followed by Japan (n = 127), Canada (n = 79), the United Kingdom (n = 34), and Germany (n = 32). We observed a stable cooperative relationship between North America and Europe as well as in Asian countries such as Japan and South Korea. The institutions listed in Fig. 3 illustrate the partnerships and cooperation between those actively publishing in the fields of geriatrics and gerontology. Xiao et al.[23] identified the economy as one of the main factors affecting the productivity of countries. Additionally, countries with high rates of population aging, such as Japan and European countries, are also significant contributors of research on older adult populations, especially those aged ≥ 80 years.[24] We observed that the keyword "80+ elderly" was cited 461 times, confirming that these countries are also studying older adult individuals in this age group.

In the co-citation analysis, the article by Jerome A. Yesavage, MD, published in 1988, titled "The Geriatric Depression Scale" (GDS) was the most cited (n = 478) (Table 2). We believe that this study made important contributions to the development of this research field. Krishnamoorthy et al.[25] described the GDS as one of the most commonly used instruments to track and detect older adults with or at risk of depression, which is a public health problem. These data are consistent with the results of our analysis of the frequency of occurrence of the 20 main keywords (Table 3) and our identified key terms such as geriatric assessment, psychological aspects, depression, and risk factors.

Classification of the studies in Table 2 by macro-themes revealed three themes: cognitive assessment (articles #1, #3, #7, and #10), functional capacity (articles #2, #4, #5, and #9), and frailty (articles #6 and #8).

Research Hotspots and Topics

We analyzed 5,278 keywords. The analysis of research hotspots showed that the main global research topics in geriatrics and gerontology were older adults (n = 663), education and training (educational research) (n = 471), and older adults aged ≥ 80 years (n = 461). These hotspots gradually expanded to include care for older adults through geriatric assessments (n = 395), geriatric nursing (n = 367), and procedures and management (n = 308) (Table 3, Fig. 4). Topics related to mental health, classified into sub-areas such as psychiatry and psychology, as well as the macro-theme of functional capacity, were also research hotspots in geriatrics and gerontology. These themes were also frequently reported in other bibliometric analyses.[13,23]

In contrast, the term dementia, which was prominently featured in the studies above, appeared in only 44 articles in the co-occurrence analysis; we attribute this contrary finding to the choice of database and search strings. However, the analysis of the co-occurrence of the term dementia with the term "oldest-old" (80+) (n = 44 publications) showed that 73% of studies on dementia focused on elderly people aged ≥ 80 years; thus, it seemed to be a research topic.[26] Original studies (n = 178), reviews (n = 93), and epidemiological prevalence studies (n = 52) appeared to be more commonly reported by researchers in geriatrics and gerontology.[27-29]

Table 1. Top-10 journal contributions

Rank	Journal title	Country	Number of articles	IF
1	*Journal of the American Geriatrics Society*	USA	100	7.538
2	*Journal of the American Medical Directors Association*	USA	27	7.802
3	*Gerontology*	Switzerland	27	5.597
4	*Gerontologist*	USA	26	5.422
5	*The Journal of Nutrition, Health & Aging*	Italy	17	5.285
6	*Archives of Gerontology and Geriatrics*	Ireland	17	4.163
7	*International Journal of Environmental and Health Research*	England	16	4.477
8	*Journal of Gerontological Social Work*	USA	15	3.608
9	*Geriatrics and Gerontology International*	Japan	14	3.387
10	*Educational Gerontology*	USA	12	1.389

IF, impact factor (Clarivate Science Citation Index-2021).

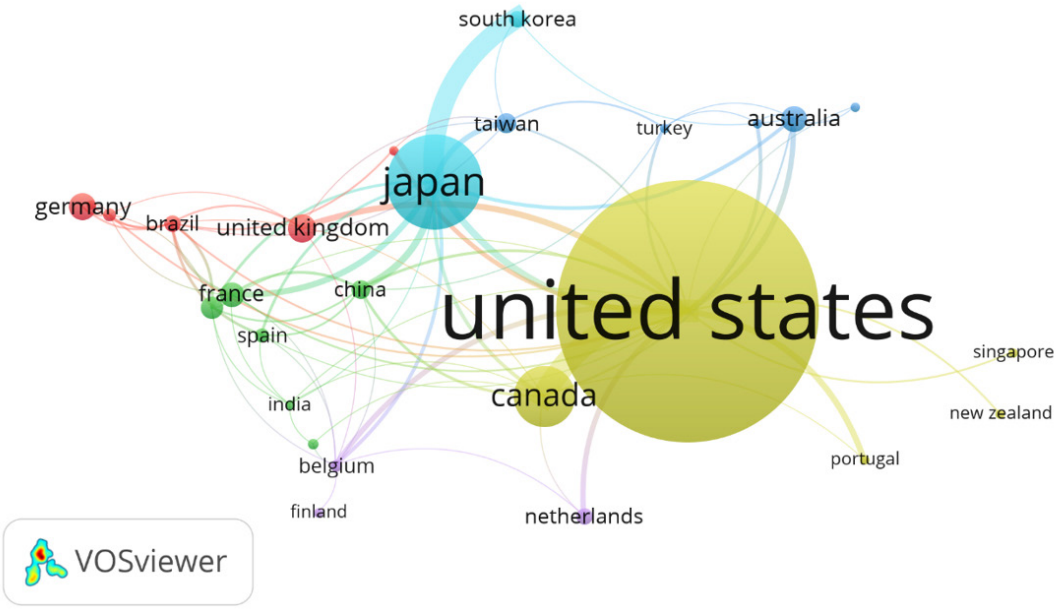

Fig. 3. Global research co-country analysis.

Table 2. Top-10 most cited articles

Rank	Title	Year	Number of citations	Journal
1	Geriatric Depression Scale	1988	478	*Psychopharmacology Bulletin*
2	Assessment of older people: self-maintaining and instrumental activities of daily living	1969	256	*The Gerontologist*
3	The mini-mental state examination	1983	177	*Archives of General Psychiatry*
4	Human aging: usual and successful	1987	175	*Science*
5	Barthel index	1965	156	*Maryland State Medical Journal*
6	Frailty in older adults: evidence for a phenotype	2001	149	*The Journals of Gerontology Series A*
7	Measurement of competence: reliability and validity of the TMIG Index of Competence	1991	136	*Archives of Gerontology and Geriatrics*
8	Frailty in elderly people	2013	132	*The Lancet*
9	The timed "Up & Go": a test of basic functional mobility for frail elderly persons	1991	126	*Journal of the American Geriatrics Society*
10	Practice parameter: Early detection of dementia: Mild cognitive impairment (an evidence-based review) [RETIRED]: Report of the Quality Standards Subcommittee of the American Academy of Neurology	2001	120	*Neurology*

TMIG, Tokyo Metropolitan Institute of Gerontology.

Table 3. Frequencies of occurrence of the top-20 keywords

Rank	Keyword	Frequency of occurrence
1	Human	782
2	Older adult	663
3	Geriatrics	598
4	Gerontology	524
5	Education and training	471
6	80+ elderly	461
7	Geriatric assessment	395
8	Geriatric nursing	367
9	Procedures	308
10	Management	290
11	Psychological aspects	237
12	Revision	192
13	Quality of life	178
14	Activities of daily life	170
15	Cognition	153
16	Health staff attitude	147
17	Depression	131
18	Risk factor	119
19	Frailty	117
20	Prevalence	113

The burst analysis of keywords did not reveal a drastic pattern of change in the searches for geriatrics and gerontology (Fig. 5). The keyword "older adults" (n = 663) showed the most robust growth in this field. Keywords related to the health of older adults were highlighted when analyzed on a macro-theme, such as geriatric assessment (n = 395), geriatric nursing (n = 367), attitudes of health personnel (n = 147), depression (n = 131), and prevalence (n = 113) (Table 3). The keyword "older adults (80+)" also appeared at a high frequency in the included studies (n = 461). A bibliometric analysis by Gonzalez-Alcaide et al.[24] reported a significant growth in scientific studies on the population aged ≥ 80 years, with a focus on cardiovascular and cerebrovascular diseases, dementia, and neoplasia. Moreover, > 96% of these studies were published in European, North American, and Asian countries. Therefore, this is a research hotspot in geriatrics and gerontology, enabling a vast field of research with new approaches, such as geriatric syndromes, as well as the social and psychosocial aspects of the population in this age group.

DISCUSSION

This study has several limitations, which should be noted when in-

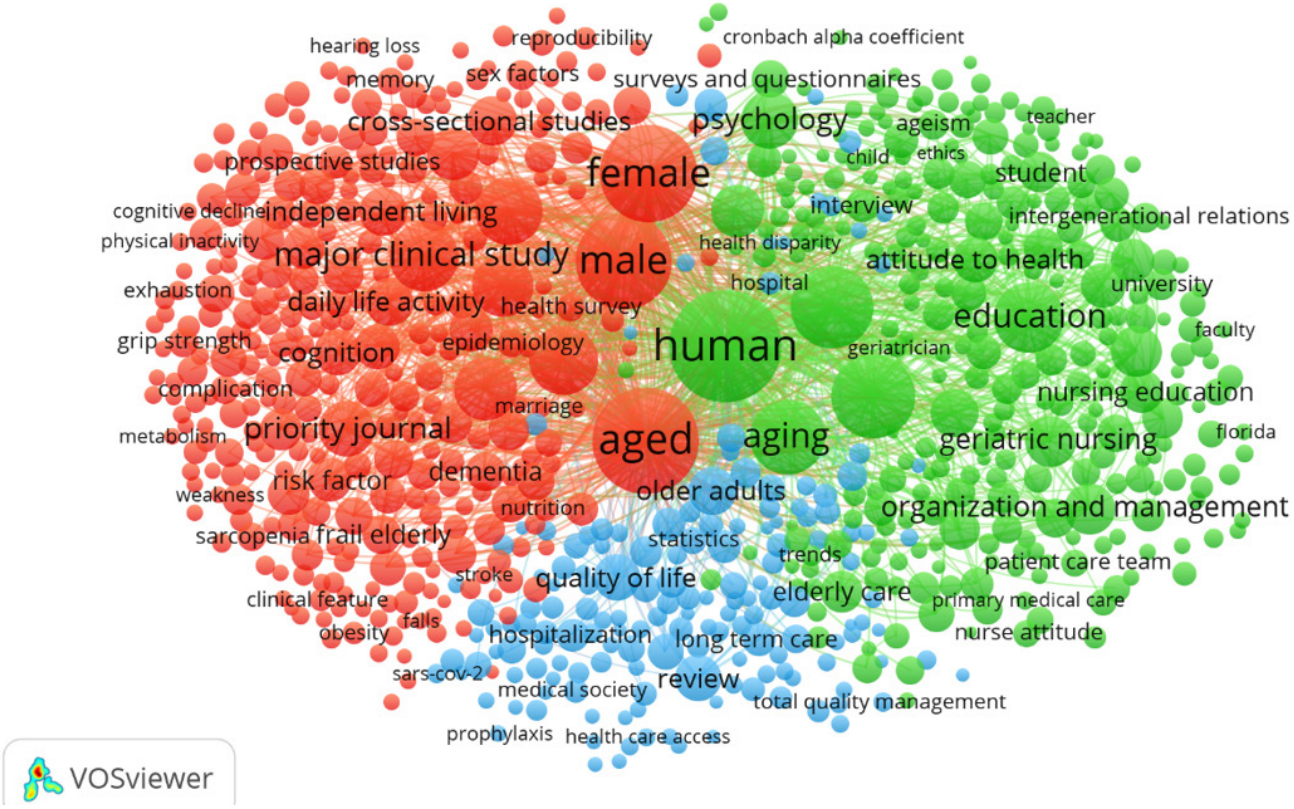

Fig. 4. Keyword co-occurrence core analysis.

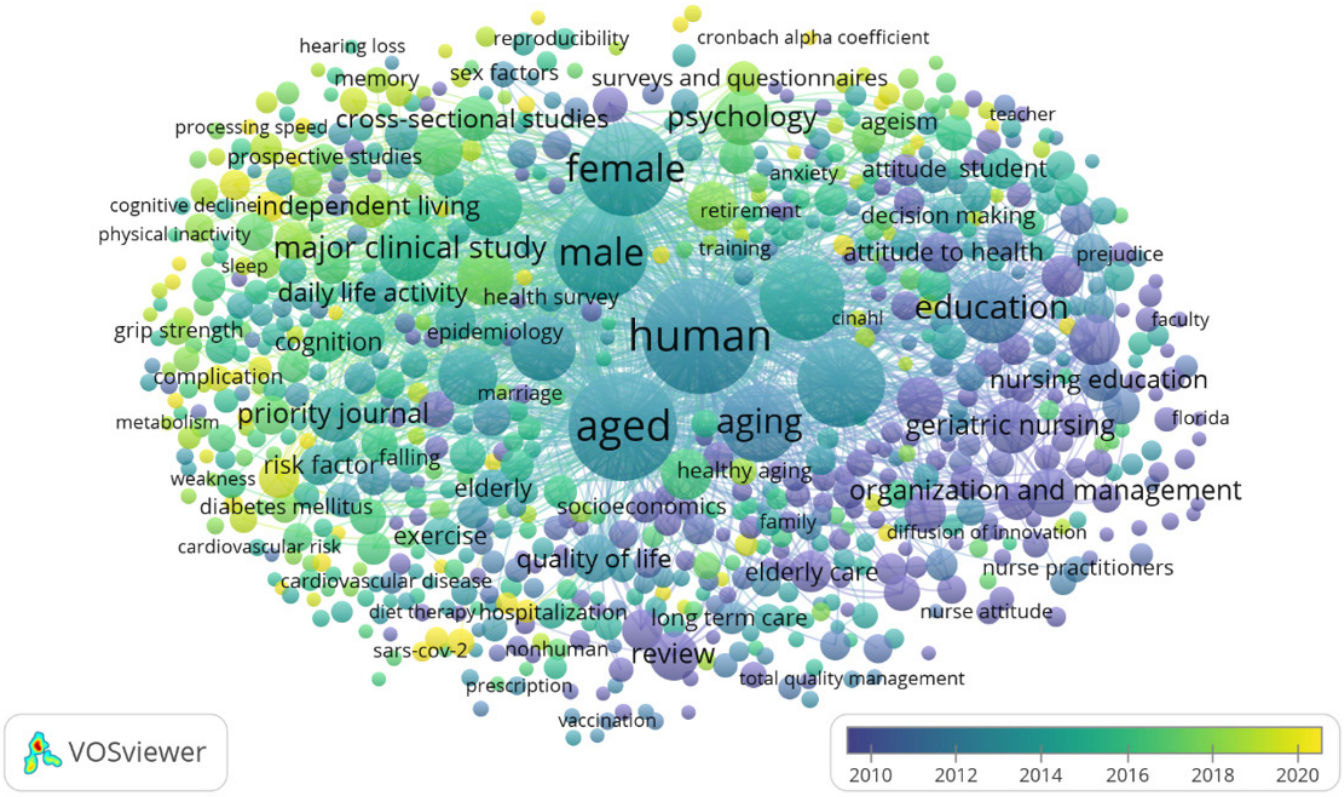

Fig. 5. Keyword burst analysis.

terpreting the results. First, we used only the Scopus database, which may have limited access to articles that are not indexed in this database. However, Scopus is one of the most widely used databases worldwide, with high-quality literature. Second, we excluded non-English articles, which may explain why some studies were missing. The VOSviewer analysis in this study was quantitative. Future studies should adopt qualitative methods to address the limitations of quantitative research. Further research is also needed to employ a more comprehensive search strategy to validate our results or to provide a broader perspective on geriatric and gerontology research. Our study has several strengths. To our knowledge, studies using holistic bibliometric analysis to assess hotspots and frontiers in the fields of geriatrics and gerontology are scarce. As aging is a priority for countries worldwide, scientometric analyses can reveal the factors driving knowledge advances in the aging agenda, such as vital academic institutions, individual researchers, and research groups. Our analysis of the Scopus database revealed a total of 340 academic journals with 858 publications in geriatrics and gerontology. We analyzed the number of publications, impact factors of the major journals, collaborations between countries/institutions, and reference co-citation and keyword analysis.

In conclusion, this study collected relevant literature on geriatrics and gerontology; analyzed information from leading countries, institutions, and journals in this field; and summarized the critical points and research frontiers. The number of publications in the analyzed field of study has increased rapidly, especially in the last decade. Most of these publications are associated with older adults, education, and training (educational research), and those aged ≥80 years, gradually expanding to care for older adults, such as geriatric assessment, geriatric nursing, procedures, and management. Topics related to mental health, classified into sub-areas such as psychiatry and psychology as well as functional capacity, appeared at high frequency among the citations in the analyzed studies. These findings suggest that reinforcing interinstitutional and interdisciplinary cooperation is essential for progress and development in this scientific field. American and European countries, especially the United States, dominate in the number of publications, journals with the highest number of co-citations, and research collaborations in geriatrics and gerontology. Asian countries, such as Japan and Taiwan, are actively seeking international cooperation to increase their global influence on the development of this field. Our results provide direction for fellow researchers to conduct studies in geriatrics and gerontology.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, LSSN, NBO; Data curation, FCFD, MDF; Investigation, FCFD, MDF; Methodology, FCFD, MDF; Writing-original draft, ABF, TSR, RCP, HLC, DVO; Writing-review & editing, LSSN, NBO.

REFERENCES

1. Ghamgosar A, Zarghani M, Nemati-Anaraki L. Bibliometric analysis on geriatric nursing research in Web of Science (1900-2020). Biomed Res Int 2021;2021:8758161.
2. Gu YH, Bai JB, Chen XL, Wu WW, Liu XX, Tan XD. Healthy aging: a bibliometric analysis of the literature. Exp Gerontol 2019;116:93-105.
3. Van Eenoo L, Declercq A, Onder G, Finne-Soveri H, Garms-Homolova V, Jonsson PV, et al. Substantial between-country differences in organising community care for older people in Europe: a review. Eur J Public Health 2016;26:213-9.
4. Chena DN, Ortolani FP, Magalhaes FG, Witter C, Rodrigues GM. [Aging and interdisciplinary: a review of the journal Estudos Interdisciplinares sobre o Envelhecimento]. Estud Interdiscipl Envelhec 2015;20:883-901.
5. Van Den Noortgate NJ, Baeyens H. Professor Jean-Pierre Baeyens. Eur Geriatr Med 2010;5:317-9.
6. Ellegaard O, Wallin JA. The bibliometric analysis of scholarly production: how great is the impact? Scientometrics 2015;105:1809-31.
7. Asghar I, Cang S, Yu H. Assistive technology for people with dementia: an overview and bibliometric study. Health Info Libr J 2017;34:5-19.
8. Ugolini D, Neri M, Cesario A, Marazzi G, Milazzo D, Volterrani M, et al. Bibliometric analysis of literature in cerebrovascular and cardiovascular diseases rehabilitation: growing numbers, reducing impact factor. Arch Phys Med Rehabil 2013;94:324-31.
9. Muller AM, Ansari P, Ebrahim NA, Khoo S. Physical activity and aging research: a bibliometric analysis. J Aging Phys Act 2016;24:476-83.
10. Zhou X, Zhang D. Multimorbidity in the elderly: a systematic bibliometric analysis of research output. Int J Environ Res Public Health 2021;19:353.
11. Zhao Z, Fan W, Chu Q. Mapping knowledge structure and global status of sarcopenia in geriatric hip fractures: a bibliometric and visualized study. Front Surg 2022;9:1019985.
12. Soytas RB. A bibliometric analysis of publications on COVID-19 and older adults. Ann Geriatr Med Res 2021;25:197-203.
13. Shen CW, Nguyen DT, Hsu PY. Bibliometric networks and analytics on gerontology research. Library Hi Tech 2019;37:88-100.
14. Vogel B, Reichard RJ, Batistic S, Cerne M. A bibliometric review of the leadership development field: How we got here, where we are, and where we are headed. Leadersh Q 2021;32:101381.
15. Agarwal A, Durairajanayagam D, Tatagari S, Esteves SC, Harlev A, Henkel R, et al. Bibliometrics: tracking research impact by selecting the appropriate metrics. Asian J Androl 2016;18:296-309.
16. Sureshbhai MG, Elizabeth H. Research on geriatric health care in BRICS countries: a scientometric investigation of Open Access Journal Articles Indexed in Scopus Database. Am J Gerentol Geriatr 2021;4:1024.
17. Aparicio-Martinez P, Perea-Moreno AJ, Martinez-Jimenez MP, Redel-Macias MD, Vaquero-Abellan M, Pagliari C. A bibliometric analysis of the health field regarding social networks and young people. Int J Environ Res Public Health 2019;16:4024.
18. van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics 2010;84:523-38.
19. Kleminski R, Kazienko P, Kajdanowicz T. Analysis of direct citation, co-citation and bibliographic coupling in scientific topic identification. J Inf Sci 2020;48:016555152096277.
20. Noh JH, Jung HW, Ga H, Lim JY. Ethical guidelines for publishing in the Annals of Geriatric Medicine and Research. Ann Geriatr Med Res 2022;26:1-3.
21. Goldman M, de Medeiros K, Cole T. Critical humanities and ageing: forging interdisciplinary dialogues. Abington, UK: Routledge; 2022.
22. Ang HM, Kwan YH. Bibliometric analysis of journals in the field of geriatrics and gerontology. Geriatr Gerontol Int 2017;17:357-60.
23. Xiao Y, Deng Z, Tan H, Jiang T, Chen Z. Bibliometric analysis of the knowledge base and future trends on sarcopenia from 1999-2021. Int J Environ Res Public Health 2022;19:8866.
24. Gonzalez-Alcaide G, Palacios-Fernandez S, Ramos-Rincon JM. Thematic research clusters in very old populations (≥ 80 years): a bibliometric approach. BMC Geriatr 2021;21:266.
25. Krishnamoorthy Y, Rajaa S, Rehman T. Diagnostic accuracy of various forms of geriatric depression scale for screening of depression among older adults: systematic review and meta-analy-

sis. Arch Gerontol Geriatr 2020;87:104002.
26. Li YX, Ye CX, Ahmad T, Khan M, Shah I, et al. The 100 most cited publications in aging research: a bibliometric analysis. Electron J Gen Med 2022;19:em342.
27. Cesário VA, Silva CR, Soares JP, Mendonca PB, Reis MK, Lima KC. [Bibliometric study of the scientific production of Brazilian Journal of Geriatrics and Gerontology between 2014 and 2019]. Rev Bras Geriatr Gerontol 2021;24:e210092.
28. Suzan V, Suzan AA. A bibliometric analysis of sarcopenia: top 100 articles. Eur Geriatr Med 2021;12:185-91.
29. Zhao Y, Zhang Z, Guo S, Feng B, Zhao X, Wang X, et al. Bibliometric analysis of research articles on pain in the elderly published from 2000 to 2019. J Pain Res 2021;14:1007-25.

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Effectiveness of Vitamin D Supplements in Reducing the Risk of Falls among Older Adults: A Meta-Analysis of Randomized Controlled Trials

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Background: The role of vitamin D in reducing the risk of falls in older adults has not been clearly demonstrated. This study examined the effectiveness of vitamin D supplementation in reducing the risk of falls in older adults. **Methods:** Four databases (Cochrane Library, Embase, PubMed, and CINAHL) were searched without language restrictions or time limitations. These articles were comprehensively screened using EndNote version 20.1 software. A manual search of the reference lists of the identified studies was also performed. The analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta–Analyses (PRISMA) guidelines. The pooled evidence was analyzed using RevMan software version 5.4. **Results:** Seventeen studies met inclusion criteria among 550 potentially relevant studies. The pooled analysis of 38,598 older adults showed that vitamin D supplementation decreased the odds of having at least one fall by 1% (odds ratio [OR]=1.01; 95% confidence interval [CI], 0.92–1.11; p=0.86); however, the difference was not statistically significant. Of eight studies with 19,946 older adults, the pooled analysis showed a 12% (OR=1.12; 95% CI, 0.97–1.29; p=0.11) decrease in the odds of having at least one fracture among older adults; however, the difference was also not statistically significant. Pooled subgroup analysis showed that neither low (<2,000 IU/day) nor high (≥2,000 and <4,000 IU/day) doses of vitamin D supplementation had any significant effect on the incidence of falls and fractures. **Conclusion:** Vitamin D supplementation had no beneficial effect in reducing fall and fracture incidence among older adults.

Key Words: Accidental falls, Bone fractures, Frail elderly, Meta-analysis

INTRODUCTION

Falls is the most frequent accident type and the main reason for injury-related hospitalizations in adults aged 65 years and older.[1] Three million older adults receive emergency room care each year for fall-related injuries.[2] Injuries caused by falls are associated with increased mortality.[3] The World Health Organization reports that falls are the second largest cause of unintentional injury death globally, leading to >684,000 deaths annually.[4] Although all people are at risk of falls, age, sex, unsafe environments, socioeconomic factors, medication, and health of an individual can impact the risk of falling.[5] Recent epidemiological studies support a relationship between vitamin D and increased muscle function related to the prevention of injurious falls.[6,7]

Ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3) are the two primary forms of vitamin D, a fat-soluble nutrient that is present in plants as vitamin D2 and as vitamin D3 in humans and animals. Vitamin D is primarily produced by the skin upon exposure to ultraviolet (UV) rays from the sun, supplements, and food. Vitamin D increases calcium and phosphate levels, which are

crucial for bone formation and muscle contractions, immune system function, and glucose metabolism.[8,9] Vitamin D deficiency is a cause for concern, especially in older adults, due to its association with poor physical performance, increased risk of falling, and osteoporosis-related fractures.[10,11] Moreover, vitamin D may play a role in preserving or enhancing muscle strength, function, physical performance, and balance in older adults, as well as in lowering hip and non-vertebral fractures.[12-14] By enhancing intestinal calcium absorption, vitamin D may enhance bone health and improve bone mineralization.[15]

One study reported that 24 weeks of vitamin D supplementation reduced the incidence of falls in older adult populations.[16] However, several systematic reviews concluded that vitamin D and calcium supplementation did not improve fracture or fall risks or bone mineral density.[17,18] Recent studies showed no significant influence of vitamin D on the risk of injuries such as fractures compared to placebo[19] and on falls among older adults.[20] Therefore, the effects of vitamin D on fall prevention remain inconclusive. Therefore, the present comprehensive review of the literature and meta-analysis of randomized controlled trials (RCTs) aimed to establish the overall effectiveness of vitamin D in reducing falls in older persons.

MATERIALS AND METHODS

Search Strategy

This study was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42022383154) and was conducted in accordance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[21] We conducted a review based on literature identified in the Cochrane Library, Embase, PubMed, and CINAHL databases. A manual search was conducted by looking at the reference lists of published studies and Google searches. The search was performed using the combinations of keywords and Medical Subject Headings (MeSH) terms of "accidental falls" OR "falling" OR "falls" OR "slip and fall" AND "vitamin deficiency" OR "vitamin D" OR "calciferol" AND "aged" OR "elderly" OR "frail elderly" OR "older people" and without date of publication and language restrictions (Table 1). The last update of the search was conducted on December 12, 2022.

Eligibility Criteria and Screening Procedures

EndNote version 20.1 was used to thoroughly screen each article in the databases. Three independent reviewers systematically screened the articles to identify relevant studies. The study inclusion criteria based on the Population, Intervention, Comparison, Outcome and Study (PICOS) criteria included: (1) older community-dwelling or institutionalized adults (≥ 60 years of age); (2) no use of vitamin D and calcium supplements at screening; (3) a control group taking a placebo or other complement such as calcium at the same dosage in all groups; (4) primary outcome of the assessment of the number of people with at least one fall and the secondary outcomes of the number of people with at least one fracture; and (5) RCT study design.

Articles meeting any of the following exclusion criteria were excluded: (1) not pertaining to the study topic; (2) irrelevant population, (3) non-research articles or inappropriate study design (such as a case-cross over, cross-sectional study, or case-control study); (4) study protocol; (5) an inappropriate outcome regarding the number of falls among the participants; (6) reporting from the same data set as other RCTs; (7) insufficient data after email

Table 1. Search string databases

Database	Result	Date of search	Search string
CINAHL	58	12/12/2022	(AB falls OR falling OR falls, accidental OR accidental fall OR fall, accidental OR slip and fall OR fall and slip) AND (AB vitamin deficiency) AND (AB aged OR elderly)
EMBASE	432	12/12/2022	'aged'/exp OR 'aged' AND 'vitamin deficiency'/exp OR 'vitamin deficiency' AND 'falls'/exp OR 'falls'
PubMed	57	12/12/2022	(("vitamin d"[MeSH Terms] OR "ergocalciferols"[MeSH Terms] OR ("vitamin d"[Title/Abstract] OR "Calciferol"[Title/Abstract])) AND ("frail elderly"[MeSH Terms] OR ("older adults"[Title/Abstract] OR "elder adults"[Title/Abstract] OR "elderly adults"[Title/Abstract] OR "older people"[Title/Abstract] OR "elder people"[Title/Abstract] OR "elderly people"[Title/Abstract])) AND ("accidental falls"[MeSH Terms] OR ("fall*"[Title/Abstract] OR "slip*"[Title/Abstract]))) AND (clinicaltrial[Filter] OR randomizedcontrolledtrial[Filter])
			Translations
			Vitamin D[Mesh]: "vitamin d"[MeSH Terms] OR "ergocalciferols"[MeSH Terms]
			Frail Elderly[MeSH Terms]: "frail elderly"[MeSH Terms]
			Accidental Falls[Mesh]: "accidental falls"[MeSH Terms]
Cochrane	3	12/12/2022	MeSH descriptor: [Vitamin D] explode all trees AND MeSH descriptor: [Frail Elderly] explode all trees AND MeSH descriptor: [Accidental Falls] explode all trees

MeSH, medical subject headings.

requests to eligible authors for missing information; and (8) lack of full text.

Extraction and Outcomes

The extracted data included study identity, study characteristics (author, year of publication, title, study design, and country), participant characteristics (study setting, sample size, mean age, and sex), intervention characteristics (frequency, duration, and dose), and outcomes (number of people who had at least one fall and/or number of people who had at least one fracture).

Quality Assessment

The risks of bias in the eligible RCTs were independently assessed by three reviewers following the approach in the Cochrane Handbook version 2 for a systematic review of interventions. Version 2 of the Cochrane risk of bias tool for randomized trials (RoB 2) is the instrument recommended for assessing the risk of bias in randomized trials. With a specific focus on various facets of trial design, conduct, and reporting, the RoB 2 is organized into a predetermined set of bias domains. A set of inquiries (referred to as "signaling questions") within each domain seeks to elicit details about trial characteristics that are important to the risk of bias. Based on the responses to the signaling questions, an algorithm generates a proposed conclusion regarding the probability of bias originating from each domain.

Statistical Analysis

We assessed the accumulated evidence using RevMan version 5.4.1 (Copenhagen, Nordic Cochrane Center; The Cochrane Collaboration, 2020). The number of participants who fell at least once and sustained a fracture was statistically estimated in a standard event and total format with 95% confidence intervals (CIs).

We calculated the Q and I^2 statistics to evaluate the heterogeneity of treatment effects across studies. I^2 indicates the consistency of a study's findings. The result is interpreted as the fraction of the overall variation across studies, which may be attributed to heterogeneity rather than random variance.[22] We applied a scale of low, moderate, and high heterogeneity, with upper limits of 25%, 50%, and 75% for I^2, respectively.[23] Models for random effects were also computed. The analysis applied a random-effects model to account for differences between the included studies.[24]

Moderator Analysis

We conducted a subgroup analysis among the included studies.[22] We conducted subgroup analyses for several potential moderator variables, including vitamin D type (vitamin D2 or vitamin D3) and doses (vitamin D2 or D3; low dose < 2,000 IU/ day, high dose ≥ 2,000 and < 4,000 IU/day).[25] We transformed the doses of vitamin D from either monthly or annual to daily intake.

RESULTS

Description of the Included Studies

Searches of the Embase, Cochrane, PubMed, and CINAHL electronic databases using the PRISMA flowchart identified 550 studies. Eighty studies were identified as duplicate records and were removed from the screening of the titles and abstracts. An additional 40 studies were excluded because of irrelevant topics, 69 studies had irrelevant populations, 36 studies were either reviews or meta-analyses, three studies were non-research articles, two studies were protocols, and 298 studies had irrelevant study designs. Therefore, the full texts of 22 studies were selected. Among these, one study was excluded because it was a duplicate publication, and 12 other studies were excluded because they did not measure the outcome of interest in this study. The manual, Google Scholar, and citation searches yielded 12 studies. Four of these studies were excluded because the populations were irrelevant. Finally, 17 studies presented sufficient information for data extraction and were eligible for enrollment in our study (Fig. 1).

Study Characteristics

Among 47,206 older adults enrolled in this study among the 17 included studies, 19,313 received vitamin D interventions, and 19,298 were assigned to placebo control groups. The mean ages ranged from 61.0 to 85.4 years. Approximately 25,361 patients (53.8%) were women. The included studies were conducted in Switzerland (17.6%), the United Kingdom (35.2%), Australia (23.6%), the United States (17.6%), and Germany (6.0%). The populations of the studies were all older adults and were heterogeneous. Most of the study participants were community-dwelling. The number of participants in the study ranged from 68 to 21,315, and the follow-up duration varied from 4 to 62 months. The vitamin D regimens in the intervention groups varied between studies in terms of the dose and method of administration. Most of the studies compared the effects of vitamin D3 supplementation among the intervention groups compared to the control group mostly administered placebos. Fifteen of the 17 studies indicated that administration occurred via the oral route (Table 2).[16,26-41]

We assessed the risk of bias for all 17 included studies using the Cochrane Library's RoB 2 tool. Among the assessed domains, all included studies had low risks of bias due to missing outcome data, measurement of outcomes, and selection of reported results. Regarding the risk of bias due to the randomization process, four studies[16,30,36,39] were of some concern, while the other studies were

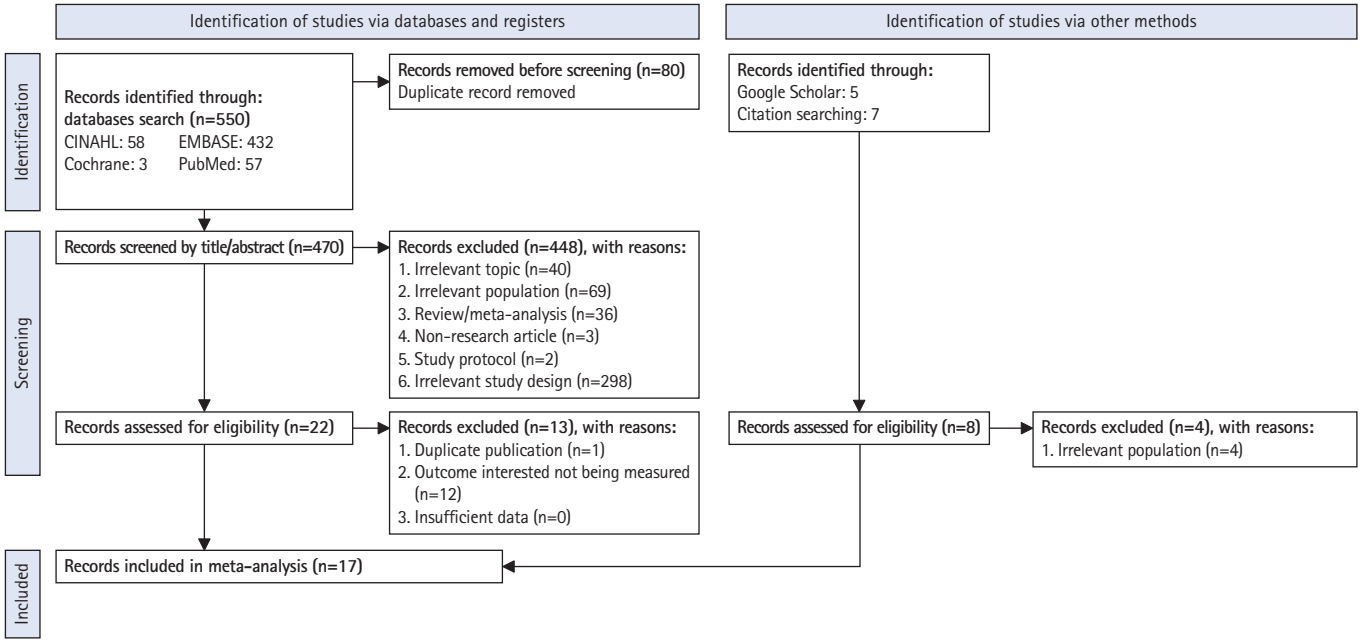

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of included studies.

of low risk. Regarding the risk of bias due to deviations from the intended interventions, only one study[39] was of concern, whereas the others were of low risk. The overall risk of bias showed 13 with low risk and four studies with "some concern" (Table 2). The risks of bias according to the five domains are presented in Supplemental Table S1.

Main Outcomes

The forest plot of the effects of vitamin D (D2 and D3) supplementation on fall incidence included 17 studies with a total population of 38,598 individuals. The pooled result showed an odds ratio (OR) of 1.01 (95% CI, 0.92–1.11), indicating that vitamin D supplementation decreased the odds of having at least one fall by only 1% compared to placebo among older adults. The incidence of falls did not differ significantly between the vitamin D and placebo groups ($p = 0.86$). We observed moderate statistical heterogeneity ($I^2 = 54\%$) (Fig. 2).

A subgroup analysis including four studies involving 10,308 participants to assess the effects of vitamin D2 supplementation showed no statistically significant reduction in fall incidence between the two groups (OR = 0.95; 95% CI, 0.88–1.03; $p = 0.22$). We observed no heterogeneity among the studies ($I^2 = 0\%$).

A subgroup analysis of 13 studies involving 28,290 participants to assess the effects of vitamin D3 supplementation showed no statistically significant reduction in fall incidence between the two groups (OR = 1.04; 95% CI, 0.93–1.17; $p = 0.52$). We observed moderate heterogeneity among the studies ($I^2 = 52\%$).

The pooled results of the forest plot of eight studies on vitamin D (D2 and D3) (Fig. 3) and fracture incidence among older adults, with a total population of 19,946 showed an OR of 1.12 (95% CI, 0.97–1.29), indicating that vitamin D supplementation decreased the odds of having at least one fracture by 12% compared to placebo among older adults. The incidence of fractures did not differ significantly between the vitamin D and placebo groups ($p = 0.11$). We observed low statistical heterogeneity in this meta-analysis ($I^2 = 24\%$).

A subgroup analysis of three studies on vitamin D2 supplementation revealed no statistically significant reduction in fracture incidences between the two groups (OR = 1.09; 95% CI, 0.82–1.45; $p = 0.56$). The analysis included a total of 13,782 participants. High heterogeneity was observed among these studies ($I^2 = 60\%$).

The results of the subgroup analysis of five studies that administered vitamin D3 supplementation showed no statistically significant reduction in fracture incidences between the two groups (OR = 1.13; 95% CI, 0.96–1.34; $p = 0.15$). The analysis included a total of 6,164 participants included in the analysis. Low heterogeneity was observed among studies ($I^2 = 4\%$).

Effects of vitamin D doses on falls and fractures

A pooled analysis of the effects of low doses ($< 2{,}000$ IU/day) including nine studies with 10,806 participants and high doses ($\geq 2{,}000$ and $< 4{,}000$ IU/day) including eight studies with 27,792

Table 2. Characteristics of randomized controlled trials included in the meta-analysis (n=17)

	Study	Year	Country	Study setting	Populations	Duration (mo)	Group type		Study quality (RoB Cochrane 2.0)
							Experiment	Control	
1	Bischoff et al.[34]	2003	Switzerland	Long-stay geriatric care	Mean age: 85.3 y Sample size: 122 Sex: male 0 (0%), female 122 (100%)	4	Vitamin D3+calcium Dose: 800 IU (vitamin D) daily Route: per oral	Calcium	Low
2	Bischoff-Ferrari et al.[37]	2022	Switzerland, Germany, Austria, France, and Portugal	Community	Mean age: 74.9 y Sample size: 2,157 Sex: male 826 (38.3%), female 1,331 (61.7%)	36	Vitamin D3 Dose: 2,000 IU daily Route: per oral	Placebo	Low
3	Dhesi et al.[30]	2004	UK	Community	Mean age: 76.8 y Sample size: 138 Sex: male 30 (21.7%), female 108 (78.3)	6	Vitamin D2 Dose: 600,000 IU per 6 month (~3,000 IU daily) Route: intramuscular	Placebo	Some concerns
4	Dukas et al.[16]	2005	Switzerland	Community	Mean age: 75.0 y Sample size: 378 Sex: male 163 (43.1%), female 215 (56.9%)	9	Vitamin D3 Dose: 1 μg alphaD3 capsules (40 IU daily) Route: per oral	Placebo	Some concerns
5	Flicker et al.[31]	2005	Australia	Nursing home	Mean age: 85.4 y Sample size: 625 Sex: male 32 (5.1%), female: 593 (94.9%)	24	Vitamin D2 Dose: 10,000 IU given once weekly (~1,000 IU daily) Route: per oral	Placebo	Low
6	Glendenning et al.[40]	2012	Australia	Community	Mean age: 76.7 y Sample size: 686 Sex: male 0 (0%), female 686 (100%)	9	Vitamin D3 Dose: 150,000 IU every 3 months (~1,600 IU daily) Route: per oral	Placebo	Low
7	Grant et al.[28]	2005	UK	Hospital	Mean age: 77.0 y Sample size: 5,292 Sex: male 811 (15.3%), female 4,481 (84.7%)	62	Vitamin D3 Dose: 800 IU daily Route: per oral	Placebo (calcium)	Low
8	Hansen et al.[26]	2015	USA	Institutionalized	Mean age: 61.0 y Sample size: 230 Sex: male 0 (0%), female: 230 (100%)	12	Vitamin D3 Dose: 50,000 IU twice monthly (~3,000 IU daily) Route: per oral	Placebo	Low
9	Hin et al.[38]	2017	UK	Community	Mean age: 72.0 y Sample size: 305 Sex: male 155 (50.8%), female 150 (49.2%)	12	Vitamin D3 Dose: 2,000 IU daily and 4,000 IU daily Route: per oral	Placebo	Low
10	Houston et al.[29]	2015	USA	Community	Mean age: 77.9 y Sample size: 68 Sex: male 19 (27.9%), female 49 (72.1%)	5	Vitamin D3 Dose: 100,000 IU per month (~3,000 IU daily) Route: per oral	Placebo (vitamin E)	Low

(Continued to the next page)

Table 3. Continued

	Study	Year	Country	Study setting	Populations	Duration (mo)	Group type		Study quality (RoB Cochrane 2.0)
							Experiment	Control	
11	Law et al.[39]	2006	UK	Nursing home	Mean age: 85.0 y Sample size: 3,717 Sex: male 892 (24.0%), female 2,825 (76.0%)	10	Vitamin D3 Dose: 1,100 IU daily Route: per oral	Control	Some concerns
12	Levis et al.[35]	2017	USA	Institutionalized	Mean age: 72.4 y Sample size: 130 Sex: male 130 (100%), female 0 (0%)	9	Vitamin D3 Dose: 4,000 IU daily Route: per oral	Placebo	Low
13	Pfeifer et al.[36]	2009	Germany	Community	Mean age: 77.0 y Sample size: 242 Sex: male 123 (50.8%), female 119 (49.2%)	12	Vitamin D3+calcium Dose: 800 IU daily (vitamin D3) Route: per oral	Placebo (calcium)	Some concerns
14	Sanders et al.[41]	2010	Australia	Community	Mean age: 76.3 y Sample size: 2,256 Sex: male 0 (0%), female 2,256 (100%)	60	Vitamin D3 Dose: 500,000 IU annually (~1,300 IU daily) Route: per oral	Placebo	Low
15	Smith et al.[32]	2007	UK	Community	Mean age: 79.4 y Sample size: 9,440 Sex: male 4,354 (46.1%), female 5,086 (53.9%)	36	Vitamin D2 Dose: 300,000 IU annually every autumn (~3,000 IU daily) Route: intramuscular	Placebo	Low
16	Waterhouse et al.[27]	2021	Australia	Community	Mean age: 69.3 y Sample size: 21,315 Sex: male 14,241 (66.8%), female 7,074 (33.2%)	60	Vitamin D3 Dose: 60,000 IU monthly (~2,000 IU daily) Route: per oral	Placebo	Low
17	Witham et al.[33]	2010	UK	Community	Mean age: 79.7 y Sample size: 105 Sex: male 69 (65.7%), female 36 (34.3%)	5	Vitamin D2 Dose: 100,000 IU per 4 months (~600 IU daily) Route: per oral	Placebo	Low

IU, international unit.

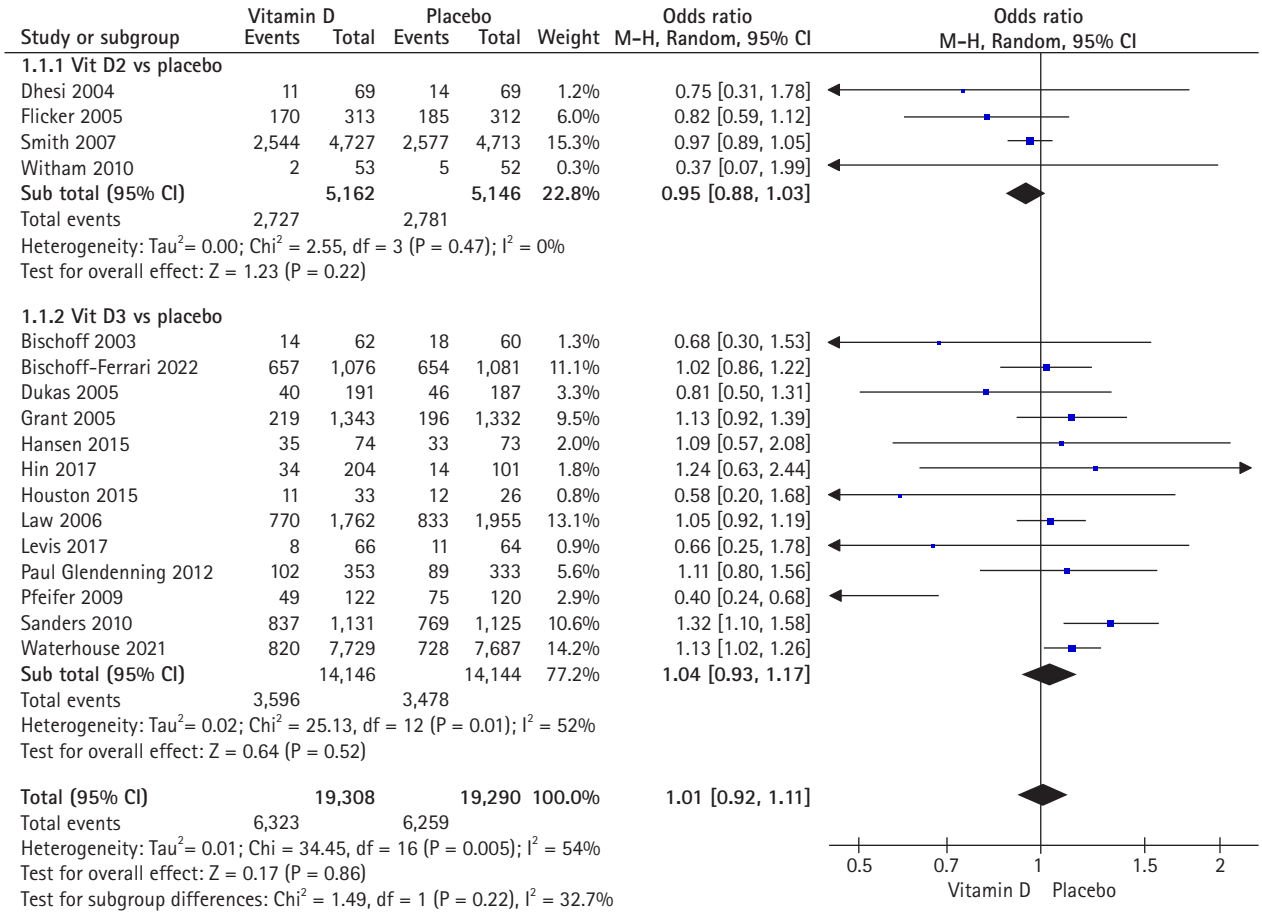

Fig. 2. Forest plot of vitamin D on the incidence of falls among older adults.

participants on fall incidence showed an OR of 0.95 (95% CI, 0.78–1.14; p=0.56) and OR of 1.03 (95% CI, 0.95–1.11; p=0.50). These results indicated no significant difference between the two groups. We observed high heterogeneity for low doses (I^2=69%) and low heterogeneity for high doses (I^2=16%) (Fig. 4).

A pooled analysis of low doses (<2,000 IU/day) including six studies with 10,201 participants and high doses (≥2,000 and <4,000 IU/day) including two studies on fracture incidence that enrolled 9,745 participants, which reported OR values of 1.10 (95% CI, 0.90–1.35; p=0.36) and OR of 1.11 (95% CI, 0.94–1.31; p=0.23). These results indicated a lack of significant difference between the two groups. Low heterogeneity was observed in both subgroups (I^2<50%) (Fig. 5).

DISCUSSION

Our meta-analysis included 17 studies with 47,206 older adults who received vitamin D supplementation or a placebo for 5 months to 5 years. The total population of all included studies and the total population of the intervention and placebo groups differed because the participants were not followed up to the end of the study,[26] they were divided into more than just vitamin D intervention or placebo groups in some studies,[26-28] or they were moved to long-term care or died during the study period.[29]

We observed no significant difference in the likelihood of falls among people who took vitamin D supplements versus the placebo group for either vitamin D2 or vitamin D3 products. The results of our meta-analysis support those of a previous study showing that vitamin D treatment alone did not result in lower falls in older persons with D3 levels >50 nmol/L.[20] However, we did not analyze the effect of vitamin D supplements based on D3 concentrations measured in the participants' bodies. More studies, like RCTs or meta-analyses, etc. are needed to analyze the effects of vitamin D supplements on the concentrations of D3 in participants' bodies measured before they take these supplements. Previous meta-analyses have also demonstrated the effectiveness of vitamin D in reducing the incidence of falls among older adults.[41-43]

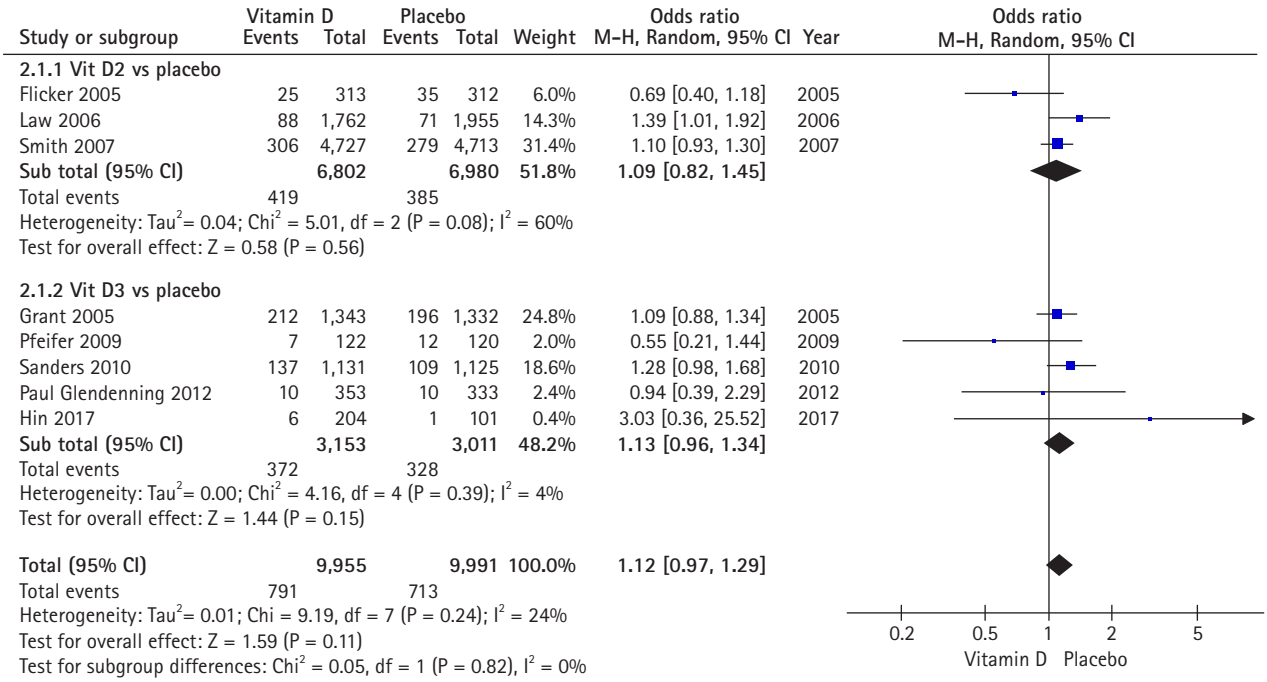

Fig. 3. Forest plot of vitamin D on the incidence of fracture among older adults.

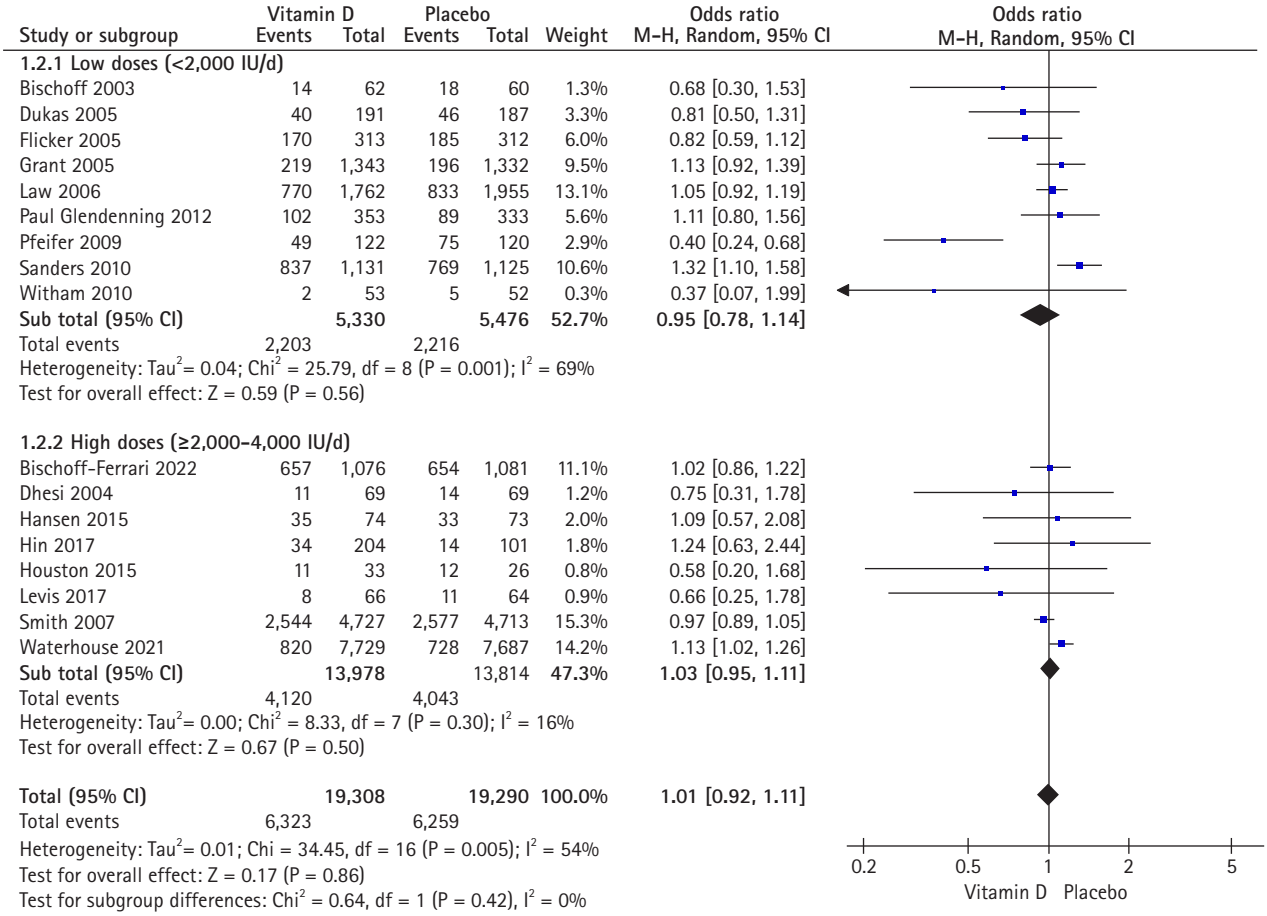

Fig. 4. Forest plot of falls incidence based on vitamin D doses among older adults.

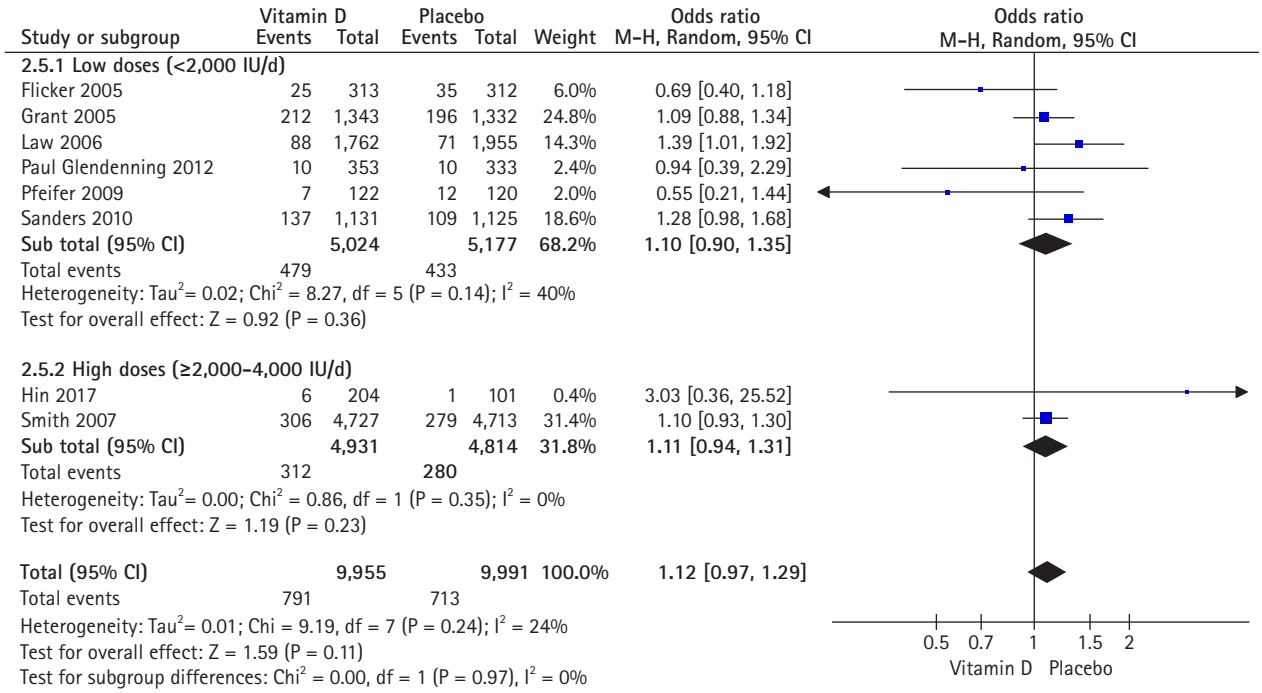

Fig. 5. Forest plot of fracture incidence based on vitamin D doses among older adults.

Our results differed due to the contradictory results of the included randomized studies. The pooled results of the analysis of four RCTs that used vitamin D2 as an intervention showed that vitamin D2 reduced the number of older adults falling in all studies, however, the difference was not statistically significant.[30-33] In contrast, among 13 studies that used vitamin D3 as an intervention, five RCTs showed that vitamin D3 reduced the risk of falls in older adults,[16,29,34-36] while the remaining eight revealed the opposite, in which that vitamin D3 supplementation increased the number of people falling.[26-28,37-41] Sanders et al.[41] and Waterhouse et al.[27] showed that vitamin D3 significantly increased the number of older adults falling compared to placebo. This raises the possibility of adverse outcomes for high doses of vitamin D3. In 2010, Sanders et al.[41] administered an annual dose of 500,000 IU of cholecalciferol to the intervention group. Similarly, in 2012, Yang[45] recommended monthly vitamin D doses of 24,000 IU as a daily supplement. Finally, a recent study by Waterhouse et al.[27] administered 60,000 IU of cholecalciferol monthly.

A major concern in studies on falls in older adults is the occurrence of fractures following falls. Similarly, analyses of fracture outcomes revealed no statistically significant difference in fracture risk between older adults who received vitamin D2, vitamin D3, or a placebo. Among the RCTs that administered vitamin D2 as an intervention, two showed that vitamin D2 increased the number of older adults with fractures[32,39]; the other showed that vitamin D2 reduced the number of fractures.[31] However, these results were not statistically significant. The same was true for vitamin D3, with two RCTs showing that vitamin D3 reduced the risk of fractures[36,40] and another three showing an increased number of fractures in the vitamin D3 group.[28,38,41] The results of our meta-analysis were similar to those of a previous study reporting that vitamin D3 supplementation did not significantly reduce fracture risk compared to placebo among older adults.[19] However, another meta-analysis on the combination of vitamin D3 and calcium showed the opposite results. Using a daily oral supplement, the results showed that supplementation with 800 IU of vitamin D3 combined with 1,200 mg of calcium reduced the risks of hip and non-vertebral fractures.[12] These findings raise the possibility of an effective combination of calcium and vitamin D to reduce the fracture risk in older adults. Future RCTs are needed to further investigate the results of this combination with different doses and timings of vitamin D administration, and with other uses such as intramuscular injection.

After converting the vitamin D dose in the intervention groups of all RCTs to daily dosing, the results of the meta-analyses showed no statistically significant differences in the number of older adults with falls and fractures between the vitamin D intervention and placebo groups. Most RCTs showed no statistically significant dif-

ference in falls; however, Pfeifer et al.[36] demonstrated the protective effect of vitamin D, specifically vitamin D3. The authors observed a statistically significant reduction in the number of older adults with falls compared with the placebo. In contrast, Sanders et al.[41] showed a higher number of older adults with falls in the vitamin D3 group compared to in the placebo group; however, the difference was not significantly significant. However, the final pooled result of all RCTs revealed no significant difference.

The major strength of our study is that it included 17 RCTs with many total participants, including 47,206 older adults from different countries worldwide. In addition to the pooled results of the total included studies, sub-analyses of vitamins D2 and D3 were also performed to determine the results for different forms of vitamin D. However, our study also has several limitations. Most of the participants were from Western countries, except for one study that included Caucasian, Afro-Caribbean, and Middle Eastern participants[30]; moreover, none of the included studies was conducted in Asian regions. Another limitation was that our meta-analysis considered only English-language publications. All of the above limitations underscore the need for future studies to identify relevant studies in populations in all regions, with no restriction on languages from databases to obtain more data to analyze the effect and safety of vitamin D supplementation. Additional meta-analyses of other subgroups such as oral administration groups, injection-using groups, and short- and long-term use are needed to support shared decision-making for a nutritionist to help patients make good choices regarding vitamin D supplementation.

In conclusion, the effects of vitamin D on the promotion of calcium and phosphate concentrations for bone growth and muscle activity are well-known. However, evidence for the effect of vitamin D in reducing falls remains inconsistent. The results of our study showed that, compared to a placebo, vitamin D supplementation did not significantly reduce the incidence of falls or fractures in older adults.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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None.

AUTHOR CONTRIBUTIONS

Conceptualization, TQ, HD; Methodology, TQ; Formal analysis, TQ, HD; Software, TQ; Data curation, TQ, HD; Visualization, TQ; Supervision, HD; Validation, MSNG, HD; Writing-original draft, TQ; Writing-review & editing, MSNG, HD.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.23.0047.

REFERENCES

1. Gale CR, Cooper C, Aihie Sayer A. Prevalence and risk factors for falls in older men and women: The English Longitudinal Study of Ageing. Age Ageing 2016;45:789-94.
2. Moreland B, Lee R. Emergency department visits and hospitalizations for selected nonfatal injuries among adults aged ≥65 years: United States, 2018. MMWR Morb Mortal Wkly Rep 2021;70:661-6.
3. Appeadu MK, Bordoni B. Falls and fall prevention in the elderly. Tampa, FL: StatPearls Publishing; 2022.
4. World Health Organization. Falls [Internet]. Geneva, Switzerland: World Health Organization; 2021 [cited 2023 Sep 10]. Available from: https://www.who.int/news-room/fact-sheets/detail/falls.
5. While AE. Falls and older people: understanding why people fall. Br J Community Nurs 2020;25:173-7.
6. Sim M, Zhu K, Lewis JR, Hodgson JM, Prince RL. Association between vitamin D status and long-term falls-related hospitalization risk in older women. J Am Geriatr Soc 2021;69:3114-23.
7. Neale RE, Wilson LF, Black LJ, Waterhouse M, Lucas RM, Gordon LG. Hospitalisations for falls and hip fractures attributable to vitamin D deficiency in older Australians. Br J Nutr 2021;126:1682-6.
8. Sintov AC, Yarmolinsky L, Dahan A, Ben-Shabat S. Pharmacological effects of vitamin D and its analogs: recent developments. Drug Discov Today 2014;19:1769-74.
9. Charoenngam N, Shirvani A, Holick MF. Vitamin D for skeletal and non-skeletal health: what we should know. J Clin Orthop Trauma 2019;10:1082-93.
10. Uusi-Rasi K, Patil R, Karinkanta S, Tokola K, Kannus P, Lamberg-Allardt C, et al. Serum 25-hydroxyvitamin D levels and incident falls in older women. Osteoporos Int 2019;30:93-101.
11. Moon H, Ko HJ, Kim AS. The relationship between serum 25-hydroxyvitamin D levels and physical performance in community-dwelling older adults. Ann Geriatr Med Res 2019;23:9-15.

12. Manoj P, Derwin R, George S. What is the impact of daily oral supplementation of vitamin D3 (cholecalciferol) plus calcium on the incidence of hip fracture in older people?: a systematic review and meta-analysis. Int J Older People Nurs 2023;18:e12492.
13. Bischoff-Ferrari HA. Relevance of vitamin D in muscle health. Rev Endocr Metab Disord 2012;13:71-7.
14. Granic A, Hill TR, Davies K, Jagger C, Adamson A, Siervo M, et al. Vitamin D status, muscle strength and physical performance decline in very old adults: a prospective study. Nutrients 2017;9:379.
15. Fleet JC, Schoch RD. Molecular mechanisms for regulation of intestinal calcium absorption by vitamin D and other factors. Crit Rev Clin Lab Sci 2010;47:181-95.
16. Dukas L, Schacht E, Mazor Z, Stahelin HB. Treatment with alfacalcidol in elderly people significantly decreases the high risk of falls associated with a low creatinine clearance of < 65 ml/min. Osteoporos Int 2005;16:198-203.
17. Gallagher JC. Vitamin D and bone density, fractures, and falls: the end of the story? Lancet Diabetes Endocrinol 2018;6:834-5.
18. Bolland MJ, Grey A, Avenell A. Effects of vitamin D supplementation on musculoskeletal health: a systematic review, meta-analysis, and trial sequential analysis. Lancet Diabetes Endocrinol 2018;6:847-58.
19. LeBoff MS, Chou SH, Ratliff KA, Cook NR, Khurana B, Kim E, et al. Supplemental vitamin D and incident fractures in midlife and older adults. N Engl J Med 2022;387:299-309.
20. Ling Y, Xu F, Xia X, Dai D, Xiong A, Sun R, et al. Vitamin D supplementation reduces the risk of fall in the vitamin D deficient elderly: an updated meta-analysis. Clin Nutr 2021;40:5531-7.
21. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev 2021;10:89.
22. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327:557-60.
23. Melsen WG, Bootsma MC, Rovers MM, Bonten MJ. The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. Clin Microbiol Infect 2014;20:123-9.
24. Serghiou S, Goodman SN. Random-effects meta-analysis: summarizing evidence with caveats. JAMA 2019;321:301-2.
25. Bleizgys A. Vitamin D dosing: basic principles and a brief algorithm (2021 update). Nutrients 2021;13:4415.
26. Hansen KE, Johnson RE, Chambers KR, Johnson MG, Lemon CC, Vo TN, et al. Treatment of vitamin D insufficiency in postmenopausal women: a randomized clinical trial. JAMA Intern Med 2015;175:1612-21.
27. Waterhouse M, Sanguineti E, Baxter C, Duarte Romero B, McLeod DS, English DR, et al. Vitamin D supplementation and risk of falling: outcomes from the randomized, placebo-controlled D-Health Trial. J Cachexia Sarcopenia Muscle 2021;12:1428-39.
28. Grant AM, Avenell A, Campbell MK, McDonald AM, MacLennan GS, McPherson GC, et al. Oral vitamin D3 and calcium for secondary prevention of low-trauma fractures in elderly people (Randomised Evaluation of Calcium Or vitamin D, RECORD): a randomised placebo-controlled trial. Lancet 2005;365:1621-8.
29. Houston DK, Tooze JA, Demons JL, Davis BL, Shertzer-Skinner R, Kearsley LB, et al. Delivery of a vitamin D intervention in homebound older adults using a meals-on-wheels program: a pilot study. J Am Geriatr Soc 2015;63:1861-7.
30. Dhesi JK, Jackson SH, Bearne LM, Moniz C, Hurley MV, Swift CG, et al. Vitamin D supplementation improves neuromuscular function in older people who fall. Age Ageing 2004;33:589-95.
31. Flicker L, MacInnis RJ, Stein MS, Scherer SC, Mead KE, Nowson CA, et al. Should older people in residential care receive vitamin D to prevent falls?: results of a randomized trial. J Am Geriatr Soc 2005;53:1881-8.
32. Smith H, Anderson F, Raphael H, Maslin P, Crozier S, Cooper C. Effect of annual intramuscular vitamin D on fracture risk in elderly men and women: a population-based, randomized, double-blind, placebo-controlled trial. Rheumatology (Oxford) 2007;46:1852-7.
33. Witham MD, Crighton LJ, Gillespie ND, Struthers AD, McMurdo ME. The effects of vitamin D supplementation on physical function and quality of life in older patients with heart failure: a randomized controlled trial. Circ Heart Fail 2010;3:195-201.
34. Bischoff HA, Stahelin HB, Dick W, Akos R, Knecht M, Salis C, et al. Effects of vitamin D and calcium supplementation on falls: a randomized controlled trial. J Bone Miner Res 2003;18:343-51.
35. Levis S, Gomez-Marin O. Vitamin D and physical function in sedentary older men. J Am Geriatr Soc 2017;65:323-31.
36. Pfeifer M, Begerow B, Minne HW, Suppan K, Fahrleitner-Pammer A, Dobnig H. Effects of a long-term vitamin D and calcium supplementation on falls and parameters of muscle function in community-dwelling older individuals. Osteoporos Int 2009;20:315-22.
37. Bischoff-Ferrari HA, Freystatter G, Vellas B, Dawson-Hughes B, Kressig RW, Kanis JA, et al. Effects of vitamin D, omega-3 fatty acids, and a simple home strength exercise program on fall prevention: the DO-HEALTH randomized clinical trial. Am J Clin Nutr 2022;115:1311-21.
38. Hin H, Tomson J, Newman C, Kurien R, Lay M, Cox J, et al. Optimum dose of vitamin D for disease prevention in older people: BEST-D trial of vitamin D in primary care. Osteoporos Int 2017;28:841-51.

39. Law M, Withers H, Morris J, Anderson F. Vitamin D supplementation and the prevention of fractures and falls: results of a randomised trial in elderly people in residential accommodation. Age Ageing 2006;35:482-6.
40. Glendenning P, Zhu K, Inderjeeth C, Howat P, Lewis JR, Prince RL. Effects of three-monthly oral 150,000 IU cholecalciferol supplementation on falls, mobility, and muscle strength in older postmenopausal women: a randomized controlled trial. J Bone Miner Res 2012;27:170-6.
41. Sanders KM, Stuart AL, Williamson EJ, Simpson JA, Kotowicz MA, Young D, et al. Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial. JAMA 2010;303:1815-22.
42. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, Orav JE, Stuck AE, Theiler R, et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomized controlled trials. BMJ 2009;339:b3692.
43. Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC, Staehelin HB, Bazemore MG, Zee RY, et al. Effect of vitamin D on falls: a meta-analysis. JAMA 2004;291:1999-2006.
44. Kalyani RR, Stein B, Valiyil R, Manno R, Maynard JW, Crews DC. Vitamin D treatment for the prevention of falls in older adults: systematic review and meta-analysis. J Am Geriatr Soc 2010;58:1299-310.
45. Yang JH. The prevention of falls. J Korean Geriatr Soc 2012;16:101-7.

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The Clinical Frailty Scale as a Risk Assessment Tool for Dysphagia in Older Inpatients: A Cross-Sectional Study

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Background: Dysphagia is a common problem with potentially serious consequences including malnutrition, dehydration, pneumonia, and death. However, there are challenges in screening for dysphagia in older adults. We assessed the feasibility of using the Clinical Frailty Scale (CFS) as a risk assessment tool for dysphagia.

Methods: This cross-sectional study was conducted at a tertiary teaching hospital from November 2021 to May 2022 and included 131 older patients (age ≥65 years) admitted to acute wards. We used the Eating Assessment Tool-10 (EAT-10), which is a simple measure for identifying individuals at risk of dysphagia, to assess the relationship between EAT-10 score and frailty status as measured using the CFS.

Results: The mean age of the participants was 74.3±6.7 years, and 44.3% were male. Twenty-nine (22.1%) participants had an EAT-10 score ≥3. The CFS was significantly associated with an EAT-10 score ≥3 after adjusting for age and sex (odds ratio=1.48; 95% confidence interval [CI], 1.09–2.02). The CFS was able to classify the presence of an EAT-10 score ≥3 (area under the receiver operating characteristic [ROC] curve=0.650; 95% CI, 0. 544–0.756). The cutoff point for predicting an EAT-10 score ≥3 was a CFS of 5 according to the highest Youden index, with a sensitivity of 82.8% and a specificity of 46.1%. The positive and negative predictive values were 30.4% and 90.4%, respectively.

Conclusion: The CFS can be used as a tool to screen for the risk of swallowing difficulty in older inpatients to determine clinical management encompassing drug administration routes, nutritional support, prevention of dehydration, and further evaluation of dysphagia.

Key Words: Dysphagia, Frailty, Clinical Frailty Scale, Older adults

INTRODUCTION

The ability to swallow is an essential aspect of human physiology and necessary for maintaining proper nutrition and hydration.[1] Dysphagia, or difficulty swallowing, is a common problem that can have serious consequences, including malnutrition, dehydration, pneumonia, and even death.[2] In addition to its negative health effects, dysphagia can affect the quality of life in older adults.[3] Swallowing difficulty can lead to social isolation and decreased enjoyment of meals, which are important aspects of overall well-being.[4,5]

As dysphagia disproportionately affects older adults with frailty, identifying dysphagia in frail individuals is crucial. The prevalence of dysphagia is up to one-third among community-dwelling older

individuals.[6] As frail older adults are more likely to have multiple chronic conditions and functional impairments,[7] these populations are more likely to experience the adverse consequences of dysphagia.[8] Furthermore, because exercise and nutritional support are important strategies to prevent the progression of frailty and improve functional status,[9-11] dysphagia may preclude the beneficial impact of such interventions on frailty.

However, challenges exist in screening for dysphagia in older adults. Individuals at risk may be unable to report symptoms of dysphagia because of cognitive or functional impairments. In addition, the symptoms of dysphagia can be vague and nonspecific, making it difficult to diagnose without specialized testing. Furthermore, individuals may not seek medical attention for dysphagia unless their symptoms are severe, which can delay diagnosis and treatment. This can be particularly problematic in older adults with frailty who may not have easy access to healthcare providers or who may not be under the care of a geriatric specialist.

The Eating Assessment Tool-10 (EAT-10) is a simple and widely used screening measure for identifying individuals at risk of dysphagia.[12] We postulated that the EAT-10 could be used as an easy screening tool for older adults with or without frailty. In this study, we assessed the relationship between the EAT-10 score and frailty status as measured using the Clinical Frailty Scale (CFS) in patients aged ≥ 65 years admitted to the acute wards at Asan Medical Center, a tertiary teaching hospital in Korea.

MATERIALS AND METHODS

Study Design and Participants

This cross-sectional study was conducted at Asan Medical Center, a tertiary teaching hospital in Seoul, Korea, between November 2021 and May 2022. The Institutional Review Board of Asan Medical Center reviewed and approved the study protocol (IRB No. 2022-1400) and waived the requirement for informed consent because evaluating the general health status of patients at admission is a routine procedure and no additional harm was anticipated. A convenience sample of older patients (age ≥ 65 years) admitted to acute wards who underwent a brief geriatric risk evaluation by a geriatric nurse specialist was included. Patients who were hemodynamically unstable or were approaching death were excluded from the study. Additionally, patients with neurological diseases such as stroke and Parkinson's disease, which can directly cause dysphagia, and patients hospitalized for respiratory infections and upper gastrointestinal diseases, which can temporarily cause or worsen dysphagia, were excluded from the analysis.

This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[13]

Patient Assessments

The CFS and EAT-10 were measured once on the day after admission by a trained geriatric nurse specialist and an occupational therapist, respectively.

Among the many tools available for measuring frailty, the CFS is a simple tool with a score ranging from 1 to 9 with brief descriptors and pictographs. It was developed to stratify older patients according to their relative degrees of frailty.[14] After its initial validation, the CFS has been widely used in multiple settings to predict the clinical outcomes of the aging population.[15] We used the Korean-translated version of the CFS, the construct validity of which has been established in Korean geriatric patients.[16,17]

Dysphagia screening was performed using the EAT-10.[18] The EAT-10 consists of 10 questions that are scored from 0 (no problem) to 4 (severe problem), resulting in a total score ranging from 0 to 40. Previous studies considered an EAT-10 score of ≥ 3 as positive for screening.[8,18] In contrast, this study, defined each EAT-10 question with a score ≥ 1 as positive. The Korean translation of EAT-10 has also been validated in Korea.[19] The baseline patient characteristics, including demographic, anthropometric, and laboratory data, were retrieved from electronic medical records. The Geriatric Nutritional Risk Index (GNRI) was calculated using the following formula derived from previous studies[20,21]:

$$\text{GNRI} = 1.489 \times \text{albumin (g/L)} + 41.7 \times (\text{body weight/WLo}).$$

WLo (Ideal weight calculated from the Lorentz equations) was calculated as follows:

$$\text{WLo} = \text{height (cm)} - 100 - \frac{\text{height} - 150}{4} \left(\text{for men}\right),$$

$$\text{WLo} = \text{height (cm)} - 100 - \frac{\text{height} - 150}{2.5} \left(\text{for women}\right).$$

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as mean ± standard deviation, while discrete variables are presented as counts and percentages. Statistical differences were assessed using t-test, Pearson chi-square test, or Fisher exact test. We performed binary logistic and linear regression analyses to evaluate the relationship between the EAT-10 score and frailty status as measured by the CFS. To assess the ability to classify for the presence of an EAT-10 score ≥ 3 and positivity for each question of the EAT-10, we performed receiver operating characteristic (ROC) analyses using the CFS as the test variable and these outcomes as the state variables. The cutoff point of the CFS was determined according to the highest Youden index, and

the sensitivity, specificity, and positive and negative predictive values were determined. All statistical analyses were two-tailed, and statistical significance was set at $p < 0.05$.

RESULTS

General Characteristics of the Study Participants

During the study period, we assessed the EAT-10 and CFS in 131 patients aged ≥65 years who were admitted to acute wards. The mean age of the patients was 74.3±6.7 years and 44.3% were male. Twenty-nine (22.1%) patients had an EAT-10 score ≥3. The general characteristics of the study participants with EAT-10 scores <3 or ≥3 are presented in Table 1. Patients with EAT-10 scores ≥3 had significantly lower body mass index and albumin levels than those with EAT-10 scores <3. In addition, their CFS scores were higher and they had a greater risk of malnutrition.

Relationship between EAT-10 Score and Frailty Status

To identify the factors associated with an EAT-10 score ≥3, we performed binary logistic regression analysis. After adjusting for age and sex, CFS was significanlty associated with an EAT-10 ≥3 (odds ratio=1.48; 95% confidence interval [CI], 1.09–2.02) (Table 2). Linear regression analysis performed to identify factors associated with the EAT-10 score revealed that CFS was significantly associated with EAT-10 score ($p = 0.027$) (Table 3).

CFS as a Dysphagia Indicator

CFS was able to classify the presence of an EAT-10 score ≥3 (area

Table 1. General characteristics of the study participants according to presence of an EAT-10 score ≥3

	Total (n=131)	EAT-10 <3 (n=102)	EAT-10 ≥3 (n=29)	p-value
Age (y)	74.3±6.7	74.4±6.9	74.0±6.0	0.765
Sex, male	58 (44.3)	41 (40.2)	17 (58.6)	0.078
BMI (kg/m^2)	24.0± 3.9	24.5±3.9	21.9±3.1	0.001
Albumin (g/dL)	3.0±0.6	3.1±0.6	2.7±0.6	0.004
EAT-10 score	2.7±6.2	0.3±0.6	11.1±9.1	<0.001
GNRI	89.4±13.2	91.7±12.6	81.0±11.9	<0.001
Clinical Frailty Scale	5.1±1.5	4.9±1.5	5.7±1.3	0.015
EAT-10 questions (positive)[a]				
My swallowing problem has caused me to lose weight.	14 (10.7)	1 (1.0)	13 (44.8)	<0.001
My swallowing problem interferes with my ability to go out for meals.	12 (9.2)	0 (0.0)	12 (41.4)	<0.001
Swallowing liquids takes extra efforts.	18 (13.7)	2 (2.0)	16 (55.2)	<0.001
Swallowing solids takes extra efforts.	25 (19.1)	1 (1.0)	24 (82.8)	<0.001
Swallowing pills takes extra efforts.	22 (16.8)	3 (2.9)	19 (65.5)	<0.001
Swallowing is painful.	21 (16.0)	1 (1.0)	20 (69.0)	<0.001
The pleasure of eating is affected by my swallowing.	18 (13.7)	0 (0.0)	18 (62.1)	<0.001
When I swallow food sticks in my throat.	20 (15.3)	2 (2.0)	18 (62.1)	<0.001
I cough when I eat.	37 (28.2)	19 (18.6)	18 (62.1)	<0.001
Swallowing is stressful.	22 (16.8)	2 (2.0)	20 (69.0)	<0.001

Values are presented as mean±standard deviation or number (%).
EAT-10, Eating Assessment Tool-10; BMI, body mass index; GNRI, Geriatric Nutritional Risk Index.
Continuous variables (age, BMI, Albumin, EAT-10 score, GNRI, Clinical Frailty Scale) were compared using the t-test. Discrete variables (sex, EAT-10 questions) were compared using either the Pearson chi-square test or Fisher exact test.
[a]Each EAT-10 question was defined as positive if the score for that question was answered as ≥1.

Table 2. Binary logistic regression analysis for the presence of an EAT-10 score ≥3

	EAT-10 score ≥3			
	Univariate		Multivariate[a]	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (1 year higher)	0.99 (0.93–1.06)	0.763	0.97 (0.90–1.04)	0.343
Sex (male)	2.11 (0.91–4.87)	0.081	2.00 (0.84–4.75)	0.115
CFS (1 higher)	**1.42 (1.06–1.89)**	**0.018**	**1.48 (1.09–2.02)**	**0.012**

A value in bold indicates statistical significance.
EAT-10, Eating Assessment Tool-10; CFS, Clinical Frailty Scale; OR, odds ratio; CI, confidence interval.
[a]All variables in the univariate analysis were entered into the multivariate analysis.

Table 3. Linear regression analysis for the EAT-10 score

	B	Beta	95% CI	p-value
Age (1 year higher)	-0.04	-0.04	-0.20–0.13	0.672
Sex (male)	2.19	0.18	0.08–4.30	0.042
CFS (1 higher)	0.85	0.20	0.10–1.59	0.027

EAT-10, Eating Assessment Tool-10; CFS, Clinical Frailty Scale; CI, confidence interval.

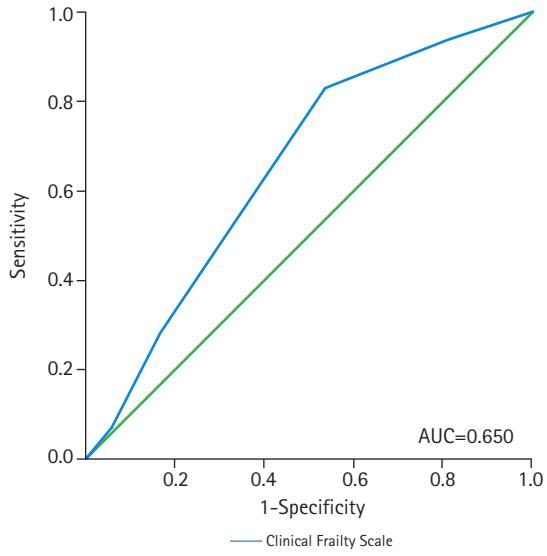

Fig. 1. Receiver operating characteristic (ROC) curve for the presence of EAT-10 score ≥3. AUC, area under ROC curve; EAT-10, Eating Assessment Tool-10.

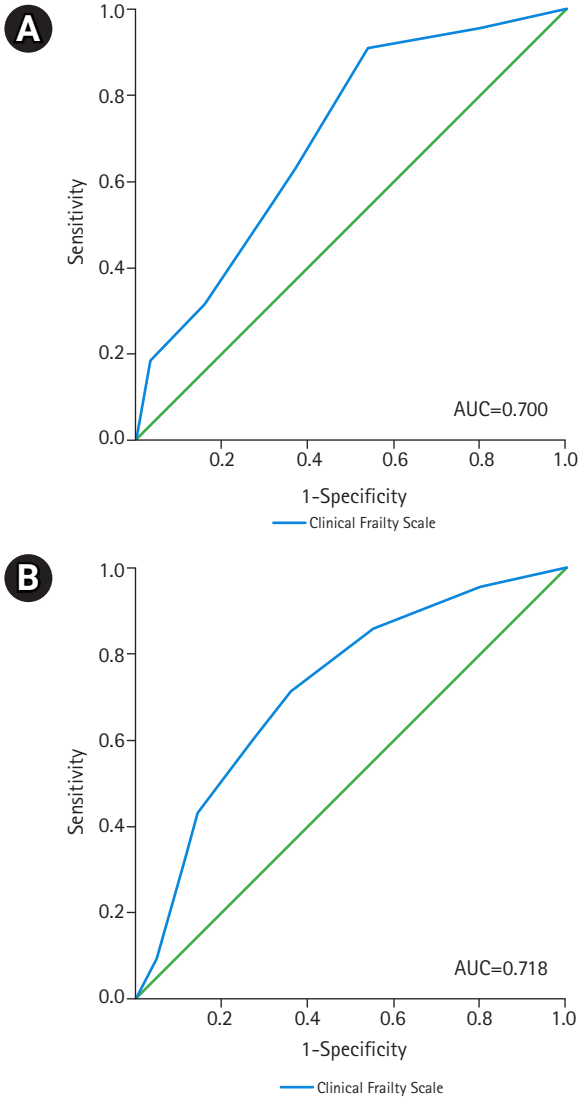

Fig. 2. Receiver operating characteristic (ROC) curves for positivity for EAT-10 questions: (A) pill-swallowing difficulty and (B) painful swallowing. AUC, area under ROC curve; EAT-10, Eating Assessment Tool-10.

under the ROC curve [AUC] = 0.650; 95% CI, 0.544– 0.756) (Fig. 1). A CFS score of 5 was the cutoff score for predicting the presence of an EAT-10 score ≥ 3, according to the highest Youden index, with a sensitivity of 82.8% and a specificity of 46.1%. The positive and negative predictive values were 30.4% and 90.4%, respectively. The CFS was able to predict positivity for two questions of the EAT-10 (Fig. 2); namely pill swallowing difficulty (AUC = 0.700; 95% CI, 0.590–0.810) and painful swallowing (AUC = 0.718; 95% CI, 0.603–0.833). The CFS cutoff score according to the highest Youden index for each question and the corresponding sensitivity, specificity, and positive and negative predictive values are shown in Table 4.

DISCUSSION

Our results showed a higher risk of malnutrition among older patients with an EAT-10 score ≥ 3 admitted to acute wards. CFS score was significantly associated with the EAT-10 score, and a CFS of 5 was the cutoff score predicting the presence of an EAT-10 score ≥ 3. Additionally, the CFS could also be used to predict pill-swallowing difficulty and swallowing pain.

Dysphagia is common in older adults and can occur due to problems during various eating phases. Oropharyngeal dysphagia commonly occurs after stroke and during the course of many neurodegenerative diseases such as dementia and Parkinson disease.[22] The prevalence of dysphagia varies among studies. Several meta-analyses have reported estimated prevalence rates of dysphagia of > 10% and > 20% in community-dwelling and hospitalized older patients, respectively.[6,23] Dysphagia is known to increase the risk of malnutrition.[24] As nutrition is considered a cornerstone in the

Table 4. The CFS cutoff points according to the highest Youden index, and the corresponding sensitivity, specificity, PPV, and NPV

	CFS cutoff points	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Swallowing pills takes extra efforts	5	90.9	45.9	25.3	96.2
Swallowing is painful	6	71.4	63.6	27.3	92.1

CFS, Clinical Frailty Scale; PPV, positive predictive value; NPV, negative predictive value.

concept of the "cycle of frailty," a self-deteriorating cycle of negative energy balance, reduced physical activity, and further decline in physical performance,[25,26] several studies have suggested that dysphagia is associated with frailty.[27,28] In addition, dysphagia is a risk factor for the development of aspiration pneumonia,[29] and increased dysphagia is associated with reduced health-related quality of life.[30] Therefore, in an aging society, identifying older adults at risk of dysphagia, performing diagnostic tests, and administering appropriate treatments based on the test results are important.

Frailty, which reflects a decline in physiological reserves, is strongly associated with biological age,[31] concurrent medical conditions, morbidity, and reduced survival in older adults.[32,33] Frailty is generally assessed through different operational definitions, and the prominent models encompass physical and biological models, deficit accumulation models, and multidimensional biopsychosocial models.[34] Among the many tools for measuring frailty, the CFS has the advantage of being able to intuitively assess the frailty status of patients. Studies have shown that the CFS can predict vulnerability to various adverse geriatric outcomes in both community-dwelling older adults and hospitalized patients. As shown in the present study, the CFS may be useful for screening for dysphagia and stratifying hospitalized older patients according to frailty status.

Assessing the presence of dysphagia in hospitalized older adult patients is essential for several reasons. First, the oral route is widely utilized and favored for drug administration owing to its benefits, including its noninvasive nature, patient compliance, and convenience in drug delivery.[35] Therefore, the presence or absence of dysphagia must be evaluated in hospitalized older adult patients who must maintain the effects of drugs through steady drug administration. The use of the CFS at the time of hospitalization and using a defined cutoff point may effectively identify patients who require evaluation for dysphagia. Following evaluation, interventions such as changing the dosage form or administration route for patients with dysphagia can be considered.

Second, screening acutely hospitalized older patients at high risk for dysphagia is useful for reducing the risk of aspiration or malnutrition and identifying patients who can benefit from nutritional interventions. Malnutrition has a severe impact on recovery from disease and is associated with increased morbidity and mortality.[36,37] Poor nutritional status is also associated with the development of geriatric syndrome.[38] Previous studies confirmed the role of malnutrition in the occurrence of delirium and pressure ulcers in hospitalized older patients.[39,40] Additionally, malnutrition upon hospital admission is a significant risk factor for falls during hospital stays.[41] A cutoff point is useful for identifying high-risk patients requiring accurate testing and close observation.

Third, older adults have decreased thirst sensation and a decline in urinary concentration ability[2]; if additional functional problems are present, dehydration can easily occur. Dehydration is very common, particularly in patients with dysphagia, with the prevalence of dehydration ranging from 44% to 75%.[42,43] As a result, dehydration ranks as one of the top 10 most commonly diagnosed medical conditions leading to hospital admission among older adults.[44] Dehydration is also associated with the development of geriatric syndromes such as delirium and falls.[45,46] Identification of the risk of dysphagia in hospitalized older adult patients is necessary to reduce the risk of dehydration.

Given the challenges in screening for dysphagia in older adults, particularly in those with cognitive or functional impairments, the use of the CFS as a dysphagia indicator can aid healthcare providers in identifying at-risk patients and facilitating early interventions. By incorporating CFS assessment into routine geriatric care, healthcare providers can enhance their ability to detect swallowing difficulties in frail older adults, ultimately reducing the risks of malnutrition, dehydration, pneumonia, and other adverse consequences of dysphagia. Additionally, timely intervention may improve the effectiveness of exercise and nutritional support in preventing the progression of frailty and improving patient functional status. Future research should explore the implementation of CFS-based screening strategies in various healthcare settings and their impact on dysphagia management and frailty outcomes.[47]

Of the 131 patients included in the study, only two underwent a videofluoroscopic swallow study (VFSS), a substantially low number considering the prevalence of patients at risk according to the EAT-10 questionnaire. Many factors may contribute to the potential underuse of formal evaluation methods for treating dysphagia, including the current bottleneck in VFSS volume per day in Korean academic hospitals.

Although the pathophysiology of dysphagia is complex and the

spectrum of its severity is wide, some issues can be addressed using this simple scale. Suspecting dysphagia in patients, especially in those with advanced frailty, may prevent delayed recognition of dysphagia after pneumonia caused by repeated aspiration. Additionally, this approach has the advantage of being widely applicable in real clinical settings due to its relatively simple predictive nature. A clinical suspicion of dysphagia using the CFS may provide healthcare professionals with an early opportunity to perform formal, in-depth assessments of this condition in patients, especially those with medical conditions that affect their swallowing ability.

This study has several limitations. First, the cross-sectional design limited our ability to establish causality between the EAT-10 score and frailty status as measured by the CFS. Longitudinal studies are needed to investigate the causal relationship between dysphagia and frailty in older adults. Second, this study was conducted at a single tertiary teaching hospital in South Korea, which may limit the generalizability of the findings to other healthcare settings and populations. Future research should include larger and more diverse samples from multiple centers to enhance the generalizability of the results. Third, this study relied on self-reported measures to assess dysphagia using the EAT-10, which may have been influenced by recall bias and subjectivity. Objective assessments of swallowing function, such as VFSS, would provide more accurate information on dysphagia presence and severity. Finally, we excluded patients who were hemodynamically unstable or approaching death, which may have led to an underestimation of the prevalence of dysphagia and its association with frailty in the overall older adult population.

In conclusion, the CFS can be used as a risk assessment tool for dysphagia in hospitalized older adults. The presence or absence of dysphagia has important implications for determining the drug administration route, nutritional intervention, and prevention of dehydration in acutely hospitalized patients. Therefore, the CFS can be effectively used to determine whether interventions can be performed to improve the prognosis of older inpatients.

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CONFLICT OF INTEREST

Hee-Won Jung cofounded Dyphi Inc, a startup company developing sensor technologies for human movement and robotics. Otherwise, authors declare that there are no potential conflicts of interest.

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None.

AUTHOR CONTRIBUTIONS

Conceptualization, MK, EL, IYJ, HWJ; Data curation, SHJ, YKP, JYB, SHL, HWJ; Investigation, SHJ, YHK, YS, SHL, HWJ; Methodology: MK, EL, IYJ, HWJ; Project administration: SHJ, YKP, JYB, YHK, YS, SHL; Supervision, EL, IYJ, HWJ; Writing-original draft: MK, HWJ; Writing-review & editing: MK, SHJ, YKP, JYB, YHK, YS, SHL, EL, IYJ, HWJ.

REFERENCES

1. Porter K, Burch N, Campbell C, Danbury C, Foster C, Gabe S, et al. Supporting people who have eating and drinking difficulties. Clin Med (Lond) 2021;21:e344-50.
2. Reber E, Gomes F, Dahn IA, Vasiloglou MF, Stanga Z. Management of dehydration in patients suffering swallowing difficulties. J Clin Med 2019;8:1923.
3. Kim DY, Park HS, Park SW, Kim JH. The impact of dysphagia on quality of life in stroke patients. Medicine (Baltimore) 2020;99:e21795.
4. Farri A, Accornero A, Burdese C. Social importance of dysphagia: its impact on diagnosis and therapy. Acta Otorhinolaryngol Ital 2007;27:83-6.
5. Ekberg O, Hamdy S, Woisard V, Wuttge-Hannig A, Ortega P. Social and psychological burden of dysphagia: its impact on diagnosis and treatment. Dysphagia 2002;17:139-46.
6. Doan TN, Ho WC, Wang LH, Chang FC, Nhu NT, Chou LW. Prevalence and methods for assessment of oropharyngeal dysphagia in older adults: a systematic review and meta-analysis. J Clin Med 2022;11:2605.
7. Lee DR, Santo EC, Lo JC, Ritterman Weintraub ML, Patton M, Gordon NP. Understanding functional and social risk characteristics of frail older adults: a cross-sectional survey study. BMC Fam Pract 2018;19:170.
8. Bahat G, Yilmaz O, Durmazoglu S, Kilic C, Tascioglu C, Karan MA. Association between dysphagia and frailty in community dwelling older adults. J Nutr Health Aging 2019;23:571-7.
9. Angulo J, El Assar M, Alvarez-Bustos A, Rodriguez-Manas L. Physical activity and exercise: strategies to manage frailty. Redox Biol 2020;35:101513.
10. Han CY, Miller M, Yaxley A, Baldwin C, Woodman R, Sharma Y. Effectiveness of combined exercise and nutrition interventions in prefrail or frail older hospitalised patients: a systematic review and meta-analysis. BMJ Open 2020;10:e040146.
11. Hsieh TJ, Su SC, Chen CW, Kang YW, Hu MH, Hsu LL, et al. Individualized home-based exercise and nutrition interventions improve frailty in older adults: a randomized controlled trial. Int J Behav Nutr Phys Act 2019;16:119.

12. Hansen T, Kjaersgaard A. Item analysis of the Eating Assessment Tool (EAT-10) by the Rasch model: a secondary analysis of cross-sectional survey data obtained among community-dwelling elders. Health Qual Life Outcomes 2020;18:139.
13. Noh JH, Jung HW, Ga H, Lim JY. Ethical guidelines for publishing in the Annals of Geriatric Medicine and Research. Ann Geriatr Med Res 2022;26:1-3.
14. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-95.
15. Church S, Rogers E, Rockwood K, Theou O. A scoping review of the Clinical Frailty Scale. BMC Geriatr 2020;20:393.
16. Jung HW, Jang IY, Back JY, Park S, Park CM, Han SJ, et al. Validity of the Clinical Frailty Scale in Korean older patients at a geriatric clinic. Korean J Intern Med 2021;36:1242-50.
17. Han SJ, Jung HW, Lee JH, Lim J, Moon SD, Yoon SW, et al. Clinical Frailty Scale, K-FRAIL questionnaire, and clinical outcomes in an acute hospitalist unit in Korea. Korean J Intern Med 2021;36:1233-41.
18. Belafsky PC, Mouadeb DA, Rees CJ, Pryor JC, Postma GN, Allen J, et al. Validity and reliability of the Eating Assessment Tool (EAT-10). Ann Otol Rhinol Laryngol 2008;117:919-24.
19. Noh DK, Choi SH, Choi CH, Lee K, Kwak SH. Validity & reliability of a Korean-version of Eating Assessment Tool (K-EAT-10): predicting the risk of aspiration in stroke patients. Commun Sci Disord 2022;27:830-43.
20. Pablo AM, Izaga MA, Alday LA. Assessment of nutritional status on hospital admission: nutritional scores. Eur J Clin Nutr 2003;57:824-31.
21. Bouillanne O, Morineau G, Dupont C, Coulombel I, Vincent JP, Nicolis I, et al. Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. Am J Clin Nutr 2005;82:777-83.
22. Takizawa C, Gemmell E, Kenworthy J, Speyer R. A systematic review of the prevalence of oropharyngeal dysphagia in stroke, Parkinson's disease, Alzheimer's disease, head injury, and pneumonia. Dysphagia 2016;31:434-41.
23. Rivelsrud MC, Hartelius L, Bergstrom L, Lovstad M, Speyer R. Prevalence of oropharyngeal dysphagia in adults in different healthcare settings: a systematic review and meta-analyses. Dysphagia 2023;38:76-121.
24. Carrion S, Cabre M, Monteis R, Roca M, Palomera E, Serra-Prat M, et al. Oropharyngeal dysphagia is a prevalent risk factor for malnutrition in a cohort of older patients admitted with an acute disease to a general hospital. Clin Nutr 2015;34:436-42.
25. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-56.
26. Goisser S, Guyonnet S, Volkert D. The role of nutrition in frailty: an overview. J Frailty Aging 2016;5:74-7.
27. Wang T, Zhao Y, Guo A. Association of swallowing problems with frailty in Chinese hospitalized older patients. Int J Nurs Sci 2020;7:408-12.
28. Yang RY, Yang AY, Chen YC, Lee SD, Lee SH, Chen JW. Association between dysphagia and frailty in older adults: a systematic review and meta-analysis. Nutrients 2022;14:1812.
29. van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM, Schols JM, de Baat C. Meta-analysis of dysphagia and aspiration pneumonia in frail elders. J Dent Res 2011;90:1398-404.
30. Jones E, Speyer R, Kertscher B, Denman D, Swan K, Cordier R. Health-related quality of life and oropharyngeal dysphagia: a systematic review. Dysphagia 2018;33:141-72.
31. Mitnitski A, Collerton J, Martin-Ruiz C, Jagger C, von Zglinicki T, Rockwood K, et al. Age-related frailty and its association with biological markers of ageing. BMC Med 2015;13:161.
32. Klein BE, Klein R, Knudtson MD, Lee KE. Frailty, morbidity and survival. Arch Gerontol Geriatr 2005;41:141-9.
33. Jung HW. Frailty as a clinically relevant measure of human aging. Ann Geriatr Med Res 2021;25:139-40.
34. Dibello V, Lozupone M, Sardone R, Ballini A, Dibello A, Daniele A, et al. Clinical indicators of oral frailty: a domain-specific frailty phenotype. Curr Top Med Chem 2022;22:2391-4.
35. Alqahtani MS, Kazi M, Alsenaidy MA, Ahmad MZ. Advances in oral drug delivery. Front Pharmacol 2021;12:618411.
36. Norman K, Pichard C, Lochs H, Pirlich M. Prognostic impact of disease-related malnutrition. Clin Nutr 2008;27:5-15.
37. Chen L, Huang Z, Lu J, Yang Y, Pan Y, Bao K, et al. Impact of the malnutrition on mortality in elderly patients undergoing percutaneous coronary intervention. Clin Interv Aging 2021;16:1347-56.
38. Saka B, Kaya O, Ozturk GB, Erten N, Karan MA. Malnutrition in the elderly and its relationship with other geriatric syndromes. Clin Nutr 2010;29:745-8.
39. Rosted E, Prokofieva T, Sanders S, Schultz M. Serious consequences of malnutrition and delirium in frail older patients. J Nutr Gerontol Geriatr 2018;37:105-16.
40. Saghaleini SH, Dehghan K, Shadvar K, Sanaie S, Mahmoodpoor A, Ostadi Z. Pressure ulcer and nutrition. Indian J Crit Care Med 2018;22:283-9.
41. Ishida Y, Maeda K, Nonogaki T, Shimizu A, Yamanaka Y, Matsuyama R, et al. Malnutrition at admission predicts in-hospital falls in hospitalized older adults. Nutrients 2020;12:541.
42. Murray J, Doeltgen S, Miller M, Scholten I. A descriptive study of the fluid intake, hydration, and health status of rehabilitation in-

patients without dysphagia following stroke. J Nutr Gerontol Geriatr 2015;34:292-304.
43. Leibovitz A, Baumoehl Y, Lubart E, Yaina A, Platinovitz N, Segal R. Dehydration among long-term care elderly patients with oropharyngeal dysphagia. Gerontology 2007;53:179-83.
44. Xiao H, Barber J, Campbell ES. Economic burden of dehydration among hospitalized elderly patients. Am J Health Syst Pharm 2004;61:2534-40.
45. George J, Rockwood K. Dehydration and delirium: not a simple relationship. J Gerontol A Biol Sci Med Sci 2004;59:811-2.
46. Hamrick I, Norton D, Birstler J, Chen G, Cruz L, Hanrahan L. Association between dehydration and falls. Mayo Clin Proc Innov Qual Outcomes 2020;4:259-65.
47. Jung HW, Baek JY, Kwon YH, Jang IY, Kim DY, Kwon HS, et al. At-point Clinical Frailty Scale as a universal risk tool for older inpatients in acute hospital: a cohort study. Front Med (Lausanne) 2022;9:929555.

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The Effect of Neuromuscular Blockade Reversal Agents on Postoperative Pulmonary Complications in Patients undergoing Femur Fracture Repair Surgery: A Retrospective Observational Study

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Background: Femoral fracture repair surgery under general anesthesia is associated with postoperative pulmonary complications (PPCs). However, information on PPCs caused by residual neuromuscular blockade following perioperative use of neuromuscular blockers is limited. This study aimed to identify the differences in the incidence of PPCs according to the type of neuromuscular blockade reversal agent used in femoral fracture repair surgery, as well as the risk factors for PPCs. **Methods:** We retrospectively analyzed the electronic medical records of 604 patients aged >18 years who underwent general anesthesia for femoral fracture repair surgery at a single university hospital between March 2017 and March 2022. Patients in whom sugammadex or anticholinesterase was used to reverse the neuromuscular block were subjected to propensity score matching. Multivariate logistic regression analysis was performed to identify risk factors for PPCs. **Results:** Among the 604 patients, 108 were matched in each group. The incidence rates of PPCs overall and in the anticholinesterase and sugammadex groups were 7.0%, 8.3%, and 5.6%, respectively, with no significant differences between the groups. Older age, higher ASA (American Society of Anesthesiologists) physical status, and lower preoperative oxygen saturation were risk factors, whereas emergency surgery was a preventive factor. **Conclusions:** Our results demonstrated that the incidence of PPC did not differ significantly between sugammadex and anticholinesterase in patients undergoing femur fracture repair under general anesthesia. Identifying the risk factors and confirming complete recovery from neuromuscular blockade might be more important.

Key Words: Femoral fractures, General anesthesia, Postoperative complications, Cholinesterase inhibitors, Sugammadex, Risk factors

INTRODUCTION

Femur fracture repair surgeries have an increased risk of postoperative pulmonary complications (PPCs), which occur in 4.1%–40% of cases, depending on the definition of PPCs.[1,2] Although the overall mortality rates when surgery is performed under general or spinal anesthesia are similar, spinal anesthesia is preferred, given the stability of respiratory function postoperatively.[3,4] However, in situations where spinal anesthesia cannot be performed, such as coagulopathy, puncture site infection, or uncooperative patients, general anesthesia is a main anesthetic method used in femoral fracture surgery. Therefore, it is important to understand the incidence of PPCs and related risk factors during general anesthesia for femoral fracture surgery.[5,6]

One of the most important elements of general anesthesia is the use of neuromuscular blockers. A neuromuscular blockade reduc-

es intraoperative movement and facilitates surgery. However, residual neuromuscular blockade is a well-known risk factor for anesthesia-related PPCs.[7] Two major drugs contribute to recovery from neuromuscular blockade: anticholinesterase, a competitive inhibitor, and sugammadex, a direct inhibitor. Traditionally, anticholinesterases competitively interfere with neuromuscular blockers. However, they have a ceiling effect that is ineffective above a specific dose, do not reverse deep neuromuscular blockade, and increase PPCs dose-dependently.[8]

Sugammadex has also recently been used. It can directly reverse all stages of neuromuscular block, regardless of the depth of the neuromuscular block. However, it is only effective for a specific class of neuromuscular blockers.[9] Various studies have compared these two drugs for residual neuromuscular block and PPCs, but not for femoral fracture repair surgery, which has a high incidence of PPCs.[10,11] Therefore, the present study aimed to identify the differences in the incidence of PPCs according to the type of neuromuscular blockade reversal agent (anticholinesterase or sugammadex) (primary aim) and identify the risk factors for PPCs (secondary aim) in patients undergoing general anesthesia for femur fracture repair surgery.

MATERIALS AND METHODS

Study Design and Populations

This retrospective observational study was conducted in accordance with the 2013 revisions of the Declaration of Helsinki, was approved by the Institutional Review Board of Konyang University Hospital (No. KYUH 2022-04-005), and was registered with the Korea Clinical Research Information Service. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines. The requirement for informed consent was waived due to the retrospective nature of the study. Also this study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[12]

We retrospectively reviewed the medical records of patients aged > 18 years who underwent femur fracture repair surgery under general anesthesia between March 2017 and March 2022 at our university hospital. We excluded patients in whom atracurium was used as a neuromuscular blocker, no neuromuscular block reversal agent was used, as well as those who underwent combined operations and with insufficient medical records.

Femoral fractures included the femoral neck, trochanter, shaft, and distal femur. The types of surgeries performed were closed reduction, open reduction, bipolar hemiarthroplasty, and total hip replacement.

Perioperative Management

The patients arrived in the operating room without premedication and were monitored using electrocardiography, noninvasive blood pressure, pulse oximetry, neuromuscular monitoring with acceleromyography or electromyography, and baseline body temperature. All medications used during anesthesia, including induction and maintenance agents for anesthesia, neuromuscular blocking agents, and hypotensive agents or vasopressors, were selected at the anesthesiologist's discretion according to each patient's condition.

Postoperatively, the neuromuscular blockade was reversed with an anticholinesterase or sugammadex at the anesthesiologist's discretion. After emergence from anesthesia, the patients were transferred to the intensive care unit (ICU) or post-anesthetic care unit, depending on their condition. Patients transferred to the post-anesthetic care unit stayed there for at least 40 minutes. Postoperative management was performed for all patients according to the protocol at our institution.

Definition and Variables

The investigation was conducted for up to 7 days postoperatively, according to the following definitions. The investigator checked for the presence of complications based on the records of the included patients. Complications were diagnosed postoperatively according to the Korean Standard Classification of Diseases. PPCs were defined as a composite of respiratory diagnoses that shared common pathophysiological mechanisms, including atelectasis, pneumonia, acute respiratory distress syndrome, and pulmonary aspiration within 7 days postoperatively. Atelectasis was detected by computed tomography or chest radiography, and pneumonia was diagnosed using the US Centers for Disease Control and Prevention criteria. Acute respiratory distress syndrome was diagnosed using the Berlin consensus definition, and pulmonary aspiration was diagnosed with a clear clinical history and radiological evidence.[13] The length of hospital stay was defined as the period from admission to discharge. Major adverse cardiac events included composites of myocardial infarction, stroke, heart transplantation, heart failure, other ischemic cardiovascular events, and death.[14] Death was defined as in-hospital death.

The following variables were collected from the electronic medical records: demographic data; preoperative status and history; preoperative laboratory findings; intraoperative data; and postoperative outcomes such as PPCs, length of hospital stay, major adverse cardiac events, and deaths (Tables 1, 2).

The primary outcome was the incidence of PPCs according to the type of neuromuscular blockade reversal agent used. The sec-

Table 1. Perioperative data before and after propensity score matching between cholinesterase inhibitor and sugammadex

	Before propensity score matching				After propensity score matching			
	Sugammadex (n = 496)	Anticholinesterase (n = 108)	p-value	Absolute SMD	Sugammadex (n = 108)	Anticholinesterase (n = 108)	p-value	Absolute SMD
Sex, male	152 (30.6)	41 (38.0)	0.173	0.151	45 (41.7)	41 (38.0)	0.677	0.076
Age (y)	79.0 (72.0–84.0)	67.0 (57.0–78.5)	< 0.001	0.567	74.0 (55.5–79.0)	67.0 (57.0–78.5)	0.553	0.048
ASA physical status			< 0.001	0.626			0.910	0.087
1	3 (0.6)	3 (2.8)			3 (2.8)	3 (2.8)		
2	197 (39.7)	72 (66.7)			67 (62.0)	72 (66.7)		
3	282 (56.9)	32 (29.6)			37 (34.3)	32 (29.6)		
4	14 (2.8)	1 (0.9)			1 (0.9)	1 (0.9)		
Body mass index (kg/m^2)	22.0 (19.6–24.5)	22.1 (19.8–24.4)	0.673	0.071	22.1 (19.8–24.4)	22.1 (19.8–24.4)	0.801	0.068
Hypertension	320 (64.5)	61 (56.5)	0.145	0.162	56 (51.9)	61 (56.5)	0.585	0.093
Cerebrovascular disease	140 (28.2)	19 (17.6)	0.031	0.279	20 (18.5)	19 (17.6)	> 0.999	0.024
Preoperative respiratory infection	7 (1.4)	0 (0)	0.456	0.132	0 (0)	0 (0)	NA	< 0.001
Preoperative anemia	204 (41.1)	39 (36.1)	0.392	0.105	38 (35.2)	39 (36.1)	> 0.999	0.019
Preoperative saturation			0.054	0.279			0.943	0.035
≥ 96%	302 (60.9)	79 (73.1)			78 (72.2)	79 (73.1)		
91%–95%	162 (32.7)	25 (23.1)			25 (23.1)	25 (23.1)		
≤ 90%	32 (6.5)	4 (3.7)			5 (4.6)	4 (3.7)		
Smoking			0.911	0.026			0.253	0.070
Nonsmoker	435 (87.7)	96 (88.9)			100 (92.6)	96 (88.9)		
Ex-smoker	28 (5.6)	5 (4.6)			1 (0.9)	5 (4.6)		
Current smoker	33 (6.7)	7 (6.5)			7 (6.5)	7 (6.5)		
Estimated blood loss	100.0 (50.0–100.0)	100.0 (50.0–100.0)	0.669	0.050	100.0 (50.0–130.0)	100.0 (50.0–100.0)	0.302	0.028
Emergency operation	107 (21.6)	20 (18.5)	0.565	0.079	21 (19.4)	20 (18.5)	> 0.999	0.024
Use of NMT	83 (16.7)	4 (3.7)	0.001	0.690	3 (2.8)	4 (3.7)	> 0.999	0.049
Time to extubation from last NMB	71.0 (48.0–92.0)	75.5 (57.0–98.0)	0.061	0.169	75.5 (53.5–101.0)	75.5 (57.0–98.0)	0.813	0.047
Use of PEEP	365 (73.6)	73 (67.6)	0.252	0.128	75 (69.4)	73 (67.6)	0.884	0.040
Duration of anesthesia	120.0 (95.0–160.0)	135.0 (107.5–185.0)	0.002	0.282	140.0 (100.0–180.0)	135.0 (107.5–185.0)	0.850	< 0.001

Values are presented as number (%) or median (interquartile range).
ASA, American Society of Anesthesiologists; NMT, neuromuscular monitoring; NMB, neuromuscular blockade; PEEP, positive end-expiratory pressure; SMD, standardized mean difference.

Table 2. Postoperative outcomes with cholinesterase inhibitor and sugammadex

	Before propensity score matching			After propensity score matching		
	Sugammadex (n = 496)	Anticholinesterase (n = 108)	p-value	Sugammadex (n = 108)	Anticholinesterase (n = 108)	p-value
Postoperative pulmonary complication	55 (11.1)	9 (8.3)	0.502	6 (5.6)	9 (8.3)	0.592
Hospital length of stay	18.0 (14.5–24.0)	21.0 (16.0–27.0)	0.007	19.0 (14.0–27.0)	21.0 (16.0–27.0)	0.224
Major adverse cardiac event	9 (1.8)	0 (0)	0.331	0 (0)	0 (0)	> 0.999
Death	8 (1.6)	0 (0)	0.387	1 (0.9)	0 (0)	> 0.999

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

ondary outcome was the risk factor for PPCs in patients who underwent femur fracture repair surgery under general anesthesia.

Statistical Analyses

To determine the incidence of PPCs, we divided the groups according to the neuromuscular blockade reversal agent used (sugammadex or anticholinesterase). All demographic and perioperative data were compared between groups before and after propensity score matching. Propensity score matching was performed using the nearest-neighbor method with a 0.2 caliper width and a 1:1 ratio. The following variables were used: age, sex, American Society of Anesthesiologists physical status (ASA PS), comorbidities, hypertension history, cerebrovascular disease history, preoperative respiratory infection, preoperative anemia, preoperative pe-

ripheral capillary oxygen saturation (SpO_2), smoking history, estimated blood loss, emergency operation, use of neuromuscular monitoring, time to extubation from the last neuromuscular blocking agent injection, use of positive end-expiratory pressure, and duration of anesthesia.

An absolute standardized mean difference (SMD) < 0.1 indicated that both groups were well-balanced.[15] Student t-test or Mann–Whitney U test was used for continuous variables after assessing the data distribution using the Kolmogorov– Smirnov test. The χ^2 test for trends (linear-by-linear association) or Fisher exact test was used to analyze categorical variables. In these analyses, a two-sided $p < 0.05$ was considered significant.

To identify variables associated with PPCs, univariate and multivariate logistic regression analyses were conducted using unmatched and matched data, respectively. The patients were divided into groups based on the occurrence of PPCs. Multivariate logistic regression analysis using backward selection included the variables with $p < 0.2$ between the two groups (PPCs and no PPCs) in the univariate analysis to identify the independent risk factors of PPCs. The analysis was performed using unmatched and matched data. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp, Armonk, NY, USA) and R 3.4.4 (www.r-project.org).

RESULTS

Among 637 patients aged > 18 years who underwent femoral fracture repair surgery under general anesthesia, 33 were excluded because of the use of atracurium, requirement for intubation after surgery, or incomplete data. Thus, the analysis included 604 patients (108 in the anticholinesterase group and 496 in the sugammadex group). After propensity score matching, 108 patients in each group were matched (Fig. 1) and all covariates were balanced (Fig. 2). Perioperative data before and after propensity score matching are shown in Table 1. The absolute SMD values of all variables were < 0.1 after propensity score matching.

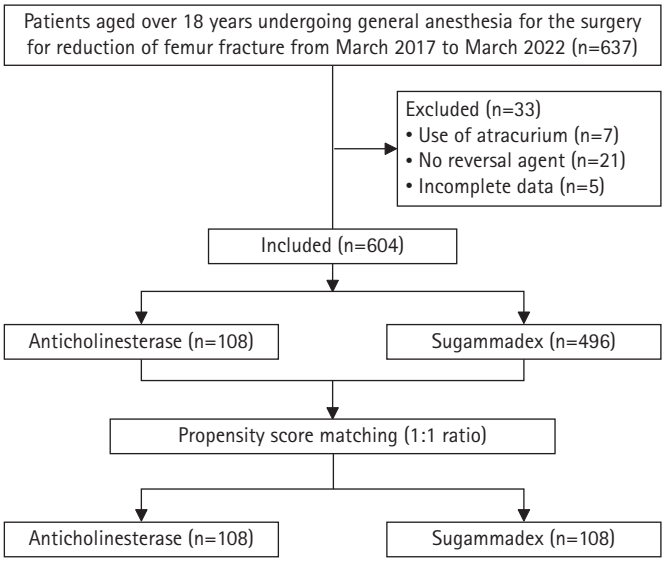

Fig. 1. Flow chart of the study.

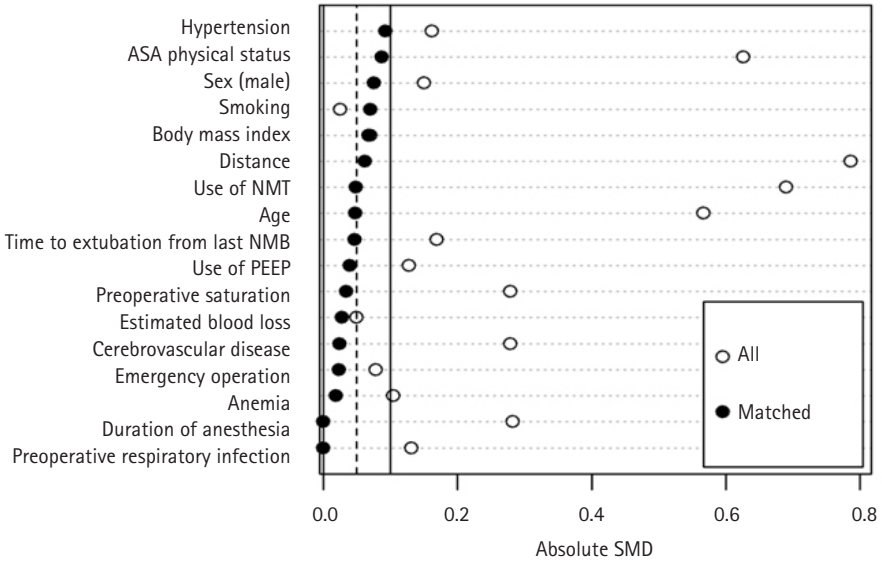

Fig. 2. Love plot of absolute standardized mean difference (SMD) before and after propensity score matching. ASA, American Society of Anesthesiologists; NMT, neuromuscular monitoring; NMB, neuromuscular blockade; PEEP, positive end-expiratory pressure.

The postoperative outcomes are presented in Table 2. The overall incidence rates of PPCs before and after matching were 10.6% and 7.0%, respectively. The incidence rates of PPCs in the matched data were 8.3% and 5.6% in the anticholinesterase and sugammadex groups, respectively, with no significant difference between the groups. The median (interquartile range) length of hospital stay was 21 (16–27) days and 19 (14–27) days in the anticholinesterase and sugammadex groups, respectively. Neither group experienced major adverse cardiac events in matched data. One patient died in the sugammadex group.

The perioperative data and results of the regression analysis according to the occurrence of PPCs before and after propensity score matching are presented in Table 3 (univariate analysis) and Table 4 (odds ratio [OR] of univariate and multivariate analyses). In the unmatched data, the variables with $p < 0.2$ were age, ASA PS, history of hypertension, preoperative saturation, smoking, and emergency operation. In the matched data, the variables with $p < 0.2$ were age, ASA PS, preoperative saturation, estimated blood loss, and time to extubation from the last neuromuscular blocker.

In the unmatched data, a higher ASA PS grade was an independent risk factor for PPCs in femur fractures (adjusted OR = 2.734; 95% confidence interval [CI], 1.61–4.631; $p < 0.001$), and emergency surgery was a preventive factor (adjusted OR = 0.229; 95% CI, 0.080–0.657; $p < 0.006$). In the matched data, age (adjusted OR = 1.050; 95% CI, 1.000–1.101; $p = 0.048$) and preoperative saturation (adjusted OR = 2.352; 95% CI, 1.020–5.424; $p = 0.045$) were independent risk factors for PPCs (Table 4).

DISCUSSION

Femur fractures, whose risk factors are old age and osteoporosis, can be corrected surgically. The postoperative complications include acute respiratory distress syndrome, fat embolism, and pneumonia caused by prolonged bed rest.[16,17] These complications are reduced through early mobilization, thereby reducing related morbidity and mortality by decreasing the ICU and hospital lengths of stay.[18,19] Various surgeries have shown differences in the incidence of PPCs according to the type of neuromuscular blockade reversal

Table 3. Perioperative data before and after propensity score matching according to the occurrence of postoperative pulmonary complications

	Before propensity score matching			After propensity score matching		
	No PPC (n = 540)	PPC (n = 64)	p-value	No PPC (n = 205)	PPC (n = 15)	p-value
Sex, male	174 (32.2)	19 (29.7)	0.788	81 (40.3)	5 (33.3)	0.796
Age (y)	78.0 (66.5–83.0)	81.0 (76.0–86.0)	0.002	69.0 (56.0–78.0)	82.0 (73.0–87.0)	0.002
ASA physical status			< 0.001			0.109
1	6 (1.1)	0 (0)		6 (3.0)	0 (0)	
2	256 (47.4)	13 (20.3)		133 (66.2)	6 (40.0)	
3	267 (49.4)	47 (73.4)		60 (29.9)	9 (60.0)	
4	11 (2.0)	4 (6.2)		2 (1.0)	0 (0)	
Body mass index (kg/m^2)	22.1 (19.6–24.5)	21.2 (20.0–23.6)	0.373	22.2 (19.7–24.4)	21.4 (20.6–23.7)	0.761
Hypertension	331 (61.3)	50 (78.1)	0.012	106 (52.7)	11 (73.3)	0.202
Cerebrovascular disease	138 (25.6)	21 (32.8)	0.273	36 (17.9)	3 (20.0)	> 0.999
Preoperative respiratory infection	4 (0.7)	3 (4.7)	0.030	0 (0.0)	0 (0)	> 0.999
Preoperative anemia	217 (40.2)	26 (40.6)	> 0.999	73 (36.3)	4 (26.7)	0.636
Preoperative saturation			0.013			0.005
≥ 96%	346 (64.1)	35 (54.7)		149 (74.1)	8 (53.3)	
91%–95%	167 (30.9)	20 (31.2)		46 (22.9)	4 (26.7)	
≤ 90%	27 (5.0)	9 (14.1)		6 (3.0)	3 (20.0)	
Smoking			0.029			0.439
Nonsmoking	478 (88.5)	53 (82.8)		181 (90.0)	15 (100)	
Ex-smoker	25 (4.6)	8 (12.5)		6 (3.0)	0 (0)	
Current smoker	37 (6.9)	3 (4.7)		14 (7.0)	0 (0)	
Estimated blood loss	100.0 (50.0–100.0)	100.0 (50.0–135.0)	0.984	100.0 (50.0–110.0)	50.0 (40.0–100.0)	0.083
Emergency operation	123 (22.8)	4 (6.2)	0.004	40 (19.9)	1 (6.7)	0.358
Use of NMT	81 (15.0)	6 (9.4)	0.306	6 (3.0)	1 (6.7)	0.983
Time to extubation from last NMB	72.5 (50.0–94.0)	68.5 (51.5–90.5)	0.513	77.0 (56.0–100.0)	60.0 (46.0–75.0)	0.050
Use of PEEP	390 (72.2)	48 (75.0)	0.747	138 (68.7)	10 (66.7)	> 0.999
Duration of anesthesia	125.0 (95.0–160.0)	115.0 (100.0–152.5)	0.775	140.0 (105.0–185.0)	115.0 (95.0–155.0)	0.102

Values are presented as number (%) or median (interquartile range).
ASA, American Society of Anesthesiologists; NMT, neuromuscular monitoring; NMB, neuromuscular blockade; PEEP, positive end-expiratory pressure.

Table 4. Logistic regression of postoperative pulmonary complications in femur fracture surgery

	Before propensity score matching				After propensity score matching			
	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Sex, male	0.89 (0.50–1.56)	0.681	-		0.74 (0.24–2.25)	0.596	-	
Age (y)	1.03 (1.01–1.03)	0.007	-		1.06 (1.015–1.117)	0.011	1.050 (1.000–1.101)	0.048
ASA physical status	3.07 (1.85–5.08)	< 0.001	2.734 (1.610–4.631)	< 0.001	2.76 (1.08–7.09)	0.035	-	
Body mass index (kg/m^2)	0.97 (0.90–1.05)	0.447	-		0.98 (0.84–1.14)	0.756	-	
Hypertension	2.26 (1.22–4.18)	0.010	-		2.46 (0.76–8.00)	0.133	-	
Cerebrovascular disease	1.42 (0.82–2.48)	0.214	-		1.15 (0.31–4.27)	0.839	-	
Preoperative respiratory infection	6.59 (1.44–30.14)	0.015	5.031 (0.941–26.892)	0.059	NA	NA	-	
Preoperative anemia	1.02 (0.60–1.73)	0.946	-		0.64 (0.20–2.07)	0.455	-	
Preoperative saturation	1.58 (1.07–2.34)	0.022	1.457 (0.975–2.178)	0.067	2.603 (1.210–5.602)	0.010	2.352 (1.020–5.424)	0.045
Smoking	1.12 (0.71–1.77)	0.616	-		0 (0–infinity)	0.993	-	
Estimated blood loss	1.00 (1.00–1.00)	0.450	-		0.99 (0.99–1.00)	0.170	-	
Emergency operation	0.23 (0.08–0.63)	0.005	0.229 (0.080–0.657)	0.006	0.29 (0.04–2.25)	0.235	-	
Use of NMT	0.59 (0.24–1.40)	0.231	-		2.32 (0.26–20.65)	0.450	-	
Time to extubation from last NMB	1.00 (0.99–1.00)	0.381	-		0.98 (0.97–1.00)	0.080	0.981 (0.961–1.002)	0.077
Use of PEEP	1.15 (0.64–2.09)	0.638	-		0.91 (0.30–2.78)	0.873	-	
Duration of anesthesia	1.00 (1.00–1.00)	0.950	-		1.00 (0.99–1.00)	0.297	-	

ASA, American Society of Anesthesiologists; NMT, neuromuscular monitoring; NMB, neuromuscular blockade; PEEP, positive end-expiratory pressure; OR, odds ratio; CI, confidence interval.

agent used.[10,11] However, we observed no difference in the incidence of PPCs between sugammadex and anticholinesterase in femur fracture surgery under general anesthesia.

General anesthesia is an important method used in femur fracture repair surgeries when regional anesthesia cannot be administered. Neuromuscular blockers are essential drugs used during general anesthesia. They facilitate surgery by preventing intraoperative movement. However, they may increase the risk of PPCs due to residual neuromuscular block, which may affect postoperative management. In femur fractures, a representative long bone fracture, immobility caused by the fracture increases the risk of pulmonary embolism due to deep vein thrombosis. It can cause fatal pulmonary complications such as fat embolism syndrome.[20] In particular, a high proportion of older patients experience femur fractures, and the incidence of residual neuromuscular block in older adults is approximately twice that in younger patients.[21]

The previously reported incidence rates of PPCs were 31% in several types of surgeries and 40% in patients with femur fractures.[2,10,11] However, the incidence in our study was 7%, which is slightly different from that in previous studies. This difference might be due to the retrospective nature of the study; additionally, underestimation was possible due to insufficient reporting and poor investigation compared to prospective studies. Additionally, unlike previous studies on PPCs in femur fracture surgeries that only included older adults, this study included all adults. The incidence might be lower in all adults than in older people.[22,23] In our data, the incidence was 12% in patients aged > 65 years.

The use of sugammadex reduces PPCs in older patients undergoing femur fracture repair surgery under general anesthesia.[24] In our study, the incidence of PPCs did not significantly differ between both types of reversal agents used in our study. However, the lower incidence with sugammadex is consistent with the results of other studies.[10,11] The reasons why the incidence of PPCs did not differ significantly between the reversal agents in our study are as follows. First, femoral fracture repair surgery is associated with a high risk of PPCs owing to the high proportion of older people and the risk of embolism. Second, the tendency to preferentially consider sugammadex for high-risk patients or those expected to have PPCs upon emergence from anesthesia could have affected the results. In addition, although our retrospective findings confirmed the relevance of PPCs related to the type of neuromuscular block reversal agent, a causal relationship could not be confirmed, and the results may have been affected by various uncontrolled influencing factors.

Some variables identified as risk factors in this study, including higher ASA PS, higher age, and lower preoperative saturation, were also representative risk factors for PPCs in previous studies.[25-27] In particular, the latter two are meaningful components of the Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) score, the only validated method for scoring PPCs risk factors.

Therefore, efforts to identify risk factors using various methods, such as prospective or large-scale studies, are necessary.[25]

In addition, unlike previous studies, we identified emergency surgery as a preventive factor.[25,26] In our hospital, we aim to perform femur fracture surgeries as emergency surgeries for patients with no specific contraindications. This is probably related to the fact that performing surgery as soon as possible reduces mortality; thus, a quick operation may have affected PPCs.[17] Moreover, it is easier to perform emergency surgery in patients without comorbidities than for those with multiple comorbidities owing to cooperation with other departments. However, as the time from injury to surgery was not recorded in this study, it was difficult to confirm this correlation.

The limitations of this study are as follows. First, as this was a retrospective study, it included many uncontrolled factors, which made it difficult to confirm a causal relationship. For PPCs in which preoperative lung status and medical history are important, the results of this study may have been influenced by several factors. However, as it is difficult to conduct a well-controlled prospective study because most patients with femoral fractures are in poor condition or are older individuals, we considered it sufficient to confirm its relevance. Second, as this was a single-center study, group bias was possible. A multicenter or big data study is required to confirm the overall effects of PPCs in patients with femoral fractures undergoing general anesthesia. Finally, the surgical site is an important risk factor for PPC. We included all types of femoral fracture repair surgeries performed in our hospital and did not analyze them by type. However, based on previous studies evaluating the risk factors of PPC, a more detailed classification of surgical types, such as closed reduction, open reduction, bipolar hemiarthroplasty, and total hip replacement, would not have significantly affected our results.[25,28]

In conclusion, we observed no significant difference in PPCs according to the type of neuromuscular block reversal agent used in patients undergoing femoral fracture repair surgery under general anesthesia. However, the relationship between PPCs and the neuromuscular blockade reversal agents remains unclear. It is important to thoroughly determine the patient's condition before surgery and to properly evaluate the patient's risk according to the risk factors identified in this study.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, TYS; Data curation, SAC, JHK, CKC; Investigation, SAC, TYS, CKC; Methodology, SAC, TYS; Supervision, TYS; Writing-original draft, SAC, SSL; Writing-review & editing, SAC, TYS.

REFERENCES

1. Bohl DD, Sershon RA, Saltzman BM, Darrith B, Della Valle CJ. Incidence, risk factors, and clinical implications of pneumonia after surgery for geriatric hip fracture. J Arthroplasty 2018;33:1552-6.
2. Clayer M, Bruckner J. Occult hypoxia after femoral neck fracture and elective hip surgery. Clin Orthop Relat Res 2000;(370):265-71.
3. Brox WT, Chan PH, Cafri G, Inacio MC. Similar mortality with general or regional anesthesia in elderly hip fracture patients. Acta Orthop 2016;87:152-7.
4. Ogurlu M, Sen S, Polatli M, Sirthan E, Gursoy F, Cildag O. The effect of spinal anesthesia on pulmonary function tests in old patients. Tuberk Toraks 2007;55:64-70.
5. Allen DJ, Chae-Kim SH, Trousdale DM. Risks and complications of neuraxial anesthesia and the use of anticoagulation in the surgical patient. Proc (Bayl Univ Med Cent) 2002;15:369-73.
6. Gimeno AM, Errando CL. Neuraxial regional anaesthesia in patients with active infection and sepsis: a clinical narrative review. Turk J Anaesthesiol Reanim 2018;46:8-14.
7. Berg H, Roed J, Viby-Mogensen J, Mortensen CR, Engbaek J, Skovgaard LT, et al. Residual neuromuscular block is a risk factor for postoperative pulmonary complications: a prospective, randomised, and blinded study of postoperative pulmonary complications after atracurium, vecuronium and pancuronium. Acta Anaesthesiol Scand 1997;41:1095-103.
8. McLean DJ, Diaz-Gil D, Farhan HN, Ladha KS, Kurth T, Eikermann M. Dose-dependent association between intermediate-acting neuromuscular-blocking agents and postoperative respiratory complications. Anesthesiology 2015;122:1201-13.
9. Schaller SJ, Lewald H. Clinical pharmacology and efficacy of sugammadex in the reversal of neuromuscular blockade. Expert Opin Drug Metab Toxicol 2016;12:1097-108.
10. Cheng KI, Tse J, Li TY. The strategy to use sugammadex to reduce postoperative pulmonary complications after Da Vinci surgery: a retrospective study. J Pers Med 2022;12:52.
11. Yu Y, Wang H, Bao Q, Zhang T, Chen B, Ding J. Sugammadex

versus neostigmine for neuromuscular block reversal and postoperative pulmonary complications in patients undergoing resection of lung cancer. J Cardiothorac Vasc Anesth 2022;36:3626-33.
12. Noh JH, Jung HW, Ga H, Lim JY. Ethical guidelines for publishing in the Annals of Geriatric Medicine and Research. Ann Geriatr Med Res 2022;26:1-3.
13. Abbott TE, Fowler AJ, Pelosi P, Gama de Abreu M, Moller AM, Canet J, et al. A systematic review and consensus definitions for standardised end-points in perioperative medicine: pulmonary complications. Br J Anaesth 2018;120:1066-79.
14. Heianza Y, Ma W, Manson JE, Rexrode KM, Qi L. Gut microbiota metabolites and risk of major adverse cardiovascular disease events and death: a systematic review and meta-analysis of prospective studies. J Am Heart Assoc 2017;6:e004947.
15. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 2009;28:3083-107.
16. Chang SM, Hou ZY, Hu SJ, Du SC. Intertrochanteric femur fracture treatment in Asia: what we know and what the world can learn. Orthop Clin North Am 2020;51:189-205.
17. Beaupre LA, Khong H, Smith C, Kang S, Evens L, Jaiswal PK, et al. The impact of time to surgery after hip fracture on mortality at 30- and 90-days: does a single benchmark apply to all? Injury 2019;50:950-5.
18. Behrman SW, Fabian TC, Kudsk KA, Taylor JC. Improved outcome with femur fractures: early vs. delayed fixation. J Trauma 1990;30:792-8.
19. Siu AL, Penrod JD, Boockvar KS, Koval K, Strauss E, Morrison RS. Early ambulation after hip fracture: effects on function and mortality. Arch Intern Med 2006;166:766-71.
20. Anwar IA, Battistella FD, Neiman R, Olson SA, Chapman MW, Moehring HD. Femur fractures and lung complications: a prospective randomized study of reaming. Clin Orthop Relat Res 2004;(422):71-6.
21. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear TD, Vender JS, et al. Residual neuromuscular block in the elderly: incidence and clinical implications. Anesthesiology 2015;123:1322-36.
22. Lv C, Chen S, Shi T, Jia M. Risk factors associated with postoperative pulmonary infection in elderly patients with hip fracture: a longitudinal study. Clin Nurs Res 2022;31:1454-61.
23. Chen J, Tian Z, Zhang H, Shi L, Bao W, Huang T, et al. Risks of postoperative respiratory failure in elderly patients after hip surgery: a retrospective study. J Orthop Surg Res 2022;17:140.
24. Oh CS, Rhee KY, Yoon TG, Woo NS, Hong SW, Kim SH. Postoperative delirium in elderly patients undergoing hip fracture surgery in the sugammadex era: a retrospective study. Biomed Res Int 2016;2016:1054597.
25. Nithiuthai J, Siriussawakul A, Junkai R, Horugsa N, Jarungjitaree S, Triyasunant N. Do ARISCAT scores help to predict the incidence of postoperative pulmonary complications in elderly patients after upper abdominal surgery? An observational study at a single university hospital. Perioper Med (Lond) 2021;10:43.
26. Miskovic A, Lumb AB. Postoperative pulmonary complications. Br J Anaesth 2017;118:317-34.
27. Choi Y, Kim N, Kim KW, Jo HH, Park J, Yoon H, et al. Gastric cancer in older patients: a retrospective study and literature review. Ann Geriatr Med Res 2022;26:33-41.
28. Davies OJ, Husain T, Stephens RC. Postoperative pulmonary complications following non-cardiothoracic surgery. BJA Educ 2017;17:295-300.

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Factors Associated with Improvement in Activities of Daily Living during Hospitalization: A Retrospective Study of Older Patients with Hip Fractures

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Background: In this study, we aimed to examine the changes in delirium during hospitalization of patients and its association with behavioral and psychological symptoms of dementia (BPSD), as well as improvements in activities of daily living (ADL). **Methods:** A longitudinal, retrospective cohort study was conducted involving 83 older adults (≥65 years) with hip fractures. We collected Mini-Mental State Examination (MMSE) and Functional Independence Measure-motor domain (m-FIM) assessment results from the medical charts at two time points: baseline (first week of hospitalization) and pre-discharge (final week before discharge). Additionally, we collected data on delirium and BPSD at three points: baseline, week 2 post-admission, and pre-discharge. We performed univariate logistic regression analysis using changes in m-FIM scores as the dependent variable and MMSE and m-FIM scores at baseline and pre-discharge, along with delirium and BPSD subtypes at baseline, week 2 post-admission, and pre-discharge, as the explanatory variables. Finally, we performed a multivariate logistic regression analysis incorporating the significant variables from the univariate analysis to identify factors associated with ADL improvement during hospitalization. **Results:** We observed significant correlations between ADL improvement during hospitalization and baseline m-FIM and MMSE scores, hypoactive delirium state, and BPSD subtype pre-discharge. Notably, all participants with hypoactive symptoms before discharge exhibited some subtype of delirium and BPSD at baseline. **Conclusion:** Besides ADL ability and cognitive function at admission, the presence of hypoactive delirium and BPSD subtype before discharge may hinder ADL improvement during hospitalization.

Key Words: Activities of daily living, Delirium, Dementia, Behavioral symptoms, Apathy, Hip fractures

INTRODUCTION

The incidence of hip fractures among older adults is increasing in many countries,[1] including Japan.[2] Falls are a common cause of hip fracture[3] and are associated with dementia and a decline in cognitive function.[4] A recent longitudinal study reported that even at 12 months post-hip fracture, activities of daily living (ADL) scores failed to recover to pre-fracture levels, with almost 60% of patients experiencing at least one ADL functional limitation.[5] These findings suggest the importance of identifying factors that influence the improvement in ADL. In the rehabilitation of older adult patients recovering hip fractures, research has demonstrated the importance of addressing delirium and behavioral and psychological symptoms of dementia (BPSD) arising from cognitive impairment during hospitalization.[6,7]

Delirium and BPSD during hospitalization hinder improve-

ments in ADL.[8-10] Marcantonio et al.[9] reported that patients with delirium at admission may experience deterioration of their mental state, and Gialanella et al.[10] reported that BPSD at admission hinders engagement in rehabilitation, potentially hindering ADL improvement during hospitalization among older adults with hip fractures. However, no longitudinal studies have investigated the subtypes of delirium and BPSD that hinder ADL improvement at specific time points.

Delirium and BPSD can be divided into several subtypes based on symptoms, such as hallucinations and delusions, disturbing speech, excitatory behavior, and an altered sleep-wake cycle[11]; it can generally be categorized into hyperactive, hypoactive, and mixed subtypes.[12] Moreover, these subtypes can change during hospitalization, suggesting the need to study these subtypes over time. However, most studies investigating the factors associated with ADL improvement among patients with hip fracture during hospitalization[13-15] have categorized delirium and BPSD as simply "present" or "not present" and few studies have investigated the subtypes. Furthermore, existing studies have only focused on assessing the status upon admission, but no studies have assessed chronological changes in delirium and BPSD.[10,16,17]

Therefore, to clarify the association of delirium and BPSD with ADL improvement, we investigated the changes in delirium and BPSD subtypes throughout the hospitalization period among older adult patients with hip fractures. By elucidating the association between ADL improvement and the timing and onset of subtypes of delirium and BPSD in patients with hip fractures, our findings study could offer valuable insights and important directions and implications for the assessment of delirium and BPSD during hospitalization at general hospitals, guiding appropriate care at each stage of hospitalization.

MATERIALS AND METHODS

Design

We conducted a retrospective cohort study using longitudinal data in accordance with the STROBE guidelines.[18] This study was approved by the Hiroshima University's Ethics Review Committee for Life Science and Medical Research with Human Participants (No. Epidemiology 3972) and Kaneda Hospital, Okayama, Japan.

Also, this study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[19]

Participants

The inclusion criteria for participating in this study were patients who were aged ≥65 years underwent hip fracture surgery and were prescribed rehabilitation at a Japanese general hospital between September 2016 and October 2022. We excluded patients who (1) did not undergo cognitive function assessment, (2) received conservative treatment, (3) were transferred to another hospital or transitioned to treatment for comorbidities, or (4) died.

Among the 261 patients, 93 underwent cognitive function assessments. The remaining 168 patients either did not have adequate cognitive function to undergo assessment or did not consent to participate in the study. Of the 93 remaining patients, six received conservative treatments due to contraindications to surgery, three were transferred to another hospital or transitioned to treatment because of complications, and one patient died. Consequently, our final analysis included 83 patients (Fig. 1).

Following hip fracture surgery, all patients were prescribed physical therapy as a part of rehabilitation plan. Additionally, we prescribed occupational and speech therapies based on each patient's comorbidities, physical function, and cognitive function, with the goal of maintaining or improving physical and cognitive capabilities.

Measures

We assessed the basic characteristics, cognitive function, delirium, BPSD, and ADL of all 83 patients using data from their medical charts. To assess cognitive function, we utilized the results of their Mini-Mental State Examination (MMSE), and for evaluating ADL, we utilized the motor domain scores of the Functional Independence Measures (m-FIM), which served as our outcome variable.

We defined the first week of hospitalization (beginning at admission) as the baseline, the second week of hospitalization (from the end of week 1 to the end of week 2) as week 2 post-admission,

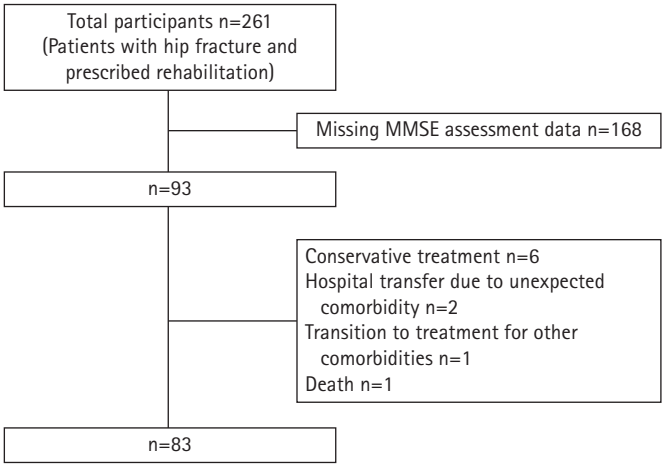

Fig. 1. Study enrollment summary. MMSE, Mini-Mental State Examination.

and the week before discharge (ending at discharge) as pre-discharge. Data on the types of medications, MMSE scores, and m-FIM scores were collected at two points: at baseline and pre-discharge. Delirium and BPSD results were collected at three time points: baseline, week 2 post-admission, and pre-discharge. As delirium is classified into cases based on whether symptoms resolved within 1 week or persisted for a longer period, cases in which delirium persists for at least 1 week are considered to be more severe.[20] Therefore, we assessed delirium and BPSD results at week 2 post-admission in addition to baseline and pre-discharge.

Patient Characteristics

We collected the following patient characteristics: age, sex, length of stay, type of surgery (arthroplasty, internal fixation), comorbidities (orthopedic disease, heart disease, lung disease, mental illness, neurodegenerative disease, and cancer), dementia diagnosis and type (Alzheimer disease, Lewy body dementia), pre-fracture walking ability (independent: yes/no), and types of medications (anti-psychotic drugs, anti-dementia drugs, and anti-anxiety drugs).

Mini-Mental State Examination

We collected data from MMSEs for the assessment of cognitive function.[21] The MMSE is a simple assessment tool with established reliability and validity. The maximum score is 30 points, with scores ≤ 23 points indicating dementia[22] and lower scores indicating more severe cognitive impairment. These assessments were performed by occupational or speech therapists.

Delirium and Behavioral and Psychological Symptoms of Dementia

Delirium and BPSD are typically observed in older adults with dementia. Although they are classified differently,[23] their clinical symptoms are similar. Thus, it is difficult to differentiate between these conditions after disease onset.[11] Therefore, we considered these two conditions as one. Delirium is classified into three subtypes, including hyperactive, hypoactive, and mixed,[24] whereas BPSD is classified into 12 subtypes:delusions, hallucinations, agitation/aggression, depression/ dysphoria, anxiety, elation/euphoria, apathy, disinhibition, irritability/lability, aberrant motor behavior, nighttime behavior disturbances, and appetite and eating abnormalities.[25] A previous study classifying BPSD using cluster analysis reported that it can be clinically classified as hyperactive or hypoactive.[26] We identified data on patients' speech and behavior corresponding to delirium and BPSD from their medical charts using these classifications.[24-26] We then categorized these into the following subtypes: hyperactive, hypoactive, and mixed.

For the hyperactive subtype, we considered delirium symptoms including abnormal verbal output, hyperalertness, irritability, euphoria, and combativeness, along with BPSD symptoms including delusions, hallucinations, agitation/ aggression, elation/euphoria, disinhibition, irritability/lability, aberrant motor behavior, nighttime behavior disturbances, and appetite and eating abnormalities. Patients with any of these symptoms were classified as hyperactive. For the hypoactive subtype, we considered delirium symptoms including apathy, decreased alertness, withdrawal, and hypersomnolence, along with BPSD symptoms including apathy, depression/dysphoria, and anxiety. Patients exhibiting any of these symptoms were classified as hypoactive. The mixed subtype was defined as a combination of symptoms from hyperactive and hypoactive subtypes. Specifically, this subtype included cases in which the patient exhibited both hyperactive and hypoactive symptoms, such as agitation followed by apathy, during a single assessment period.

Functional Independence Measure

The FIM is used to evaluate the extent of an individual's ADL care needs. In this study, we used the assessment results for the motor domain (m-FIM).[27] The m-FIM comprises self-care, sphincter control, and transfers. The m-FIM is known for its high reliability, sensitivity to changes in the functional status of patients undergoing rehabilitation, and ease of implementation.[28-30] Each item is assessed on a 7-point scale, ranging from requiring total assistance to being completely independent. The total scores range from 13 to 91 points, with a lower score indicating lower ADL independence. These assessments were performed by physiotherapists.

Data Analysis

We calculated the mean, standard deviation, and percentage based on the descriptive statistics of the patient characteristics and assessment results. Statistical analyses were performed using R software (version 4.0.5; R Foundation for Statistical Computing, Vienna, Austria). All tests were performed at a significance level of 0.05.

First, we calculated the median change in the m-FIM score. Subsequently, we categorized the patients into high and low groups based on the changes in their ADL scores, with those at or above the median categorized into the high group and those below the median categorized into the low group.

Thereafter, using a univariate logistic regression model, we analyzed the factors associated with changes in m-FIM scores. The high or low group change in m-FIM scores was set as the outcome variable, whereas the explanatory variables encompassed basic characteristics, types of medications (baseline and pre-discharge), MMSE scores (baseline and pre-discharge), m-FIM scores (baseline and pre-discharge), and delirium and BPSD subtypes (base-

line, week 2 post-admission, and pre-discharge).

Finally, we performed multivariate logistic regression analysis to organize and investigate the multiple factors associated with changes in m-FIM. The high or low group change in m-FIM scores was set as the outcome variable, whereas the explanatory variables comprised those with significant associations in the univariate logistic regression analysis. Notably, we observed multicollinearity for m-FIM scores, MMSE scores, and types of medications; therefore, only the baseline values were used as explanatory variables for these items. We confirmed the goodness of fit of the explanatory variables to the outcome variable using the Hosmer–Lemeshow test.

RESULTS

Patient Characteristics

Table 1 presents the patients' basic characteristics. In this study, 72 patients (86.7%) were women, 63 (75.9%) had comorbidities, 69 (83.1%) had not been diagnosed with dementia, and 38 (45.8%) could walk independently before admission. The mean age was 89.1 ± 7.2 years, the mean length of stay was 51.9 ± 19.8 days, and the mean MMSE score at baseline was 15.5 ± 8.4 points. Among the patients, 73 (88.0%) exhibited delirium or BPSD at least one of the three data collection points.

Factors Associated with Changes in ADL (Univariate Analysis)

The median change in the m-FIM score was 27. Thus, the high (n = 41) and low (n = 42) groups comprised patients with changes in their m-FIM scores of ≥ 27 points and ≤ 26 points, respectively. The univariate analysis, performed to identify factors associated with the change in m-FIM scores, revealed significant associations with age (odds ratio [OR] = 0.94; 95% confidence interval [CI], 0.87–9.97), independent walking before admission (OR = 3.17; 95% CI, 1.31–7.99), anti-psychotic type medications (OR = 0.34; 95% CI, 0.19–0.59), m-FIM scores (OR = 1.07; 95% CI, 1.01–1.15), MMSE scores (OR = 1.27; 95% CI, 1.16– 1.42), and pre-discharge hypoactive symptomology (OR = 0.17; 95% CI, 0.03–0.57) (Table 2).

Factors Associated with Changes in ADL (Multivariate Analysis)

The results of the multivariate analysis revealed significant associations among low baseline m-FIM score (OR = 0.86; 95% CI, 0.77–0.95), high baseline MMSE score (OR = 1.41; 95% CI, 1.22–1.71), and pre-discharge hypoactive symptomology (OR = 0.07; 95% CI, 0.01–0.43) (Table 3). The result of the Hosmer–Lemeshow test was not significant ($X^2(8) = 0.64$).

Table 1. Demographic and characteristics data (n=83)

Characteristic	Value
Age (y)	89.1 ± 7.2
Sex	
Male	11 (13.2)
Female	72 (86.7)
Length of stay (day)	52.0 ± 19.8
Type of surgery	83 (100)
Arthroplasty	28 (33.7)
Internal fixation	55 (66.3)
Comorbidity	63 (75.9)
Orthopedic disease	14 (16.9)
Heart disease	19 (22.9)
Lung disease	8 (9.6)
Mental illness	15 (18.1)
Neurodegenerative disease	4 (4.8)
Cancer	3 (3.6)
Type of dementia	14 (16.9)
No dementia	69 (83.1)
Alzheimer's disease	13 (15.6)
Lewy body dementia	1 (1.2)
Pre-fracture walking ability	
Independent	38 (45.8)
Number of drugs for anti-psychotic	
Baseline	46 (55.4)
Pre-discharge	36 (43.3)
Number of drugs for anti-dementia	
Baseline	7 (8.4)
Pre-discharge	5 (6.0)
Number of drugs for anti-anxiety	
Baseline	18 (21.7)
Pre-discharge	18 (21.7)
FIM motor score (13–91)	
Baseline	20.5 ± 9.1
Pre-discharge	50.4 ± 27.0
MMSE total score (0–30)	
Baseline	15.5 ± 8.4
Pre-discharge	16.3 ± 8.3
Delirium and BPSD	60 (72.3)
Hyperactive	
Baseline[a]	42 (50.6)
Week 2[b]	33 (39.6)
Pre-discharge[c]	33 (39.6)
Hypoactive	28 (33.7)
Baseline[a]	7 (8.4)
Week 2[b]	12 (14.5)
Pre-discharge[c]	16 (19.3)
Mixed	33 (39.8)
Baseline[a]	19 (22.9)
Week 2[b]	14 (16.9)
Pre-discharge[c]	8 (9.6)

Values are presented as mean ± standard deviation or number (%).
FIM, Functional Independent Measure motor score; MMSE, Mini-Mental State Examination; BPSD, behavioral and psychological symptoms of dementia.
[a]First week of hospitalization, [b]second week of hospitalization, [c]1-week period before discharge.

Table 2. Univariate logistic regression for each variable

Variable	m-FIM gain		p-value
	Low group	High group	
Age (y)	90.8 ± 6.5	87.6 ± 7.7	0.047*
Sex			
Male	7 (8.4)	4 (4.8)	0.320
Female	34 (40.9)	38 (45.8)	-
Length of stay (day)	49.0 ± 22.8	54.9 ± 16.2	0.180
Type of surgery			
Arthroplasty	13 (15.7)	15 (18.1)	-
Internal fixation	28 (33.7)	27 (32.5)	0.700
Comorbidity			
Orthopedic disease	6 (7.2)	8 (9.6)	0.590
Heart disease	7 (8.4)	12 (14.5)	0.220
Lung disease	2 (2.4)	6 (7.2)	0.170
Mental illness	10 (12.0)	5 (6.0)	0.150
Neurodegenerative disease	2 (2.4)	2 (2.4)	0.980
Cancer	-	3 (3.6)	0.990
Types of dementia			
Alzheimer's disease	9 (10.8)	4 (4.8)	0.130
Lewy body dementia	1 (1.2)	-	0.990
Pre-fracture walking ability			
Independent	13 (15.7)	25 (30.1)	0.010*
Number of drugs for anti-psychotic			
Baseline	31 (37.3)	15 (18.1)	< 0.001*
Pre-discharge	28 (33.7)	8 (9.6)	< 0.001*
Number of drugs for anti-dementia			
Baseline	5 (6.0)	2 (2.4)	0.210
Pre-discharge	3 (3.6)	2 (2.4)	0.460
Number of drugs for anti-anxiety			
Baseline	7 (8.4)	11 (13.3)	0.200
Pre-discharge	7 (8.4)	11 (13.3)	0.200
FIM motor score (13–91)			
Baseline	18.3 ± 9.9	22.5 ± 7.8	0.046*
Pre-discharge	27.0 ± 14.3	73.2 ± 13.0	< 0.001*
MMSE total score (0–30)			
Baseline	10.0 ± 7.2	20.8 ± 5.7	< 0.001*
Pre-discharge	11.3 ± 7.5	21.2 ± 5.7	< 0.001*
Delirium and BPSD			
Hyperactive			
Baseline[a]	25 (59.5)	17 (40.5)	0.060
Week 2[b]	20 (60.6)	13 (39.4)	0.100
Pre-discharge[c]	17 (51.5)	16 (48.5)	0.750
Hypoactive			
Baseline[a]	4 (57.1)	3 (42.9)	0.670
Week 2[b]	7 (58.3)	5 (41.7)	0.510
Pre-discharge[c]	13 (81.3)	3 (18.8)	0.009*
Mixed			
Baseline[a]	11 (57.9)	8 (42.1)	0.400
Week 2[b]	9 (64.3)	5 (35.7)	0.230
Pre-discharge[c]	7 (87.5)	1 (12.5)	0.051

Values are presented as mean±standard deviation or number (%).
m-FIM, Functional Independent Measure motor score; MMSE, Mini-Mental State Examination; BPSD, behavioral and psychological symptoms of dementia.
[a]First week of hospitalization, [b]second week of hospitalization, [c]1-week period before discharge.
*p<0.05

Table 3. Multivariate logistic regression

Variable	Estimate	SE	OR (95% CI)	p-value
Age	-0.04	0.06	0.96 (0.85–1.08)	0.490
FIM motor score	-0.15	0.05	0.86 (0.77–0.95)	0.003*
Drugs for anti-psychotic	-0.58	0.45	0.56 (0.22–1.36)	0.200
Walking ability	1.06	0.74	2.89 (0.68–13.27)	0.150
MMSE total score	0.34	0.09	1.41 (1.22–1.71)	< 0.001*
Hypoactive	-2.66	1.02	0.07 (0.01–0.43)	0.008*

FIM motor score, drugs for anti-psychotic, and MMSE score are mentioned at the baseline level. Walking ability was recorded as pre-fracture (independent: yes/no); hypoactive status was recorded pre-discharge.
FIM, Functional Independent Measure motor score; MMSE, Mini-Mental State Examination; SE, standard error; OR, odds ratio; CI, confidence interval.
*p<0.05.

Subtypes at Baseline and Week 2 Post-admission among Patients with Pre-discharge Hypoactive Symptomology

In this study, we classified 16 patients as having the hypoactive subtype of delirium and BPSD pre-discharge. We confirmed the subtypes that these participants exhibited at baseline and week 2 post-admission, as shown in Fig. 2. All 16 patients exhibited some form of delirium and BPSD at baseline. However, four patients (25%) did not show delirium or BPSD at week 2 post-admission. Furthermore, eight (50%) and six (37.5%) patients exhibited hyperactive symptomology at baseline and week 2 post-admission, respectively. Finally, two participants (12.5%) exhibited hypoactive symptomology at baseline and three (18.8%) exhibited hypoactive symptomology at week 2 post-admission.

DISCUSSION

Our investigation of the factors associated with ADL improvement during hospitalization among older adult patients with hip fractures revealed better improvement among patients with higher cognitive function at admission and non-hypoactive delirium and BPSD symptomology before discharge than those among patients without these symptomologies. We also observed that the lower a patient's ADL independence at admission, the greater the improvement in ADL.

Factors Associated with Changes in ADL

Our results indicated that ADL improved during hospitalization among patients with higher MMSE scores at admission. One explanation for this finding may be that patient cooperation with rehabilitation following hip fracture surgery is easier to achieve when cognitive function is better at admission. Thus, patients with better cognitive function at admission may have been open to future ADL improvement and proactive engagement in rehabilitation,

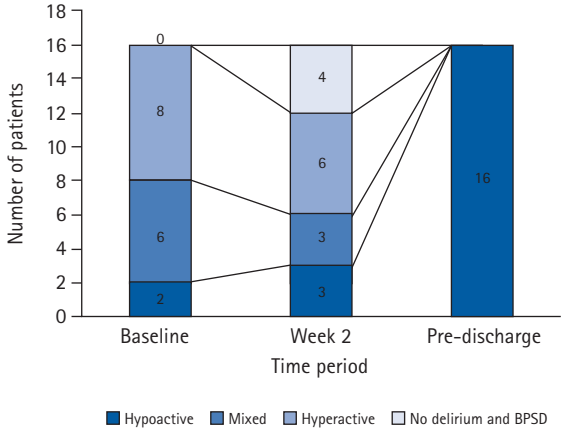

Fig. 2. The changes in the subtypes of the 16 pre-discharge hypoactive participants at baseline and week 2 post-admission. BPSD, behavioral and psychological symptoms of dementia.

even with the presence of postoperative pain and physical dysfunction. Regarding the association between rehabilitation and ADL improvement, Lenze et al.[31] reported that executive dysfunction and apathy caused by cognitive impairment may impede engagement in rehabilitation and act as barriers to ADL improvement. Similarly, Kang et al.[32] observed that higher MMSE scores are positively associated with improved walking ability. Although we did not investigate patients' engagement in rehabilitation, we conjecture that ADL improvement was better among patients with stronger cognitive function at admission as they were proactively engaged in rehabilitation.

Furthermore, our results demonstrated that ADL improvement was more difficult in participants who had hypoactive symptoms as discharge approached. In a study conducted in an acute-phase hospital with similar results, Lenze et al.[33] reported reduced ADL improvement in patients with apathy and hypoactive symptoms before discharge, suggesting that a hypoactive state before discharge may impede engagement in rehabilitation and negatively impact ADL improvement. However, Gialanella et al.[16] reported that hyperactive symptoms at admission may impede ADL improvement. Although, in our study, a hyperactive state at admission was not identified as a barrier to ADL improvement, further research on the association between the timing of the onset of hyperactive symptoms and ADL is required.

Patients in a hypoactive state are unlikely to regularly exhibit this behavior in everyday context. Thus, they are often misdiagnosed by hospital staff as being "well-behaved" with no symptomatic behaviors.[34] However, if hospital staffs do not diagnose a patient's hypoactivity, ADL improvement may be impeded by the patient's decreased motivation for rehabilitation and ADL, ultimately reducing opportunities for their participation.[35] Thus, hospital staffs must pay close attention to changes in patients' hypoactivity not only after admission and surgery but also on a daily basis to ensure that they do not overlook hypoactive symptoms during hospitalization. Moreover, providing rehabilitation and everyday care is particularly important to prevent the development of hypoactive symptoms before discharge.

Finally, our results demonstrated that patients with lower ADL independence at admission (i.e., lower FIM scores) exhibited better ADL improvement. Previous studies have reported similar results suggesting that the lower a patient's FIM score at admission, the greater is the improvement.[36] When the FIM score was high at the time of admission, any subsequent improvement in their ADL might have been constrained, due to limitation for further increase in the maximum FIM score. Since the FIM includes tasks with a relatively low difficulty level, the possibility of a ceiling effect cannot be ruled out. This may explain the lack of association between high ADL independence upon admission and ADL improvement in our study.

Subtype Fluctuations among Patients with Pre-discharge Hypoactivity

Considering that most patients in a hypoactive state with subtype symptoms of delirium and BPSD during the study period were in a hyperactive state at admission, only a few remained hypoactive throughout the hospitalization period. Hospitalization phase for these patients included the acute stage after surgery, in which patients experienced a combination of physical factors, such as limited movement; psychological factors including interaction with unfamiliar hospital staff; and environmental factors that differ from their ordinary lives, such as the presence of intravenous drips. This combination of factors may lead them to transition into a hyperactive state. Furthermore, studies have indicated that the use of pharmacotherapy to treat hyperactive patients upon admission may lead to a hypoactive state.[37-39] Similarly, based on the number of anti-psychotic drugs used at admission and week 2 after admission compared to pre-discharge, we conjecture that hypoactivity induced by pharmacotherapy cannot be ruled out. Considering these findings, hospital staffs may contribute to ADL improvement during hospitalization through careful multidisciplinary observation and communication of any changes in the patient's delirium and BPSD subtypes after the first 2 weeks of hospitalization and address these symptoms primarily through non-pharmacological methods.[37,40]

Limitations and Future Directions This study had several limitations. First, due to the retrospective nature of our delirium and BPSD assessments, we could not perform detailed quantitative evaluation of subtype categories. Second, we could not perform a

follow-up on pre-discharge hypoactive symptoms, as a factor impeding ADL improvement beyond the first 2 weeks after admission, preventing us from determining the timing and persistence of the hypoactive state until pre-discharge. Third, we could not consider the impact of physical functioning, such as muscle strength, on ADL improvement. Future prospective longitudinal studies using qualitative assessments of delirium and BPSD along with extended follow ups beyond the second week of hospitalization are necessary. Moreover, future studies are required to examine whether subtypes continue to change after discharge, and if so, how hospital care may influence such changes as well as their impact on ADL post-discharge.

Despite these limitations, the results of our investigation of the change in delirium and BPSD subtypes over time during hospitalization among older patients with hip fractures demonstrated that ADL improvement may be impeded in patients with hypoactive pre-discharge delirium and BPSD symptoms. Previous studies have demonstrated that delirium and BPSD at admission can hinder ADL improvement. However, only a few studies have investigated the chronological changes and subtypes of delirium and BPSD that can hinder ADL improvement during hospitalization. The significance of this study lies in elucidating the potential negative effects of pre-discharge hypoactivity on ADL improvement. These results have implications for patient care in clinical practice. They further underscore the importance of continuous monitoring of changes in delirium and BPSD subtypes throughout hospitalization and preventing any shift to hypoactivity to effectively improve ADL outcomes.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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None.

AUTHOR CONTRIBUTIONS

Conceptualization, KT, HH; Data curation, KT, KY; Formal analysis, KT; Investigation, KT; Methodology, KT, KY, YH, TW, HH; Project administration, KT, HH; Supervision, MW, HH; Writing-original draft, KT; Writing-review & editing, MW, HH.

REFERENCES

1. Dhanwal DK, Dennison EM, Harvey NC, Cooper C. Epidemiology of hip fracture: worldwide geographic variation. Indian J Orthop 2011;45:15-22.
2. Orimo H, Yaegashi Y, Hosoi T, Fukushima Y, Onoda T, Hashimoto T, et al. Hip fracture incidence in Japan: Estimates of new patients in 2012 and 25-year trends. Osteoporos Int 2016;27:1777-84.
3. Fernandez MA, Griffin XL, Costa ML. Management of hip fracture. Br Med Bull 2015;115:165-72.
4. Friedman SM, Menzies IB, Bukata SV, Mendelson DA, Kates SL. Dementia and hip fractures: development of a pathogenic framework for understanding and studying risk. Geriatr Orthop Surg Rehabil 2010;1:52-62.
5. Abeygunasekara T, Lekamwasam S, Lenora J, Alwis G. Quality of life and functional independence of hip fracture patients: data from a single center follow-up study in Sri Lanka. Ann Geriatr Med Res 2021;25:98-104.
6. Carrillo CB, Barr C, George S. Cognitive status and outcomes of older people in orthopedic rehabilitation? A retrospective-cohort study. Geriatrics (Basel) 2020;5:14.
7. Small GW. Treating dementia and agitation. JAMA 2014;311:677-8.
8. Heruti RJ, Lusky A, Barell V, Ohry A, Adunsky A. Cognitive status at admission: does it affect the rehabilitation outcome of elderly patients with hip fracture? Arch Phys Med Rehabil 1999;80:432-6.
9. Marcantonio ER, Flacker JM, Michaels M, Resnick NM. Delirium is independently associated with poor functional recovery after hip fracture. J Am Geriatr Soc 2000;48:618-24.
10. Gialanella B, Prometti P, Monguzzi V, Ferlucci C. Neuropsychiatric symptoms and rehabilitation outcomes in patients with hip fracture. Am J Phys Med Rehabil 2014;93:562-9.
11. Tanaka T. Factors predicting perioperative delirium and acute exacerbation of behavioral and psychological symptoms of dementia based on admission data in elderly patients with proximal femoral fracture: a retrospective study. Geriatr Gerontol Int 2016;16:821-8.
12. Liptzin B, Levkoff SE. An empirical study of delirium subtypes. Br J Psychiatry 1992;161:843-5.
13. Shibasaki K, Asahi T, Mizobuchi K, Akishita M, Ogawa S. Rehabilitation strategy for hip fracture, focused on behavioral psychological symptoms of dementia for older people with cognitive impairment: a nationwide Japan rehabilitation database. PLoS One 2018;13:e0200143.
14. Heyman N, Nili F, Shahory R, Seleznev I, Ben Natan M. Preva-

lence of delirium in geriatric rehabilitation in Israel and its influence on rehabilitation outcomes in patients with hip fractures. Int J Rehabil Res 2015;38:233-7.
15. Adunsky A, Levy R, Heim M, Mizrahi E, Arad M. The unfavorable nature of preoperative delirium in elderly hip fractured patients. Arch Gerontol Geriatr 2003;36:67-74.
16. Gialanella B, Ferlucci C, Monguzzi V, Prometti P. Determinants of functional outcome in hip fracture patients: the role of specific neuropsychiatric symptoms. Disabil Rehabil 2015;37:517-22.
17. Gialanella B, Ferlucci C, Monguzzi V, Prometti P. Determinants of outcome in hip fracture: role of daily living activities. Eur J Phys Rehabil Med 2015;51:253-60.
18. Vandenbroucke JP, von Elm E, Altman DG, Gotzsche PC, Mulrow CD, Pocock SJ, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. PLoS Med 2007;4:e297.
19. Noh JH, Jung HW, Ga H, Lim JY. Ethical guidelines for publishing in the Annals of Geriatric Medicine and Research. Ann Geriatr Med Res 2022;26:1-3.
20. Wada Y, Yamaguchi N. Delirium in the elderly: relationship of clinical symptoms to outcome. Dementia 1993;4:113-6.
21. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.
22. Fayers PM, Hjermstad MJ, Ranhoff AH, Kaasa S, Skogstad L, Klepstad P, et al. Which mini-mental state exam items can be used to screen for delirium and cognitive impairment? J Pain Symptom Manage 2005;30:41-50.
23. Hessler JB, Schaufele M, Hendlmeier I, Junge MN, Leonhardt S, Weber J, et al. Behavioural and psychological symptoms in general hospital patients with dementia, distress for nursing staff and complications in care: results of the General Hospital Study. Epidemiol Psychiatr Sci 2018;27:278-87.
24. Meagher DJ, Moran M, Raju B, Gibbons D, Donnelly S, Saunders J, et al. Motor symptoms in 100 patients with delirium versus control subjects: comparison of subtyping methods. Psychosomatics 2008;49:300-8.
25. Cummings JL. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. Neurology 1997;48:S10-6.
26. Miyagawa A, Kunii Y, Gotoh D, Hoshino H, Kakamu T, Hidaka T, et al. Effects of the Great East Japan Earthquake and the Fukushima Daiichi Nuclear Power Plant accident on behavioural and psychological symptoms of dementia among patients. Psychogeriatrics 2021;21:709-15.
27. Kidd D, Stewart G, Baldry J, Johnson J, Rossiter D, Petruckevitch A, et al. The Functional Independence Measure: a comparative validity and reliability study. Disabil Rehabil 1995;17:10-4.
28. Hetherington H, Earlam RJ, Kirk CJ. The disability status of injured patients measured by the functional independence measure (FIM) and their use of rehabilitation services. Injury 1995;26:97-101.
29. Ottenbacher KJ, Mann WC, Granger CV, Tomita M, Hurren D, Charvat B. Inter-rater agreement and stability of functional assessment in the community-based elderly. Arch Phys Med Rehabil 1994;75:1297-301.
30. Granger CV, Hamilton BB. The Uniform Data System for Medical Rehabilitation report of first admissions for 1992. Am J Phys Med Rehabil 1994;73:51-5.
31. Lenze EJ, Munin MC, Dew MA, Rogers JC, Seligman K, Mulsant BH, et al. Adverse effects of depression and cognitive impairment on rehabilitation participation and recovery from hip fracture. Int J Geriatr Psychiatry 2004;19:472-8.
32. Kang JH, Lee G, Kim KE, Lee YK, Lim JY. Determinants of functional outcomes using clinical pathways for rehabilitation after hip fracture surgery. Ann Geriatr Med Res 2018;22:26-32.
33. Lenze EJ, Munin MC, Dew MA, Marin RS, Butters MA, Skidmore ER, et al. Apathy after hip fracture: a potential target for intervention to improve functional outcomes. J Neuropsychiatry Clin Neurosci 2009;21:271-8.
34. Rigney TS. Delirium in the hospitalized elder and recommendations for practice. Geriatr Nurs 2006;27:151-7.
35. Resnick B, Zimmerman SI, Magaziner J, Adelman A. Use of the Apathy Evaluation Scale as a measure of motivation in elderly people. Rehabil Nurs 1998;23:141-7.
36. Ogawa T, Koike M. Independent factors that attenuate the effectiveness of fracture rehabilitation in improving activities of daily living in female patients aged 80 years and above. Aging Clin Exp Res 2022;34:793-800.
37. van Velthuijsen EL, Zwakhalen SM, Mulder WJ, Verhey FR, Kempen GI. Detection and management of hyperactive and hypoactive delirium in older patients during hospitalization: a retrospective cohort study evaluating daily practice. Int J Geriatr Psychiatry 2018;33:1521-9.
38. Leentjens AF, Molag ML, Van Munster BC, De Rooij SE, Luijendijk HJ, Vochteloo AJ, et al. Changing perspectives on delirium care: the new Dutch guideline on delirium. J Psychosom Res 2014;77:240-1.
39. Scholtens RM, van Munster BC, Adamis D, de Jonghe A, Meagher DJ, de Rooij SE. Variability of delirium motor subtype scale-defined delirium motor subtypes in elderly adults with hip fracture: a longitudinal study. J Am Geriatr Soc 2017;65:e45-50.
40. Smith TO, Drew BT, Meek TH, Clark AB. Knee orthoses for treating patellofemoral pain syndrome. Cochrane Database Syst Rev 2015;2015:CD010513.

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Predictive Ability of the 2-Minute Step Test for Functional Fitness in Older Individuals with Hypertension

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Background: The 2-minute step test (2MST) is a simple and inexpensive functional test that measures an individual's ability to perform continuous stepping up and down on a step platform for two minutes. This study evaluated the 2MST as a tool for assessing functional fitness in older individuals with hypertension and determined the correlation between the 2MST and physical fitness tests. **Methods:** A total of 91 older individuals with hypertension performed physical fitness tests, including the 2MST, 6-minute walk test (6MWT), five times sit-to-stand test (FTSST), grip strength and leg strength assessments, and timed up and go test (TUG) to collectively assess their physical fitness. **Results:** A cutoff score of ≤60 steps in the 2MST had 87.50% sensitivity and 70.59% specificity in predicting functional exercise performance in older individuals with hypertension. Additionally, the number of steps in the 2MST was positively correlated with the distance covered in the 6MWT, isometric grip strength, and isometric leg strength and negatively correlated with the duration of the FTSST and TUG. **Conclusions:** A cutoff score of ≤60 steps in the 2MST predicted functional exercise performance in older individuals with hypertension with 87.50% sensitivity and 70.59% specificity and was correlated with other physical fitness tests, suggesting that the 2MST is a useful tool for assessing functional exercise performance.

Key Words: Hypertension, Aging, Step test, Physical fitness testing

INTRODUCTION

The world's aging population is increasing, and the elderly population is projected to constitute approximately 30% of the global population by 2050.[1] Aging is a significant risk factor for chronic diseases and can trigger the onset of geriatric syndromes and illnesses owing to changes in physiological systems.[2-4] Hypertension is a prevalent condition in older adults, affecting > 70% of the population. This condition is associated with increased risks of cardiovascular disease, cognitive decline, and physical disability.[5] Moreover, sarcopenia is characterized by the age-related loss of muscle mass and strength; hypertension can exacerbate this process, leading to further deterioration in physical capabilities.[6,7]

Functional fitness, which is the ability to perform daily tasks safely and independently without exhaustion or discomfort, is a critical component of healthy aging. It enables individuals to maintain their independence and quality of life.[8] The increase in the number of functionally limited individuals with hypertension highlights the need for early detection and interventions to alleviate the burden of hypertension-aging-disability.[5] Therefore, the accurate identification of functional impairment can assist in tailoring interventions to improve fitness, set achievable goals, and educate individuals about the importance of physical fitness for daily tasks and overall health.

Aerobic capacity, a key aspect of physical fitness, is commonly assessed in healthy and diseased populations.[9] The 6-minute walk test (6MWT) is a common method used to evaluate the submaximal functional aerobic capacity in older adults[9-11] but its adminis-

tration requires a 30-m hallway and can be time-consuming for routine outpatient consultations. Simple and quick office-based field exercise tests, such as the 2-minute step test (2MST)[12,13] may be valuable options as first screening tools before a detailed assessment of functional status and subsequent treatment. The 2MST is highly correlated with the 6MWT[14-16] indicating its potential as a measure of functional aerobic capacity. Its correlation with the timed up and go test (TUG),[16] five times sit-to-stand test (FTSST), and leg strength[15] highlights the close relationship between cardiovascular endurance, muscle strength, and functional mobility.[17]

Evaluating functional fitness using the available tools can be difficult because of variations in body composition, physical capacity, and perceptions of physical functioning among different populations and research settings.[12,18] The assessment of functional capacity is particularly critical in estimating the functional consequences and disability among patients with hypertension. Owing to the limitations of studies evaluating the tests to assess the functional capacity evaluation test specifically in individuals with hypertension, the present study investigated the predictive ability of the 2MST to identify functional impairment in hypertensive older adults and its correlation with other functional measures, including the 6MWT, FTSST, TUG, grip strength, and leg strength.

MATERIALS AND METHODS

1. Participants

This cross-sectional study included on 91 older individuals with hypertension in Phayao Province, Thailand, who were undergoing routine antihypertensive medication therapy. We identified and recruited eligible participants during their routine appointments at a primary healthcare center, and informed consent was obtained from all individuals before their participation. The study included participants who met specific criteria, including a diagnosis of hypertension, age >60 years, body mass index (BMI) <30 kg/m^2, and absence of any physical limitations that would impact their ability to walk or perform stepping movements. Participants with respiratory diseases or clinical conditions such as cognitive impairment, uncontrolled hypertension, unstable angina, and infectious diseases were excluded from the study. This study was approved by the Human Research Ethics Committee of the University of Phayao (No. 1.2/056/65). The minimum estimated sample size required was 62 participants for a diagnostic study, with a 90% power, 0.05 p-value, and 80% sensitivity based on a previous study.[19]

This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[20]

2. Procedure

The experimental protocol was divided into two visits. On the first visit, we assessed the participants' general information using a self-reported questionnaire, and collected socio-demographic (age and sex), anthropometric (height and weight to compute BMI), and general clinical data (duration of hypertension, medical conditions, and physical activity) using the Physical Activity Questionnaire for Elderly Japanese.[21] Subsequently, a physical fitness test, handgrip strength measurement, leg strength measurement, TUG, FTSST, and 2MST were performed for each participant with a 30-minute rest between tests. During the second visit on the following week, the participants performed the 6MWT.

Hand grip strength was measured with a Jamar Hand Dynamometer (Sammons Preston, Bolingbrook, IL, USA). After a practice test, participants were instructed to stand with their arms extended, and squeeze the dynamometer twice as hard as possible for 3 seconds with the dominant arm. The participants were allowed to rest between measurements. Three trials were performed and the average values were recorded, regardless of hand dominance.[22]

In the 6MWT protocol, the participants were asked to sit on a chair for 5 minutes to record their vital signs, dyspnea, and leg fatigue. They were then instructed to walk as fast as possible for 6 minutes without running and to continue at the same pace without stopping. The distance covered by each participant was recorded.[9] One minute after the test, the participants' vital signs, dyspnea, and leg fatigue were recorded.

In the 2MST protocol, the participants were instructed to stand against a wall, and marks were made on the wall at the level of the anterior superior iliac crest and patella. Half of the distance between the two marks was marked using a piece of tape. The participants were asked to lift their knees to the height marked by the tape while treading in place as quickly as possible for 2 minutes. The number of steps taken on the right side to reach the criterion height was counted for each participant and recorded.[23]

In the FTSST protocol, the participants were asked to stand up and sit down as fast as possible five times with their arms folded across their chests. Two trials were conducted with a rest period of 1 minute between trials. The average time of two trials was recorded as the test result.[24]

In the leg strength protocol, the participants were instructed to stand with their feet shoulder-width apart on the dynamometer base and hold onto a bar with their hands. The chain was adjusted such that the knees were flexed at 110°. The participants were then asked to pull as hard as possible on the chain while trying to straighten their legs and keep their upper limbs straight without flexing their backs. Each subject performed two trials and the max-

imum performance was recorded.[25]

The TUG protocol involved measuring the time required for the participants to rise from a chair with an approximate seat height of 46 cm, walk 3 m to a line on the floor, turn, walk back to the chair, and sit down again. The participants had one practice walk-through before being timed for three attempts with 1-minute rest intervals and verbal encouragement. The shortest time was recorded for analysis.[26-28]

3. Statistical Analysis

We computed the descriptive statistics, including means, standard deviations, and percentages, for the participant characteristics and study outcomes. Receiver operating characteristic (ROC) curve analysis was used to identify the accuracy of the 2MST in differentiating older adults with hypertension with and without functional impairment. We used a 6MWT cut-off of 320 m,[14] which is associated with low exercise endurance in older adults. Based on these cutoffs, we identified the threshold for the 2MST to identify functional impairments. The area under the curve (AUC), best cut-off point, sensitivity, and specificity were identified. We compared older adults with hypertension below or above the cut-off point in the 2MST using the independent samples t-test or Mann–Whitney U test, as appropriate. Physiological responses—blood pressure (BP), heart rate (HR), and oxygen saturation (O_2 sat)—and differences between the 2MST and 6MWT were evaluated using dependent samples t-test or signed-rank test. Leg fatigue and dyspnea scores were measured using the signed-rank test. Pearson correlation coefficient was used to verify the correlation between the 2MST and 6MWT, handgrip strength, leg strength, TUG, FTSST, and 6MWT. Data were analyzed using Stata 14.0 (StataCorp LLC, College Station, TX, USA), with a significance level of 5%.

RESULTS

This study enrolled 91 older individuals with hypertension, with a mean age of 70.29 ± 4.95 years and an almost equal distribution of men (49.45%) and women (50.55%). The participants had a mean body weight of 58.59 ± 0.71 kg, a mean height of 160.94 ± 12.02 cm, and a mean BMI of 22.59 ± 3.85 kg/m^2. The average duration of hypertension since diagnosis was 8.87 ± 3.54 years, and most participants had comorbidities including diabetes (48.4%), dyslipidemia (38.46%), and orthopedic problems (9.89%). A small proportion of participants had cardiovascular disease (8.79%). The participants' level of physical activity was 8.77 ± 5.23 metabolic equivalents (METs) hr/wk, indicating moderate physical activity levels. Table 1 summarizes the participants' characteristics.

Table 1. Characteristics of hypertensive older adults (n=91)

Variable	Hypertensive older adults
Age (y)	70.29 ± 4.95
Sex	
Male	45 (49.45)
Female	46 (50.55)
Body weight (kg)	58.59 ± 0.71
Height (cm)	160.94 ± 12.02
BMI (kg/m^2)	22.59 ± 3.85
PAQ-EJ score (METs, hr/wk)	8.77 ± 5.23
SBP (mmHg)	135.91 ± 16.55
DBP (mmHg)	73.31 ± 9.20
Duration of hypertension (y)	8.87 ± 3.54
Comorbidities	
None	8 (8.79)
Diabetes	44 (48.4)
Dyslipidemia	35 (38.46)
Orthopedic problems (gout, rheumatoid disease)	9 (9.89)
Cardiovascular disease	8 (8.79)

Values are presented as mean±standard deviation or number (%).
BMI, body mass index; PAQ-EJ, Physical Activity Questionnaire for Elderly Japanese; METs, metabolic equivalents; SBP, systolic blood pressure; DBP, diastolic blood pressure.

As shown in Table 2, the 2MST had an optimal cut-off score of ≤ 60 steps, with a sensitivity of 87.50% and a specificity of 70.59%. The AUC was 0.91 (95% confidence interval, 0.84–0.97).

Compared to the group of participants that completed the 2MST with ≥ 60 steps, those that completed the test with < 60 steps had significantly lower handgrip strength, leg strength, TUG, FTSST, and 6MWT distances ($p < 0.001$), as well as significantly lower systolic blood pressure (SBP) and diastolic blood pressure (DBP) ($p < 0.001$ and $p = 0.036$, respectively). The HR, HR as a percentage of the predicted maximum, O_2 sat, and dyspnea grade did not differ significantly between the groups (Table 3).

Table 4 shows the results of the comparison of physiological responses, dyspnea, and leg fatigue between the 2MST and 6MWT in older adults with hypertension. The HR in beats per minute (bpm) during the 2MST was significantly increased when compared to the 6MWT (86.91 ± 14.10 bpm vs. 83.02 ± 15.36 bpm; $p < 0.001$), as well as the HR in percentage of predicted maximum HR (57.10% ± 2.56% vs. 54.69% ± 2.20%; $p < 0.001$). SBP during the 2MST was also significantly higher than that during the 6MWT (154.33 ± 21.61 mmHg vs. 144.42 ± 18.71 mmHg; $p < 0.001$). The DBP and O_2 sat levels did not differ significantly between the two tests ($p = 0.452$ and $p = 0.050$, respectively).

Regarding the subjective responses, the dyspnea and leg fatigue levels were significantly higher during the 2MST than those during the 6MWT (11.48 ± 2.73 vs. 10.54 ± 2.92, $p = 0.004$ and 2.12 ± 1.67 vs. 1.45 ± 1.33, $p < 0.001$, respectively). These results suggested

Table 2. Optimal cut-off score, sensitivity, specificity, and AUC of the 2MST in all participants

Number of participants	Cut-off (steps)	Sensitivity (%)	Specificity (%)	AUC (95% CI)
91	≤ 60	87.50	70.59	0.91 (0.84–0.97)

2MST, 2-minute step test; AUC, area under the curve; CI, confidence interval.

Table 3. Comparing physiological responses, dyspnea, leg fatigue, and functional ability in individuals below (n=31) or above (n=60) the 2MST cut-off point

Variable	Total (n = 91)	2MST		p-value
		< 60 steps (n = 31)	≥ 60 steps (n = 60)	
HR (beats/min)	85.26 ± 6.36	83.58 ± 10.20	88.63 ± 15.53	0.080
HR (%pred)	57.10 ± 2.56	56.21 ± 6.74	58.61 ± 10.69	0.182
SBP (mmHg)	153.16 ± 28.28	143.61 ± 18.62	159.87 ± 21.09	< 0.001*
DBP (mmHg)	78.03 ± 1.41	76.13 ± 10.22	81.13 ± 10.79	0.036*
O_2 sat (%)	97.26 ± 0.00	97.65 ± 1.11	97.82 ± 1.23	0.357
Dyspnea (6–20 grade)	9.77 ± 0.00	11.26 ± 2.71	11.60 ± 2.76	0.595
Leg fatigue (0–10 grade)	1.47 ± 3.54	2.58 ± 1.54	1.88 ± 1.69	0.040*
2MST (step)	62.47 ± 14.68	47.23 ± 11.94	70.35 ± 8.43	< 0.001*
Handgrip strength (kg)	23.15 ± 7.04	18.21 ± 4.60	25.70 ± 6.74	< 0.001*
Leg strength (kg)	50.04 ± 24.65	34.84 ± 12.89	57.90 ± 25.65	< 0.001*
TUGT (s)	11.71 ± 3.88	14.25 ± 5.12	10.40 ± 2.14	< 0.001*
FTSST (s)	12.21 ± 3.57	14.07 ± 4.12	11.25 ± 2.83	< 0.001*
6MWT (m)	334.56 ± 83.11	266.68 ± 77.81	369.62 ± 61.53	< 0.001*

Values are presented as mean±standard deviation.
HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; O_2 sat, oxygen saturation; 2MST, 2-minute step test; TUG, timed up and go test; FTSST, five time sit-to-stand test; 6MWT, 6-minute walk test.
*p<0.05, statistically significant.

Table 4. A comparison of physiological responses, dyspnea, and leg fatigue between 6MWT and 2MST in hypertensive older adults (n=91)

Variable	2MST	6MWT	p-value
HR (beats/min)	86.91 ± 14.10	83.02 ± 15.36	< 0.001*
HR (%pred)	57.10 ± 2.56	54.69 ± 2.20	< 0.001*
SBP (mmHg)	154.33 ± 21.61	144.42 ± 18.71	< 0.001*
DBP (mmHg)	79.43 ± 10.81	78.58 ± 11.34	0.452
O_2 sat (%)	97.76 ± 1.19	97.46 ± 1.30	0.050
Dyspnea (6–20 grade)	11.48 ± 2.73	10.54 ± 2.92	0.004*
Leg fatigue (0–10 grade)	2.12 ± 1.67	1.45 ± 1.33	< 0.001*

Values are presented as mean±standard deviation.
6MWT, 6-minute walk test; 2MST, 2-minute step test; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; O_2 sat, oxygen saturation.
*p<0.05, statistically significant.

Table 5. Relationships between the 2MST and demographic factors, handgrip strength, leg strength, TUG, and FTSST in hypertensive older adults

Variable	2MST	
	r	p-valve
Age	-0.294	0.005*
Height	0.332	0.001*
Weight	0.144	0.172
6MWT	0.747	< 0.001*
Handgrip strength	0.567	< 0.001*
Leg strength	0.472	< 0.001*
FTSST	-0.491	< 0.001*
TUG	-0.632	< 0.001*

2MST, 2-minute step test; 6MWT, 6-minute walk test; FTSST, five times sit to stand test; TUG, timed up and go test.
*p<0.05, statistically significant.

that the 2MST may be more challenging in terms of cardiovascular and subjective responses than the 6MWT in older adults with hypertension (Table 4).

Table 5 presents the associations between the number of steps taken in the 2MST and various demographic and physical factors in older adults with hypertension. The results demonstrated a negative correlation between 2MST and age (r = -0.294, p = 0.005), a positive correlation with height (r = 0.332, p = 0.001), and no significant correlation with body weight (r = 0.144, p = 0.172).

The results of several physical fitness tests in the same population, including the 6MWT distance, grip strength, leg strength, TUG duration, and FTSST duration showed that the number of steps in the 2MST was positively associated with the distance of the 6MWT (r = 0.747, p < 0.0001), isometric grip strength (r = 0.567,

$p < 0.0001$), and isometric leg strength ($r = 0.472$, $p < 0.0001$). In contrast, the number of steps in the 2MST was negatively associated with FTSST ($r = -0.491$, $p < 0.0001$) and TUG ($r = -0.632$, $p < 0.0001$) duration (Table 5).

DISCUSSION

This study investigated the usefulness of the 2MST for assessing functional fitness in older individuals with hypertension and its correlation with other physical fitness tests. The results showed that the 2MST was effective in identifying functional limitations in this population, with a cutoff score of ≤ 60 steps indicating lower functional ability and physiological responses. Furthermore, the 2MST was more challenging than the 6MWT and was significantly correlated with demographic factors, handgrip strength, leg strength, TUG, and FTSST.

The 2MST was originally developed as a component of the Senior Fitness Test (SFT) by Rikli and Jones in 1999.[16] The SFT is a comprehensive set of tests designed to evaluate physical fitness in older adults, with the 2MST specifically assessing aerobic endurance and lower body strength.[29] Various studies have demonstrated the 2MST's usefulness in assessing functional capacity and found it to be a reliable and valid measure of physical fitness in older adults.[30] Our study found that a cutoff of 60 steps in the 2MST accurately distinguished older individuals with hypertension with or without functional impairment. This result is consistent with those of a previous study that identified the 2MST as the best predictor of functional capacity in hypertensive individuals, with an average of 69 repetitions and an AUC of 0.7.[19] Individuals who performed < 60 repetitions in the 2MST exhibited longer times on the TUG and FTSST, indicating potential mobility and balance issues. These findings, along with lower handgrip and leg strength and higher leg fatigue, may suggest a decrease in overall physical fitness, including reduced endurance and physical capacity. Therefore, < 60 repetitions in the 2MST may serve as a useful marker for identifying functional impairment, indicating the need for interventions to improve physical fitness and functional capacity in individuals with hypertension.

The 2MST is a good measure of cardiorespiratory fitness when other submaximal fitness tests cannot be undertaken, such as the 6MWT, and involves lifting the knees to the mid-level between the patella and iliac crest[8]; thus, it requires more intensity and a longer duration of single-leg support than the standard step.[31] In our study of older adults with hypertension, the 2MST elicited a higher HR, SBP, dyspnea, and leg fatigue compared to the 6MWT. The biomechanics of the 2MST require greater lower-body strength, physical skills, and longer periods of single-leg support,[32,33] which explained the higher physiological demand and RPE compared with the 6MWT. The RPE was significantly higher in the 2MST group than in the 6MWT group.

The 2MST and 6MWT exhibit a strong correlation, indicating that both tests are reliable measures of cardiorespiratory fitness.[34] Our results are consistent with those of previous studies, which suggests that the 2MST can complement the 6MWT in various populations, including those with coronary artery disease,[35] hypertension in older adults,[16] symptomatic peripheral artery disease,[34] and systolic heart failure.[36] Additionally, other studies have reported an association between these tests in both healthy older individuals[8] and those with pathologies[16,36] suggesting that the 2MST can assess the integrated global response to exercise of all human body systems. We observed correlations between age, height, weight, and 2MST, suggesting that these factors may impact test performance and should be considered.

Our study results revealed significant inverse correlations between the 2MST and two functional mobility tests, the FTSST and TUG, which assess the ability to complete tasks such as standing up from a chair or standing on one leg. These results reinforce the strong relationship between cardiovascular endurance and functional mobility. A negative correlation implies that poor cardiovascular endurance may lead to poor functional mobility, and vice versa. These results are consistent with those of previous studies reporting a correlation between functional capacity and functional mobility in older adults with hypertension.[16,17] Moreover, we observed a significant positive correlation between 2MST, handgrip strength, and leg strength. This supports prior research indicating a relationship between the 2MST and quadriceps strength in patients with systolic heart failure.[36] In older adults, maintaining strong handgrip and leg muscles is crucial not only for completing daily tasks but also for reducing the risks of mortality, functional decline, disability, and falls.[37-39] Moreover, poor aerobic endurance and leg strength contribute significantly to slow gait velocity in community-dwelling patients with stroke.[40]

In conclusion, the 2MST is a useful tool for assessing functional capacity in older individuals with hypertension, with a cut-off of 60 steps accurately identifying functional impairment. The 2MST was positively correlated with the 6MWT, grip strength, and leg strength and negatively associated with the FTSST and TUG duration.

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CONFLICT OF INTEREST
The researcher claims no conflicts of interest.

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AUTHOR CONTRIBUTIONS
Conceptualization, AS; Data curation, AS, PP; Funding acquisition, AS; Investigation, AS, TP, NS; Methodology, AS, TP, NS; Writing-original draft, AS, PA; Writing-review and editing, AS, PA, PP.

REFERENCES

1. United Nations. World population prospects: the 2015 revision. New York, NY: United Nations, Department of Economic and Social Affairs; 2015.
2. Boss GR, Seegmiller JE. Age-related physiological changes and their clinical significance. West J Med 1981;135:434-40.
3. Guo J, Huang X, Dou L, Yan M, Shen T, Tang W, et al. Aging and aging-related diseases: from molecular mechanisms to interventions and treatments. Signal Transduct Target Ther 2022;7:391.
4. Buford TW. Hypertension and aging. Ageing Res Rev 2016;26:96-111.
5. Mitchell WK, Williams J, Atherton P, Larvin M, Lund J, Narici M. Sarcopenia, dynapenia, and the impact of advancing age on human skeletal muscle size and strength: a quantitative review. Front Physiol 2012;3:260.
6. Kara M, Kara O, Ceran Y, Kaymak B, Kaya TC, Citir BN, et al. SARcopenia Assessment in Hypertension: The SARAH Study. Am J Phys Med Rehabil 2023;102:130-6.
7. Rikli RE, Jones CJ. Senior fitness test manual. 2nd ed. Champaign, IL: Human Kinetics; 2013.
8. Lim JY. Aging with disability: what should we pay attention to? Ann Geriatr Med Res 2022;26:61-2.
9. Thaweewannakij T, Wilaichit S, Chuchot R, Yuenyong Y, Saengsuwan J, Siritaratiwat W, et al. Reference values of physical performance in Thai elderly people who are functioning well and dwelling in the community. Phys Ther 2013;93:1312-20.
10. Bohannon RW. Hand-grip dynamometry predicts future outcomes in aging adults. J Geriatr Phys Ther 2008;31:3-10.
11. Galhardas L, Raimundo A, Del Pozo-Cruz J, Marmeleira J. Physical and motor fitness tests for older adults living in nursing homes: a systematic review. Int J Environ Res Public Health 2022;19:5058.
12. Amput P, Wongphon S, Srithawong A, Konsanit S, Naravejsakul K. The correlation among 2-minute step test, time up and go test, and sit to stand test in Phayao hypertensive older adults. J Med Assoc Thail 2021;104:1706-10.
13. Pedrosa R, Holanda G. Correlation between the walk, 2-minute step and TUG tests among hypertensive older women. Braz J Phys Ther 2009;13:252-6.
14. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111-7.
15. Enright PL, McBurnie MA, Bittner V, Tracy RP, McNamara R, Arnold A, et al. The 6-min walk test: a quick measure of functional status in elderly adults. Chest 2003;123:387-98.
16. Rikli RE, Jones CJ. Development and validation of a functional fitness test for community-residing older adults. J Aging Phys Act 1999;7:129-61.
17. Bohannon RW, Crouch RH. Two-minute step test of exercise capacity: systematic review of procedures, performance, and clinimetric properties. J Geriatr Phys Ther 2019;42:105-12.
18. Jones CJ, Rikli RE. Measuring functional. J Act Aging 2002;1:24-30.
19. Srithawong A, Poncumhak P, Manoy P, Kumfu S, Promsrisuk T, Prasertsri P, et al. The optimal cutoff score of the 2-min step test and its association with physical fitness in type 2 diabetes mellitus. J Exerc Rehabil 2022;18:214-21.
20. Noh JH, Jung HW, Ga H, Lim JY. Ethical guidelines for publishing in the Annals of Geriatric Medicine and Research. Ann Geriatr Med Res 2022;26:1-3.
21. Rikli RE, Jones CJ. Development and validation of criterion-referenced clinically relevant fitness standards for maintaining physical independence in later years. Gerontologist 2013;53:255-67.
22. Guedes MB, Lopes JM, Andrade AD, Guedes TS, Ribeiro JM, Cortez LC. Validation of the two minute step test for diagnosis of the functional capacity of hypertensive elderly persons. Rev Bras Geriatr Gerontol 2015;18:921-6.
23. Yasunaga A, Park H, Watanabe E, Togo F, Park S, Shephard RJ, et al. Development and evaluation of the physical activity questionnaire for elderly Japanese: the Nakanojo study. J Aging Phys Act 2007;15:398-411.
24. He H, Pan L, Wang D, Liu F, Du J, Pa L, et al. Normative values of hand grip strength in a large unselected Chinese population: evidence from the China National Health Survey. J Cachexia Sarcopenia Muscle 2023;14:1312-21.
25. Bandinelli S, Benvenuti E, Del Lungo I, Baccini M, Benvenuti F, Di Iorio A, et al. Measuring muscular strength of the lower limbs by hand-held dynamometer: a standard protocol. Aging (Mila-

no) 1999;11:287-93.
26. Barry E, Galvin R, Keogh C, Horgan F, Fahey T. Is the timed Up and Go test a useful predictor of risk of falls in community dwelling older adults: a systematic review and meta-analysis. BMC Geriatr 2014;14:14.
27. Rydwik E, Bergland A, Forsen L, Frandin K. Psychometric properties of timed up and go in elderly people: a systematic review. Phys Occup Ther Geriatr 2011;29:102-25.
28. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991;39:142-8.
29. Schaubert KL, Bohannon RW. Reliability and validity of three strength measures obtained from community-dwelling elderly persons. J Strength Cond Res 2005;19:717-20.
30. Goldberg A, Chavis M, Watkins J, Wilson T. The five-times-sit-to-stand test: validity, reliability and detectable change in older females. Aging Clin Exp Res 2012;24:339-44.
31. Rikli RE, Jones CJ. The reliability and validity of a 6-minute walk test as a measure of physical endurance in older adults. J Aging Phys Act 1998;6:363-75.
32. Zhao Y, Chung PK. Differences in functional fitness among older adults with and without risk of falling. Asian Nurs Res (Korean Soc Nurs Sci) 2016;10:51-5.
33. Beutner F, Ubrich R, Zachariae S, Engel C, Sandri M, Teren A, et al. Validation of a brief step-test protocol for estimation of peak oxygen uptake. Eur J Prev Cardiol 2015;22:503-12.
34. Dreher M, Walterspacher S, Sonntag F, Prettin S, Kabitz HJ, Windisch W. Exercise in severe COPD: is walking different from stair-climbing? Respir Med 2008;102:912-8.
35. Oliveros MJ, Seron P, Roman C, Galvez M, Navarro R, Latin G, et al. Two-minute step test as a complement to six-minute walk test in subjects with treated coronary artery disease. Front Cardiovasc Med 2022;9:848589.
36. Braghieri HA, Kanegusuku H, Corso SD, Cucato GG, Monteiro F, Wolosker N, et al. Validity and reliability of 2-min step test in patients with symptomatic peripheral artery disease. J Vasc Nurs 2021;39:33-8.
37. Węgrzynowska-Teodorczyk K, Mozdzanowska D, Josiak K, Siennicka A, Nowakowska K, Banasiak W, et al. Could the two-minute step test be an alternative to the six-minute walk test for patients with systolic heart failure? Eur J Prev Cardiol 2016;23:1307-13.
38. Benichou O, Lord SR. Rationale for strengthening muscle to prevent falls and fractures: a review of the evidence. Calcif Tissue Int 2016;98:531-45.
39. Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum A Jr, Orlandini A, et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. Lancet 2015;386:266-73.
40. Taylor-Piliae RE, Latt LD, Hepworth JT, Coull BM. Predictors of gait velocity among community-dwelling stroke survivors. Gait Posture 2012;35:395-9.

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Balance Ability and Quality of Life in Older Adult with Recovery from Mild COVID-19

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Background: In this study, we aimed to assess the ability to balance and quality of life (QoL) among older adults without a history of coronavirus disease 2019 (COVID-19) and those who had recovered from mild COVID-19. **Methods:** We recruited 80 older adults and categorized them into the following two groups based on their history of COVID-19: those without COVID-19 (n=40) and those who had recovered from mild COVID-19 (n=40). We assessed the participants' ability to balance using the multi-directional reach test and timed up and go (TUG) test, and evaluated their QoL using the Short Form-36. **Results:** Compared with older adults without a history of COVID-19, those who had recovered from mild COVID-19 demonstrated no differences in the scores of the forward, backward, right, and left directions (p>0.05), but a significantly longer duration for the TUG test (p=0.02) and a reduced QoL. **Conclusion:** Our study results demonstrated decreased ability to balance and poor QoL among older adults who had recovered from mild COVID-19.

Key Words: Post-COVID-19, Older adult, Balance, Quality of life, Mild-COVID-19, TUG test

INTRODUCTION

The coronavirus disease 2019 (COVID-19) first appeared in Wuhan, China, and spread rapidly worldwide.[1)] It is known to cause serious health problems including croup, cold, and bronchiolitis.[2)] In addition, COVID-19 affects the neurological system, particularly the ability to balance.[3)] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) binds to angiotensin-converting enzyme 2 (ACE2) receptors and invades human cells, resulting in adverse effects on the central nervous system (CNS)[4,5)] and leading to blood-brain barrier damage.[6)] Moreover, SARS-CoV-2 activates neuroinflammation resulting from the influx of cytokines into different sites of the CNS.[6)] These factors lead to neurological and neuromuscular systems dysfunction, resulting in postural instability and impaired ability to balance.[3,4,7)] Furthermore, these impairments are not present in the acute phase of COVID-19 but rather appear post-COVID-19.[7)] Previous studies have reported that patients post-COVID-19 experience memory loss, headache, vertigo, sleep disturbances, myalgia, brain fog, peripheral neuropathies, fatigue, and depression.[3,7)] Therefore, neuromuscular changes caused by SARS-CoV-2 infection lead to poor postural balance, resulting in a low patient quality of life (QoL) post-COVID-19.[8,9)] Previous studies have reported poorer postural balance in patients post-COVID-19 compared to healthy controls, which is related to fatigue and low QoL.[8,9)] Older adults with COVID-19 show symptoms of multisystem involvement and an increased risk of death.[10,11)] In addition, older adults with prolonged COVID-19 infection exhibit neurocognitive symptoms, such as mood disorders, mental conditions, and anxiety.[12)] However, the ability to balance and QoL in older adults who have recovered from mild COVID-19 have not yet been evaluated. Therefore, in this study, we aimed to assess the ability to balance using the multi-directional reach test (MDRT) and timed up and go (TUG) test and evaluate QoL using the Short Form-36 (SF-36) in older adults who had re-

covered from mild COVID-19 and those with a history of COVID-19. This study would offer valuable insights to older adults who are recovering from mild COVID-19, aiding in the identification of balance disorders. We hypothesized that older adults recovering from mild COVID-19 would have reduced ability to balance and poor QoL than those of older adults without a history of COVID-19.

MATERIALS AND METHODS

Study Design and Participants

This cross-sectional study assessed the ability to balance using the MDRT and TUG tests and evaluated QoL using the SF-36 in older adults without a history of COVID-19 and older adults who had recovered from mild COVID-19. This study was approved by the Clinical Research Ethics Committee of the University of Phayao, Phayao, Thailand (IRB Code 1.3/032/65). Also, this study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[13]

We recruited 80 older adults without a history of COVID-19 and those who had recovered from mild COVID-19 and categorized them into two groups (n = 40/group). The sample size was calculated using a power of 0.90, power analysis with an alpha of 0.05, and effect size d of 0.4.[14] The inclusion criteria were as follows: patients aged 60 years or above, without a history of COVID-19 or those recovering from mild COVID-19 with confirmation of infection by SARS-CoV-2 using polymerase chain reaction (PCR) or antigen test kit performed at least 3 months before the evaluation procedure, with normal body mass index (BMI) values (18.5–24.9 kg/m^2),[15] and ability to stand and walk without assistive walking devices. The exclusion criteria were participants who had problems with hearing, communication, vision, standing, or walking; balance impairment; history of back or lower limb surgery, inability to raise the arms to 90°; or scoliosis affecting the ability to stand or walk.

Procedures

The MDRT protocol encompassed assessments in forward, backward, right-sided, and left-sided directions. A 100-cm yardstick attached to a tripod was set parallel to the floor at the height of the participant's acromion process. The participants were instructed to stand on the floor without wearing shoes and to lift an outstretched arm to shoulder height. We recorded the lengths at the fingertips as the initial reach data. Subsequently, the participants were instructed to reach as far as they could while maintaining alignment with the yardstick, without moving their feet or taking a step from the floor.[16] They were then instructed to lean back as far as possible to determine the extent of reach in the backward direction. For the right and left directions, they were instructed to lean as far as possible toward the right and left, respectively. The distance score for each direction was calculated from the initial reach. We recorded three successful trials for each direction.[16]

In the TUG test protocol, the participants were instructed to get up from the chair at the signal, walk to a marker, go around it, return to the chair, and sit down promptly resuming a sitting posture. The test commenced with participants seated upright with a vertical posture, hands resting on the thighs, and feet planted flat on the ground. The participants were reminded that the test was time-bound and the goal was to walk expeditiously without running.[17]

We assessed the participants' QoL using the SF-36. This questionnaire includes eight dimensions comprising a list of questions about various aspects of QoL, including physical functioning, physical role limitations, bodily pain, general health perceptions, vitality, social functioning, emotional role limitations, and mental health.[18] The result is a score ranging from 0 to 100, with higher scores indicating a better QoL.[18] Fig. 1 is a flow diagram of the participants at each stage of the study.

Statistical Analysis

Descriptive statistics were used to present the demographic data. The independent sample t-test was used to compare MDRT scores, TUG test duration, and SF-36 scores between older adults without a history of COVID-19 and those who had recovered from mild COVID-19. We performed the statistical analysis using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA), with a p-value < 0.05 indicating significance.

RESULTS

A total of 80 older adults without COVID-19 and those who recovered from mild COVID-19 voluntarily participated in this

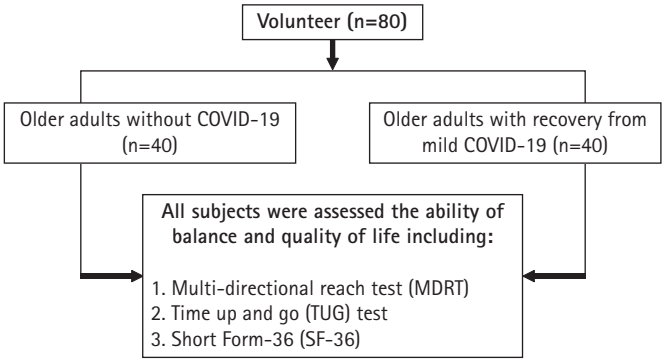

Fig. 1. The flow diagram of the subjects though each stage of this study.

study. The participants' characteristics are summarized in Table 1. Most participants were female, and the average age and BMI did not differ between the two groups.

All participants completed the MDRT. We observed no differences in the scores of the forward, backward, right-side, and left-side directions between older adults who had recovered from mild COVID-19 and those without a history of COVID-19 ($p > 0.05$). The highest and lowest MDRT scores were observed in the forward and backward directions, respectively (Table 2).

All participants successfully completed the TUG test. Older adults who had recovered from mild COVID-19 demonstrated a significantly longer duration for the TUG test than those of the older adults without a history of COVID-19 ($p = 0.02$) (Table 3).

Our results demonstrated significantly lower scores in terms of physical functioning, physical role limitations, bodily pain, general health perceptions, vitality, social functioning, emotional role limitations, and mental health among older adults who had recovered from mild COVID-19 than among those without a history of COVID-19 ($p < 0.05$) (Table 4).

DISCUSSION

The results of the present study demonstrated decreased ability to balance and poor QoL among older adults who had recovered from mild COVID-19. Additionally, this group demonstrated longer duration for the TUG test and worse scores for the eight dimensions of the SF-36 questionnaire than those of the older adults without a history of COVID-19; however, no difference was observed for the scores in the four directions of the MDRT.

We observed no difference in MDRT scores in any direction between older adults with no history of COVID-19 and those who had recovered from mild COVID-19. These results may be because the participants in both the groups had similar BMI. A previous study reported lower ability to balance among older adults who were overweight or obese than among those with normal weight.[19] Moreover, older adults who were overweight or obese had significantly reduced MDRT scores in the forward, backward, right-side, and left-side directions than those of older adults with normal weight.[19] The amount of adipose tissue is increased in individuals with overweight and obesity, leading to reduced stability of postural control in these individuals.[20] In addition, individuals

Table 1. Characteristics of the older adults without COVID-19 and older adults with recovery from mild COVID-19

Variable	Older adults without COVID-19 (n = 40)	Older adults with recovery from mild COVID-19 (n = 40)	p-value
Age (y)	68.95 ± 4.40	67.53 ± 4.55	0.97
Sex			
Male	15	15	
Female	25	25	
Weight (kg)	52.13 ± 6.16	53.35 ± 6.45	0.81
High (cm)	155.38 ± 0.06	156.83 ± 0.08	0.22
BMI (kg/m^2)	21.70 ± 1.98	21.66 ± 1.70	0.17

Values are presented as mean±standard deviation.
COVID-19, coronavirus disease 2019; BMI, body mass index.

Table 2. The comparison between score of MDRT in older adults without COVID-19 and older adults with recovery from mild COVID-19

Variable	Older adults without COVID-19 (n = 40)	Older adults with recovery from mild COVID-19 (n = 40)	p-value
Forward (cm)	18.77 ± 4.18	17.29 ± 3.03	0.10
Backward (cm)	11.75 ± 2.79	11.20 ± 62.44	0.24
Right-side (cm)	14.43 ± 2.57	14.35 ± 2.79	0.39
Left-side (cm)	13.85 ± 3.06	13.05 ± 2.76	0.71

Values are presented as mean±standard deviation.
COVID-19, coronavirus disease 2019; MDRT, multi-directional reach test.

Table 3. Comparison between duration TUG in older adults without COVID-19 and older adults with recovery from mild COVID-19

Variable	Older adults without COVID-19 (n = 40)	Older adults with recovery from mild COVID-19 (n = 40)	p-value
TUG (s)	7.30 ± 0.86	10.61 ± 1.31	0.02

Values are presented as mean±standard deviation.
COVID-19, coronavirus disease 2019; TUG, time up and go test.

Table 4. Comparison between quality of life assessed by the Short Form-36 in older adults without COVID-19 and older adults with recovery from mild COVID-19

Variable	Older adults without COVID-19 (n = 40)	Older adults with recovery from mild COVID-19 (n = 40)	p-value
Physical functioning	74.90 ± 11.96	61.75 ± 5.94	0.001
Physical role limitations	76.95 ± 10.50	62.28 ± 6.56	0.004
Bodily pain	58.75 ± 11.81	54.75 ± 16.17	0.011
General health perceptions	70.75 ± 10.95	57.25 ± 8.16	0.007
Vitality	68.50 ± 11.89	59.50 ± 9.04	0.035
Social functioning	70.18 ± 11.11	60.08 ± 7.03	0.007
Emotional role limitations	86.50 ± 8.34	63.25 ± 11.63	0.042
Mental health	85.00 ± 5.99	65.75 ± 9.64	0.018

Values are presented as mean±standard deviation.
COVID-19, coronavirus disease 2019.

with overweight and obesity have an increased base of support and decreased walking velocity due to increased ankle muscle activity, which leads to an abnormal gait pattern.[21] Additionally, our results revealed the highest and lowest MDRT scores in the forward and backward directions, respectively, among older adults without a history of COVID-19 and those who had recovered from mild COVID-19. This is because the ankle and foot biomechanical arrangements provide greater forward walking ability than backward walking ability.[16] Moreover, humans have greater control over balance in the forward direction because they are involved in moving the body forward in activities of daily life (ADL).[16] Additionally, significant energy is required to shift the body weight to the rear because a person cannot exert visual control over the feet during movement.[22] These findings indicate that older adults without a history of COVID-19 and those who had recovered from mild COVID-19 exhibit greater ability to balance in the forward direction than in the backward direction or to the right or left direction.

Balance is important not only for posture stability but also for performing safe ADL. ADL are associated with multiple tasks, including rising from a chair, standing, walking, and turning.[23] Therefore, the TUG test was used to assess these conditions. This test can assess various aspects of ability to balance, including posture, mobility, agility, transitioning from sitting to standing position, walking stability, and gait speed, in older adults.[17,24] Older adults with TUG test duration of > 13.5 seconds are at a higher risk of experiencing falls.[25,26] However, in the present study, older adults without a history of COVID-19 and those who had recovered from mild COVID-19 had average TUG test duration of < 13.5 seconds, indicating adequate ability to balance. However, older adults who had recovered from mild COVID-19 required significantly more time to complete the tests than that of older adults without a history of COVID-19. These findings suggested that older adults who had recovered from mild COVID-19 had reduced ability to balance than those without a history of COVID-19. These findings are consistent with those of a previous study demonstrating lower postural balance among patients with post-acute COVID-19 syndrome than among healthy controls.[8] These results may be due to the activation of neuroinflammation by SARS-CoV-2 resulting from the influx of cytokines into different sites of the CNS, leading to prolonged generalized symptoms such as impaired postural balance and fatigue.[6]

Compared to older adults without a history of COVID-19, those who had recovered from mild COVID-19 exhibited lower QoL, including physical functioning, physical role limitations, bodily pain, general health perceptions, vitality, social functioning, emotional role limitations, and mental health. These results are consistent with those of previous studies demonstrating significant decreases in the eight domains of the SF-36 questionnaire among patients post-COVID-19 compared to a healthy controls.[9,27] In addition, a previous study reported notable declines in the domains of physical functioning, physical role limitations, bodily pain, general health perceptions, and mental health in the SF-36 among patients with post-acute COVID-19 syndrome than among healthy controls.[8] These results may be attributed to dyspnea, impaired mental health, and neuropsychological disorders, resulting in decreased QoL in patients with prolonged COVID-19 infection.[28,29] Therefore, the reduced QoL in older adults recovering from mild COVID-19 may occur from their reduced ability to balance.

This study may be limited by variables that can influence an individual's ability to balance. Factors, including muscle strength and endurance of the lower limbs, may attain statistical significance with more suitable variables. Future studies should investigate these variables to enrich our understanding of balance dynamics and its implications for individuals' well-being.

In conclusion, the present study is the first to comprehensively assess the impact of COVID-19 on individuals' ability to balance in various directions and performing ADL. The findings from the

present study indicated a decreased ability to balance and poor QoL among older adults recovering from mild COVID-19 than in those without a history of COVID-19.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, PA; Data curation, PA, SW; Funding acquisition, PA; Investigation, PA, SW; Methodology, PA, WT, NS, SK, SW; Writing-original draft, PA, SW; Writing-review & editing, PA, WT, NS, SK, SW.

REFERENCES

1. Abboah-Offei M, Salifu Y, Adewale B, Bayuo J, Ofosu-Poku R, Opare-Lokko EB. A rapid review of the use of face mask in preventing the spread of COVID-19. Int J Nurs Stud Adv 2021;3:100013.
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases fr om the Chinese Center for Disease Control and Prevention. JAMA 2020;323:1239-42.
3. Augustin M, Schommers P, Stecher M, Dewald F, Gieselmann L, Gruell H, et al. Post-COVID syndrome in non-hospitalised patients with COVID-19: a longitudinal prospective cohort study. Lancet Reg Health Eur 2021;6:100122.
4. Divani AA, Andalib S, Biller J, Di Napoli M, Moghimi N, Rubinos CA, et al. Central nervous system manifestations associated with COVID-19. Curr Neurol Neurosci Rep 2020;20:60.
5. Pergolizzi JV, Raffa RB, Varrassi G, Magnusson P, LeQuang JA, Paladini A, et al. Potential neurological manifestations of COVID-19: a narrative review. Postgrad Med 2022;134:395-405.
6. De Felice FG, Tovar-Moll F, Moll J, Munoz DP, Ferreira ST. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the central nervous system. Trends Neurosci 2020;43:355-7.
7. Gervasoni F, LoMauro A, Ricci V, Salce G, Andreoli A, Visconti A, et al. Balance and visual reliance in post-COVID syndrome patients assessed with a robotic system: a multi-sensory integration deficit. Neurol Sci 2022;43:85-8.
8. de Sousa KC, Gardel DG, Lopes AJ. Postural balance and its association with functionality and quality of life in non-hospitalized patients with post-acute COVID-19 syndrome. Physiother Res Int 2022;27:e1967.
9. Liska D, Liptakova E, Babicova A, Batalik L, Banarova PS, Dobrodenkova S. What is the quality of life in patients with long COVID compared to a healthy control group? Front Public Health 2022;10:975992.
10. Perrotta F, Corbi G, Mazzeo G, Boccia M, Aronne L, D'Agnano V, et al. COVID-19 and the elderly: insights into pathogenesis and clinical decision-making. Aging Clin Exp Res 2020;32:1599-608.
11. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054-62.
12. Bull-Otterson L, Baca S, Saydah S, Boehmer TK, Adjei S, Gray S, et al. Post-COVID conditions among adult COVID-19 survivors aged 18-64 and ≥ 65 years: United States, March 2020-November 2021. MMWR Morb Mortal Wkly Rep 2022;71:713-7.
13. Noh JH, Jung HW, Ga H, Lim JY. Ethical guidelines for publishing in the Annals of Geriatric Medicine and Research. Ann Geriatr Med Res 2022;26:1-3.
14. Perrot JC, Segura M, Beranuy M, Gich I, Nadal MJ, Pintor A, et al. Comparison of post-COVID symptoms in patients with different severity profiles of the acute disease visited at a rehabilitation unit. PLoS One 2022;17:e0274520.
15. Barbosa MH, Bolina AF, Luiz RB, de Oliveira KF, Virtuoso JS, Rodrigues RA, et al. Body mass index as discriminator of the lean mass deficit and excess body fat in institutionalized elderly people. Geriatr Nurs 2015;36:202-6.
16. Newton RA. Validity of the multi-directional reach test: a practical measure for limits of stability in older adults. J Gerontol A Biol Sci Med Sci 2001;56:M248-52.
17. Bohannon RW. Reference values for the timed up and go test: a descriptive meta-analysis. J Geriatr Phys Ther 2006;29:64-8.
18. Nandasena HM, Pathirathna ML, Atapattu AM, Prasanga PT. Quality of life of COVID 19 patients after discharge: systematic review. PLoS One 2022;17:e0263941.
19. Amput P, Wongphon S, Naravejsakul K. Balance assessment using multi-directional reach test in community-dwelling elderly people with different body mass index. J Med Assoc Thai 2021;104:1908-12.
20. Ku PX, Abu Osman NA, Yusof A, Wan Abas WA. Biomechani-

cal evaluation of the relationship between postural control and body mass index. J Biomech 2012;45:1638-42.
21. Ko S, Stenholm S, Ferrucci L. Characteristic gait patterns in older adults with obesity: results from the Baltimore Longitudinal Study of Aging. J Biomech 2010;43:1104-10.
22. Hao WY, Chen Y. Backward walking training improves balance in school-aged boys. Sports Med Arthrosc Rehabil Ther Technol 2011;3:24.
23. Mancini M, Horak FB. The relevance of clinical balance assessment tools to differentiate balance deficits. Eur J Phys Rehabil Med 2010;46:239-48.
24. Mathias S, Nayak US, Isaacs B. Balance in elderly patients: the "get-up and go" test. Arch Phys Med Rehabil 1986;67:387-9.
25. Barry E, Galvin R, Keogh C, Horgan F, Fahey T. Is the Timed Up and Go test a useful predictor of risk of falls in community dwelling older adults: a systematic review and meta-analysis. BMC Geriatr 2014;14:14.
26. Schoene D, Wu SM, Mikolaizak AS, Menant JC, Smith ST, Delbaere K, et al. Discriminative ability and predictive validity of the timed up and go test in identifying older people who fall: systematic review and meta-analysis. J Am Geriatr Soc 2013;61:202-8.
27. Lemhofer C, Sturm C, Loudovici-Krug D, Best N, Gutenbrunner C. The impact of post-COVID-syndrome on functioning: results from a community survey in patients after mild and moderate SARS-CoV-2-infections in Germany. J Occup Med Toxicol 2021;16:45.
28. Malik P, Patel K, Pinto C, Jaiswal R, Tirupathi R, Pillai S, et al. Post-acute COVID-19 syndrome (PCS) and health-related quality of life (HRQoL): a systematic review and meta-analysis. J Med Virol 2022;94:253-62.
29. Yardley L, Redfern MS. Psychological factors influencing recovery from balance disorders. J Anxiety Disord 2001;15:107-19.

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The Risk Factors of COVID-19 Infection and Mortality among Older Adults in South Korea

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Background: This study aimed to identify the risk factors associated with coronavirus disease 2019 (COVID-19) infection and mortality among older adults in South Korea. **Methods:** Using Korean National Health Insurance data from January 1, 2020, to March 31, 2022, we analyzed the impact of various factors, including age, comorbidity burden, and insurance type, on COVID-19 infection and mortality rates. **Results:** Age was the most significant risk factor for mortality in older adults. A higher comorbidity burden was also associated with increased infection (odds ratio [OR]=1.33 for Charlson Comorbidity Index [CCI] ≥2, 95% confidence interval [CI] 1.321–1.339) and mortality (OR=1.537 for CCI ≥2, 95% CI 1.459–1.618) rates. While Medical Aid recipients exhibited lower infection rates (OR=0.898, 95% CI 0.89–0.906) than National Health Insurance beneficiaries, they had higher mortality rates (OR=1.692, 95% CI 1.623–1.763). **Conclusion:** These results emphasized the need to prioritize vaccination and allocate healthcare resources for older adults, particularly those with multiple comorbidities. Addressing socioeconomic disparities and ensuring equitable access to testing and healthcare services are crucial for mitigating the impact of COVID-19 on older adults.

Key Words: COVID-19, Mortality, Aged, Republic of Korea, Risk factors

INTRODUCTION

Since the World Health Organization (WHO) declared the coronavirus disease 2019 (COVID-19) pandemic on March 12, 2020, as of July 3, 2023, a total of 32,131,606 cumulative confirmed cases of COVID-19 in Korea have been recorded by the WHO.[1)] COVID-19 is primarily transmitted through respiratory droplets when an infected person coughs, sneezes, talks, or breathes. The symptoms range from mild to severe, with the common symptoms including fever, cough, shortness of breath, fatigue, and loss of taste or smell.[2-4)] However, some individuals, particularly older adults, and those with underlying health conditions, may experience severe respiratory distress and other complications.

Previous COVID-19-related research in Korea examined the impact of the comorbidity burden on mortality in patients infected with the virus. However, these studies were limited in scope, relying on data from only 7,590 patients registered until May 15, 2020, and did not specifically focus on older adults.[5)] Although studies have been conducted in Wuhan, China, to examine the association between acute respiratory distress syndrome (ARDS), mortality,

and risk factors, these studies used data from the overall age range of infected individuals.[6] Another study conducted in South Korea that evaluated the COVID-19 case fatality risk found that, while younger age groups had higher infection rates, older adults had higher mortality rates. However, that study had limitations owing to its relatively small sample size.[7]

The COVID-19 pandemic has majorly impacted global health, particularly among older adults who are more vulnerable to severe illness and mortality.[5,6] Understanding the risk factors associated with COVID-19 infection and mortality in this population is crucial for effective prevention and management strategies. South Korea has implemented comprehensive healthcare systems including universal health coverage, providing an ideal setting for investigating these risk factors.

This study aimed to identify key risk factors contributing to COVID-19 infection and mortality among older adults in South Korea. Age, comorbidity burden, disease severity, and insurance type were examined to assess their associations with infection and mortality rates. By utilizing a large-scale nationwide cohort, this study provides robust evidence of specific risk factors affecting this population.

MATERIALS AND METHODS

Data Source

We used the Korea Disease Control and Prevention Agency-COVID-19-National Health Insurance Service (K-COV-N) cohort data from the National Health Insurance Service (NHIS). The data are provided through the universal health coverage for Koreans. Data from the population aged ≥65 years registered between January 1, 2019, and December 31, 2019, were used for analysis. Death was defined as the loss of national health insurance qualification. For COVID-19 confirmation, individuals who claimed with the coronavirus code from January 1, 2020, to March 31, 2022, were included in the analysis. COVID-19 mortality was defined as death within 30 days from the coronavirus code entered for the last time until April 30, 2022.

Using data from the National Health Insurance Corporation's qualification information for 2020, specifically the data related to insured individuals in the 0th percentile of the calculated insurance premium for January 2020, we indirectly reflected the income level by considering the eligibility for NHIS beneficiaries or Medical Aid recipients. In South Korea, the national social security system, known as Medical Aid, provides medical assistance to low-income individuals who lack the means to sustain their livelihoods or who face financial difficulties.

Study Population

Data from a total of 7,802,796 (n=6,725,628 of non-COVID-19; n=1,077,168 of COVID-19) patients registered between January 1, 2020, and March 31, 2022, were obtained from the NHID database. Based on the qualification data for 2020, those aged ≥65 years were included. Among them, cases where the "C" code (cancer diagnosis),was entered more than once in the primary diagnosis or sub-diagnosis during the 10 years from January 1, 2010, to December 31, 2019, were excluded. Among the group of patients with confirmed COVID-19, only data from those aged ≥65 years were included, and the number of people entered by combining the coronavirus codes from January 1, 2020, to March 31, 2022, was confirmed. Death from COVID-19 was defined as death within 30 days of the last entry of the code U07.1 as a primary or sub-diagnosis, and deaths up to April 30, 22 were included (Fig. 1).

Data Collection

We utilized data on sex, age, type of insurance, residential area, Charlson Comorbidity Index (CCI), and disease severity. The CCI was calculated based on the diagnosis codes recorded from January 1, 2019, to December 31, 2019. Age groups were categorized as 65–74, 75–84, and ≥85 years. The mean and standard deviation were rounded to the nearest decimal place, while the percentages were rounded to the second decimal place. Insurance eligibility was divided into National Health Insurance and Medical Aid recipients. Residential areas were classified as capital regions, including Seoul, Gyeonggi Province, and Incheon.

Disease severity was classified by assessing whether specific treatment codes were present within the infectious period, enabling us to categorize hospitalization and the condition severity.

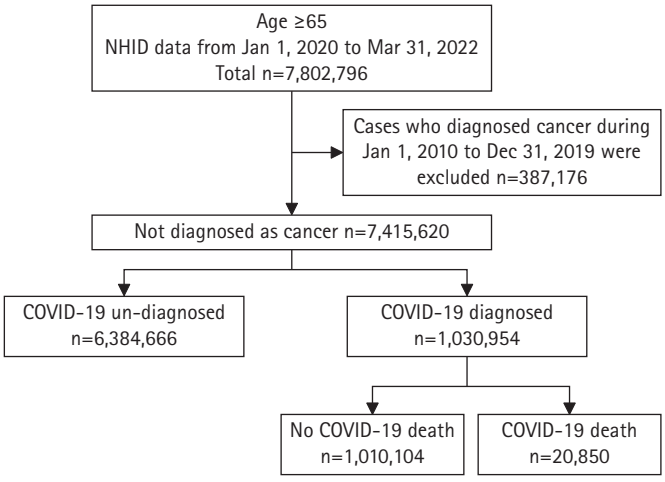

Fig. 1. Flow chart of this study. COVID-19, coronavirus disease 2019; NHID, National Health Information Database.

The treatment levels of "oxygen therapy" and "oxygen by mask or nasal prongs" were defined as "hospitalized mild disease," while "non-invasive ventilation or high-flow oxygen," "intubation and mechanical ventilation," and "ventilation + additional organ support (continuous renal replacement therapy [CRRT], extracorporeal membrane oxygenation [ECMO])" were categorized as "hospitalized severe disease" if implemented. The classification was based on the most severe point of the condition.

Ethical Consideration

This study was approved by the Institutional Review Board of Kyung Hee University Hospital (No. KHUH 2022-11-059). The requirement for informed consent was waived because this study used de-identified administrative data. Also, this study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[8]

Statistical Analysis

Using frequencies and percentages, we compared the characteristics of COVID-19 patients and individuals without confirmed infection. Additionally, we conducted a multivariate logistic regression analysis to identify the factors associated with the occurrence of and death due to COVID-19. We calculated adjusted odds ratios (ORs) for nine factors: region, sex, age group, CCI, four specific diseases, and MA status. We defined the significance level as two-tailed p-values < 0.05.

In the analysis of disease severity, we first compared confirmed cases that were not hospitalized with those that were hospitalized. Second, we compared "hospitalized severe disease" and deceased patients with other patients. Finally, we compared deceased patients with the remaining patients.

RESULTS

Characteristics and Risk Factors for COVID-19 Infection

Among the 7,415,620 participants, 44.33% resided in the capital region. Of the 1,030,954 infected individuals, 49.26% resided in the capital region. A total of 43.53% of non-infected individuals also lived in the capital region. Men comprised 41.87%, and 41.05% of the entire study population and infected individuals, respectively. The 65–74-year age group accounted for 4,263,439 individuals, representing 57.49% of the total population. Among them, 643,625 were affected by COVID-19, corresponding to 62.43% of the 1,030,954 infected individuals. In the 75–84-year age group, 286,940 individuals were affected by COVID-19. The OR for this age group compared with the 65–74-year age group was 0.756 (95% confidence interval [CI], 0.753–0.76), indicating a lower risk of infection. The population aged ≥ 85 years (790,234

Table 1. Baseline characteristics of study and COVID-19 infection risk factor analysis

	All (n = 7,415,620)	Undiagnosed (n = 6,384,666)	Diagnosed (n = 1,030,954)	OR (95% CI)	
				Crude	Adjusted
Residential area (other areas)[a]	4,128,628 (55.67)	3,605,488 (56.47)	523,140 (50.74)	0.794 (0.791–0.797)	0.790 (0.787–0.793)
Sex, female	4,310,600 (58.13)	3,702,839 (58)	607,761 (58.95)	1.040 (1.036–1.044)	1.066 (1.062–1.071)
Age (y)	74.2 ± 7.4	74.4 ± 7.4	73.5 ± 7.3		
65–74	4,263,439 (57.49)	3,619,814 (56.7)	643,625 (62.43)	1 (ref)	1 (ref)
75–84	2,361,947 (31.85)	2,075,007 (32.5)	286,940 (27.83)	0.778 (0.774–0.781)	0.756 (0.753–0.760)
≥ 85	790,234 (10.66)	689,845 (10.8)	100,389 (9.74)	0.818 (0.813–0.824)	0.789 (0.783–0.795)
Morbidity status (Charlson Comorbidity Index)					
0	1,866,266 (25.17)	1,640,556 (25.7)	225,710 (21.89)	1 (ref)	1 (ref)
1	1,816,419 (24.49)	1,560,782 (24.45)	255,637 (24.8)	1.190 (1.183–1.198)	1.217 (1.209–1.224)
≥ 2	3,732,935 (50.34)	3,183,328 (49.86)	549,607 (53.31)	1.255 (1.248–1.261)	1.330 (1.321–1.339)
Disease					
Cardiovascular disease	4,657,874 (62.81)	4,009,958 (62.81)	647,916 (62.85)	1 (0.6134–0.4335)	0.974 (0.969–0.978)
Cerebrovascular disease	1,129,908 (15.24)	963,240 (15.09)	166,668 (16.17)	1.085 (1.079–1.092)	1.057 (1.051–1.063)
Diabetes mellitus	2,411,182 (32.51)	2,065,802 (32.36)	345,380 (33.5)	1.053 (1.049–1.058)	0.963 (0.958–0.968)
Chronic respiratory disease	1,495,683 (20.17)	1,270,376 (19.9)	225,307 (21.85)	1.126 (1.120–1.132)	1.066 (1.061–1.072)
Socioeconomic status represented by national insurance status					
Insurance beneficiaries	6,920,374 (93.32)	5,952,515 (93.23)	967,859 (93.88)	1 (ref)	1 (ref)
Medical Aid	495,246 (6.68)	432,151 (6.77)	63,095 (6.12)	0.898 (0.890–0.906)	0.898 (0.890–0.906)

Values are presented as mean±standard deviation or number (%).
COVID-19, coronavirus disease 2019; OR, odd ratio; CI, confidence interval.
[a]Area except Seoul metropolitan area (Seoul, Gyeonggi Province, Incheon).

individuals, 10.66%) included 100,389 confirmed cases (9.74%). The OR was 0.789 (95% CI, 0.783–0.795), indicating a lower infection risk than that in the 65–74-year age group. These results suggested that the infection risk of COVID-19 did not necessarily increase with age and that the infection rate was lower in older age groups (Table 1).

Among the 1,030,954 confirmed cases, 225,710 (21.89%), 255,637(24.8%), and 549,607(53.31%) had CCI scores of 0, 1, and 2, respectively. Compared with the reference group with CCI scores of 0, the ORs were 1.217 (95% CI, 1.209–1.224) for a CCI score of 1 and 1.33 (95% CI, 1.321–1.339) for a CCI score ≥2. Thus, the infection rate increased with higher CCI scores.

Regarding the relationship between income level and susceptibility to infection, when considering medical insurance status, the OR for Medical Aid recipients compared to that for insurance beneficiaries was 0.898 (95% CI, 0.89–0.906). Thus, Medical Aid recipients had a lower risk of infection than insurance beneficiaries.

Characteristics and COVID-19 Mortality

Comparison of the risk of death based on residential area showed that 47.54% of the deceased individuals resided in the capital region. When using individuals residing in the capital region as the reference, the OR for non-capital region residents confirmed to have COVID-19 was 0.928 (95% CI, 0.903–0.955). Among all confirmed and deceased cases, 41.05% and 42.35% were men, respectively. The OR for the risk of death in women compared to men was 0.607 (95% CI, 0.59– 0.625), indicating a higher risk of death in men. The average age of the confirmed cases was 73.5 years, while the average age of the deceased after confirmation was 82.4 years. Among all confirmed cases, 61.43% were aged 65–74 years, 27.83% were aged 75–84 years, and 9.74% were aged ≥85 years. Comparison of the risk of progression to death using the group aged 65–74 years as a reference, the OR for the 75–84 years age group was 4.406 (95% CI, 4.236–4.582), while that for the ≥85 years age group was 16.032 (95% CI, 15.399–16.691). Compared to the reference group with a CCI score of 0, the ORs for the risk of death after confirmation among patients with CCI scores of 1 and ≥2 were 1.172 (95% CI, 1.111–1.236) and 1.537 (95% CI, 1.459–1.618), respectively. This indicates that as the burden of comorbidities increased (higher CCI score), the risk of death also increased. Compared to the general population with medical insurance, patients with Medical Aid showed a higher risk of death

Table 2. Multivariate analysis of factors associated with COVID-19 death

	All diagnosed (n = 1,030,954)	No COVID-19 death (n = 1,010,104)	COVID-19 death (n = 20,850)	OR (95% CI)	
				Crude	Adjusted
Demographic					
Seoul metropolitan area	507,814 (49.26)	497,902 (49.29)	9,912 (47.54)	1 (ref)	1 (ref)
Other areas[a)]	523,140 (50.74)	512,202 (50.71)	10,938 (52.46)	1.073 (1.044–1.103)	0.928 (0.903–0.955)
Sex, female	607,761 (58.95)	595,741 (58.98)	12,020 (57.65)	0.947 (0.921–0.973)	0.607 (0.590–0.625)
Age (y)	73.5 ± 7.3	73.4 ± 7.1	82.4 ± 8.1		
65–74	643,625 (62.43)	639,753 (63.34)	3,872 (18.57)	1 (ref)	1 (ref)
75–84	286,940 (27.83)	278,933 (27.61)	8,007 (38.4)	4.743 (4.563–4.930)	4.406 (4.236–4.582)
≥85	100,389 (9.74)	91,418 (9.05)	8,971 (43.03)	16.214 (15.604–16.847)	16.032 (15.399–16.691)
Morbidity status (Charlson Comorbidity Index)					
0	225,710 (21.89)	223,402 (22.12)	2,308 (11.07)	1 (ref)	1 (ref)
1	255,637 (24.8)	251,803 (24.93)	3,834 (18.39)	1.474 (1.399–1.552)	1.172 (1.111–1.236)
≥2	549,607 (53.31)	534,899 (52.95)	14,708 (70.54)	2.661 (2.546–2.781)	1.537 (1.459–1.618)
Disease					
Cardiovascular disease	647,916 (62.85)	632,423 (62.61)	15,493 (74.31)	1.727 (1.674–1.782)	1.018 (0.984–1.052)
Cerebrovascular disease	166,668 (16.17)	160,495 (15.89)	6,173 (29.61)	2.227 (2.161–2.295)	1.338 (1.295–1.383)
Diabetes mellitus	345,380 (33.5)	336,990 (33.36)	8,390 (40.24)	1.345 (1.308–1.383)	1.142 (1.107–1.178)
Chronic respiratory disease	225,307 (21.85)	220,460 (21.83)	4,847 (23.25)	1.085 (1.050–1.121)	0.887 (0.857–0.918)
Socioeconomic status represented by national insurance status					
Insurance beneficiaries	967,859 (93.88)	949,945 (94.04)	17,914 (85.92)	1 (ref)	1 (ref)
Medical Aid	63,095 (6.12)	60,159 (5.96)	2,936 (14.08)	2.588 (2.487–2.693)	1.692 (1.623–1.763)

Values are presented as mean±standard deviation or number (%).
COVID-19, coronavirus disease 2019; OR, odd ratio; CI, confidence interval.
[a)]Area except Seoul metropolitan area (Seoul, Gyeonggi Province, Incheon).

(OR = 1.692; 95% CI, 1.623–1.763) (Table 2).

Correlation between Age and COVID-19 Severity and Length of Hospitalization

A total of 173,816 of 1,030,954 confirmed cases aged ≥ 65 years were hospitalized. The analysis was conducted by categorizing individuals into four groups based on the severity of hospitalization: non-hospitalized, hospitalized mild disease, hospitalized severe disease, and death. We evaluated severity based on the most severe condition during the treatment period.

First, using the non-hospitalized group as a reference, we divided the hospitalized patients into age groups and assessed the risk of hospitalization according to the OR. Taking the age group of 65–74 years as the reference, the ORs of hospitalization for the 75–84 and ≥ 85 years age groups were 2.007 (95% CI, 1.983–2.032) and 4.933 (95% CI, 4.857–5.01), respectively, indicating a higher risk of hospitalization with increasing age.

The group exhibiting severe disease during hospitalization was compared with the group showing lower disease severity. Age-specific risks were also compared. Taking the age group of 65–74 years as the reference, the OR for the 75–84 and ≥ 85 years age groups were 3.129 (95% CI, 3.032–3.228) and 10.012 (95% CI, 9.685–10.35), respectively. Thus, the risk of progression to severe or higher COVID-19 severity increased with age. Comparison of mortality rates by age group showed an OR for the ≥ 85-years age group of 16.032 (95% CI, 15.399–16.691), indicating a significantly higher mortality rate as age increased, especially in the ≥ 85 years age group compared to that in the youngest age group. Finally, we compared the length of hospitalization by age, specifically among patients who were hospitalized for more than a week, with other confirmed cases as the control group. Among all infected individuals, 126,964 (12.32%) required hospitalization for more than 1 week.

Among the 643,625 infected individuals aged 65–74 years, 56,253 (8.74%) required hospitalization for more than one week. In comparison, 15.3% of those aged 75–84 years (OR = 1.762; 95% CI, 1.738–1.786) and 26.69% of those aged ≥ 85 years (OR = 3.515; 95% CI, 3.455–3.576) required hospitalization for more than one week. These findings confirmed that as age increases, the duration of hospitalization also tends to increase, indicating a higher need for hospitalization as individuals age. Table 3 shows the severities and hospitalization dates of COVID-19 patients classified by age, and Table 4 shows the results of the multivariate analysis.

DISCUSSION

Our study was conducted using a large-scale population-based cohort. The most influential factor in the severity and mortality rate of COVID-19 in older Korean adults was age. Furthermore, being an Medical Aid recipient and having multiple comorbidities increased the risk of COVID-19 infection progressing to mortality.

The risk of infection was lower for individuals with cardiovascular disease (OR = 0.974; 95% CI, 0.969–0.978) and diabetes (OR = 0.963; 95% CI; 0.958–0.968). In contrast, the risk of infection was higher in individuals with cerebrovascular disease (OR = 1.057; 95% CI, 1.051–1.063) and chronic respiratory disease (OR = 1.066; 95% CI, 1.061–1.072).

The risk of mortality increased significantly with cerebrovascular disease (OR = 1.338; 95% CI, 1.295–1.383) and diabetes (OR = 1.142; 95% CI, 1.107–1.178) but not for cardiovascular disease (OR = 1.018; 95% CI, 0.984–1.052) and chronic respirato-

Table 3. Data of COVID-19 confirmed patients based on severity and length of hospitalization

	Total (n = 1,030,954)	Age group (y)		
		65–74 (n = 643,625)	75–84 (n = 286,940)	≥ 85 (n = 100,389)
COVID-19 severity[a]				
Not hospitalized	857,138 (83.14)	572,423 (88.94)	225,171 (78.47)	59,544 (59.31)
Hospitalized mild	146,648 (14.22)	64,147 (9.97)	51,550 (17.97)	30,951 (30.83)
Hospitalized severe	6,318 (0.61)	3,183 (0.49)	2,212 (0.77)	923 (0.92)
Death	20,850 (2.02)	3,872 (0.6)	8,007 (2.79)	8,971 (8.94)
Hospitalization day (wk)				
< 1	903,990 (87.68)	587,372 (91.26)	243,025 (84.7)	73,593 (73.31)
≥ 1	126,964 (12.32)	56,253 (8.74)	43,915 (15.3)	26,796 (26.69)

Values are presented as number (%).
COVID-19, coronavirus disease 2019.
[a]Hospitalized mild includes oxygen therapy, oxygen by mask or nasal prongs, hospital severe includes non-invasive ventilation, high-flow oxygen, intubation and mechanical ventilation, ventilation+additional organ support (continuous renal replacement therapy, extracorporeal membrane oxygenation); classification was based on the most severe point of the condition.

Table 4. Multivariate analysis on the correlation between age, severity, and length of hospitalization

	Total[a]	Event[b]	Adjusted OR[c] (95% CI)
Hospitalized, mild disease or more severe severity[d]	1,030,954	173,816 (16.86)	
65–74 y	643,625	71,202 (11.06)	1 (ref)
75–84 y	286,940	61,769 (21.53)	2.007 (1.983–2.032)
≥ 85 y	100,389	40,845 (40.69)	4.933 (4.857–5.010)
Hospitalized, severe disease or more severe severity[d]	1,030,954	27,168 (2.64)	
65–74 y	643,625	7,055 (1.1)	1 (ref)
75–84 y	286,940	10,219 (3.56)	3.129 (3.032–3.228)
≥ 85 y	100,389	9,894 (9.86)	10.012 (9.685–10.350)
Death	1,030,954	20,850 (2.02)	
65–74 y	643,625	3,872 (0.6)	1 (ref)
75–84 y	286,940	8,007 (2.79)	4.406 (4.236–4.582)
≥ 85 y	100,389	8,971 (8.94)	16.032 (15.399–16.691)
Admission ≥ 1 week	1,030,954	1,26,964 (12.32)	
65-74 y	643,625	56,253 (8.74)	1 (ref)
75-84 y	286,940	43,915 (15.3)	1.762 (1.738–1.786)
≥ 85 y	100,389	26,796 (26.69)	3.515 (3.455–3.576)

Values are presented as number (%).
COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval.
[a]Number of diagnosed, [b]number of hospitalized patients, [c]adjusted ORs for nine factors (region, gender, age group, Charlson Comorbidity Index, four specific diseases, medical aid status); [d]hospitalized mild includes oxygen therapy, oxygen by mask or nasal prongs, hospital severe includes non-invasive ventilation, high-flow oxygen, intubation and mechanical ventilation, ventilation+additional organ support (continuous renal replacement therapy, extracorporeal membrane oxygenation); classification was based on the most severe point of the condition.

ry disease (OR = 0.887; 95% CI, 0.857–0.918).

Previous studies compared factors such as sex, medical history, disease severity, and mortality related to COVID-19 infection between older and younger age groups.[9-11] One study found that in all age groups, men had a higher oxygen demand and greater disease severity ($p < 0.01$, $p = 0.0083$).[9] Furthermore, univariate analysis revealed that the risk of non-mild COVID-19 was significantly higher ($p < 0.05$) in middle-aged and older adults than in young adults.[9] Another study using data from a total of 1,537 patients reported that in-hospital mortality was associated with older age after adjusting for age, hypertension, diabetes mellitus, and corticosteroid use (risk ratio [RR] = 2.01; 95% CI, 1.59–2.52).[10] These findings are consistent with the main findings of the present study. However, the previous study had limitations in terms of a smaller sample size and shorter observation period (from May 2020 to August 2020) compared to our study.

A previous study conducted using COVID-19-confirmed case data registered in South Korea until May 15, 2020, that evaluated the association between CCI values (3, 4, and 5 or higher) and mortality also found an increasing trend in mortality with increasing age-adjusted CCI score.[11] Although this study included data from a younger age group, a similar trend was observed in the present study.

In this study, patients with diabetes and cerebrovascular diseases had a higher COVID-19-related mortality rate, which is consistent with previously reported findings.[12] However, we observed no significant relationship between cardiovascular disease and COVID-19-related mortality rates. In this study, the cardiovascular disease categories included hypertension, ischemic heart disease, cardiomyopathy, atrial fibrillation, and heart failure. Previous studies have demonstrated that each of these conditions contributes to increased mortality in COVID-19 patients. A review reported that hypertension, which is the most common underlying disease, can increase the severity and mortality rates of COVID-19. However, the use of renin–angiotensin–aldosterone system (RAAS) inhibitors may provide benefits in the course of the disease.[13] Another study found that angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) mitigate COVID-19 mortality rates in patients with hypertension.[14] In the management of hypertension in South Korea, the most commonly used monotherapy is ARB (50.1%). Even in combination therapies (dual therapy), ARB/ACEi regimens dominate, accounting for 89.9% of cases.[15] This contradictory relationship may explain the lack of significance between cardiovascular disease and COVID-19 mortality.

The chronic respiratory disease categories in the present study included obstructive pulmonary disease, chronic bronchitis, emphysema, asthma, persistent asthma, and bronchiectasis. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 report, chronic obstructive pulmonary disease

(COPD) is more likely to worsen with severe COVID-19. However, the impact of COPD on the risk of COVID-19 is unclear, which is consistent with the low risk of infection in our study.[16] In another study investigating the relationship between obstructive pulmonary disease (OPD) and COVID-19, a total of 7,549 patients with a history of COPD were included for comparison of mortality rate. The study found that patients with COPD had higher hospitalization rates (62% vs. 28%) and higher mortality rates (15% vs. 4%; adjusted OR = 2.1; 95% CI, 1.96–2.26; $p < 0.001$) compared to those without COPD.[17] Regarding asthma, a cohort study compared the risk of COVID-19-related mortality between adults using low-dose inhaled corticosteroids (ICS) and those without asthma. The study did not observe a significant difference in mortality risk between patients with and without asthma.[18] Another study suggested that one mechanism of asthma, involving type 2 airway inflammation and ACE2/TMPRSS2 receptor downregulation and the use of controllers such as ICS, might underrepresent COVID-19 symptoms.[19]

In our study, patients with chronic respiratory disease showed decreased mortality rates (OR = 0.887; 95% CI, 0.857–0.918), which could be due to asthma. Second, the prevalence of COPD in South Korea is relatively high, reaching 13.4% in individuals aged ≥ 40 years. However, in COPD, symptoms may remain mild or go unnoticed until the lung function is compromised by > 50%. Moreover, many cases are attributed to aging-related symptoms, leading to underdiagnosis.[20] Lastly, our study has some limitations in the results as we did not consider data on the severity of chronic respiratory disease.

Previous domestic studies examining the association between mortality from COVID-19 and socioeconomic income levels, considering characteristics such as age, sex, and underlying diseases, observed no significant difference in the risk of death between Medical Aid recipients and health insurance beneficiaries.[21] In contrast, in our study, after adjusting for factors such as region, sex, age group, CCI, and major underlying diseases, we observed a higher mortality rate than infection rate in the Medical Aid patient group. This aligns with the findings of another systematic review and meta-analysis of 4.3 million patients from 68 studies which found that socioeconomic determinants were strongly associated with COVID-19 outcomes in racial and ethnic minority populations.[22] The previous domestic study included only 7,590 confirmed cases as of May 15, 2020, which may explain the discordant results.

We identified age as the factor with the greatest impact on the infection rates and subsequent mortality. Therefore, prioritizing the vaccination of older adults may be warranted in future infectious disease situations. Additionally, as age increased, the length of hospitalization tended to increase. Given the gradual aging of society and the increasing elderly population, policies aimed at securing an adequate number of hospital beds are needed. Analysis of the data by insurance type showed a lower infection rate among Medical Aid recipients than among NHIS beneficiaries; however, the mortality rate of Medical Aid recipients was higher. This can be attributed not only to socioeconomic differences, as pointed out in previous studies on COVID-19 infection and mortality rates in the domestic healthcare environment with universal health coverage, but also to other factors that may have had a marked impact, such as poor underlying health conditions, rapid early testing and treatment, transmission-reducing behaviors, and regional preparedness.[23] Considering the relatively high cost of self-testing kits and the surge in demand for masks, which have increased personal hygiene expenses, it is important to implement national policies that provide appropriate support and resources to Medical Aid recipients. This is crucial for preventing economic differences from translating into differences in infection and mortality rates.

Limitations and Strengths

This study has several strengths. First, it benefits from a nationwide cohort in which the entire population is enrolled in health insurance programs. This resulted in a large sample size, which increased the statistical significance of the findings. Additionally, the study focused exclusively on the elderly population aged ≥ 65 years. By identifying the most significant factors related to disease outcomes in older adults, who are generally considered vulnerable to infections due to the high prevalence of underlying health conditions, our findings can be utilized to prioritize management with limited resources in the event of future infectious diseases.

In addition, a previous study comparing age and COVID-19-related mortality in South Korea identified malignant neoplasms as having the highest hazard ratio among comorbidities.[23] In the present study, we excluded patients diagnosed with cancer within the past 10 years to ensure distinctiveness in our analysis. However, this study had some limitations. First, as the population decreases with increasing age, the infection rate among older adults may have been underestimated in the OR. However, the sufficiently large OR for mortality suggests that the results remain valid for evaluating the severity of COVID-19 and the importance of age in policy decisions. Second, statistical errors may have occurred due to the relatively low proportion of Medical Aid recipients compared with that in the total population. According to the "2021 Medical Aid Statistical Yearbook" jointly published by the National Health Insurance Corporation and Health Insurance Review and Assessment Service in October 2022, the number of Medical Aid recipients was 1,516,525, accounting for approximately 2.9% of

the total population (approximately 52.92 million).[24] However, as 39.1% of Medical Aid recipients were aged ≥65 years and this study focused on this age group, our findings are highly significant in evaluating the relationship between COVID-19 and insurance status.

The study's limitation lies in the use of insurance type as a proxy for access to healthcare without accounting for other factors such as living conditions,[25] exposure to smoking, and work environments, which could also contribute to higher infection rates. Reports have suggested an association between smoking and COVID-19 progression and mortality.[26] However, the present study did not include such data, indicating the need for further research in this area. Moreover, the reduction in mortality among individuals surveyed later in the data collection period could be attributed to the commencement of the national COVID-19 vaccination in South Korea.

In this study, the incidence of COVID-19 among Medical Aid beneficiaries was lower than that among NHIS beneficiaries, and the mortality of COVID-19 among Medical Aid beneficiaries was higher than that among NHIS beneficiaries. These findings are in stark contrast to the results of previous studies.[27,28] While other studies have examined the early phase of the COVID-19 pandemic, our study covered a longer period of exceeding 2 years. Therefore, our study better reflects the trend of the COVID-19 pandemic. Because Medical Aid beneficiaries have relatively poor jobs, they may have lost their jobs due to the prolonged COVID-19 pandemic. Due to the COVID-19 pandemic, these individuals could not use community services such as welfare centers and senior citizen centers and likely spent more time at home. This may have reduced human contact, and consequently, reduced the prevalence of COVID-19. However, this is merely speculation, and no precise analysis has been performed. Further studies are needed to confirm this hypothesis. Our results may have been better supported if we had conducted a comparative analysis between COVID-19 infection status and COVID-19-related deaths. However, this analysis was not possible, which is a limitation of our study.

Lastly, as long COVID syndrome has gained attention, discussion continues regarding its long-term effects. However, this study did not evaluate long-term complications, which is a limitation that warrants further investigation.

Conclusion

The most significant factor for COVID-19 infection was the severity of the underlying health conditions, whereas age and socioeconomic status were the most critical factors for post-infection mortality. The results of this study suggest that in the event of a large-scale respiratory infection, policies should prioritize vaccination and the provision of hospital beds for the elderly, rather than focusing solely on underlying health conditions. For individuals receiving Medical Aid, it is crucial to implement measures such as rapid screening tests and ensure the availability of healthcare supplies to correct the pathways contributing to the worsening of infection.

Overall, the results of this study provide valuable insights for the development of policies and interventions in response to respiratory infections, emphasizing the importance of age, underlying health conditions, and socioeconomic factors in determining infection and mortality rates.[29]

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, HL, SK; Data curation, JL, HL, JYL; Formal analysis, JL, HL; Investigation, JL, HL, JYL; Methodology; HL, SK; Project administration, HL, JL; Supervision, HL, JL, SK; Validation, HL, SK, JL, JYL; Writing-original draft, SL, SK; Writing-review & editing, SL, JL, JYL, BK, CWW, CK, JP, HL, SK.

REFERENCES

1. World Health Organization. WHO coronavirus (COVID-19) dashboard: situation by region, country, territory & area [Internet]. Geneva, Switzerland: World Health Organization; 2022 [cited 2023 Sep 10]. Available from: https://covid19.who.int/table.
2. Chams N, Chams S, Badran R, Shams A, Araji A, Raad M, et al. COVID-19: a multidisciplinary review. Front Public Health 2020;8:383.
3. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497-506.
4. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical

characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708-20.
5. Cho SI, Yoon S, Lee HJ. Impact of comorbidity burden on mortality in patients with COVID-19 using the Korean health insurance database. Sci Rep 2021;11:6375.
6. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med 2020;180:934-43.
7. Shim E. Delay-adjusted age-specific COVID-19 case fatality rates in a high testing setting: South Korea, February 2020 to February 2021. Int J Environ Res Public Health 2021;18:5053.
8. Noh JH, Jung HW, Ga H, Lim JY. Ethical guidelines for publishing in the Annals of Geriatric Medicine and Research. Ann Geriatr Med Res 2022;26:1-3.
9. Statsenko Y, Al Zahmi F, Habuza T, Almansoori TM, Smetanina D, Simiyu GL, et al. Impact of age and sex on COVID-19 severity assessed from radiologic and clinical findings. Front Cell Infect Microbiol 2021;11:777070.
10. Mas-Ubillus G, Ortiz PJ, Huaringa-Marcelo J, Sarzo-Miranda P, Munoz-Aguirre P, Diaz-Ramos A, et al. High mortality among hospitalized adult patients with COVID-19 pneumonia in Peru: a single centre retrospective cohort study. PLoS One 2022;17:e0265089.
11. Katoto PD, Aboubacar I, Oumarou B, Adehossi E, Anya BM, Mounkaila A, et al. Clinical features and predictors of mortality among hospitalized patients with COVID-19 in Niger. Confl Health 2021;15:89.
12. Kim DW, Byeon KH, Kim J, Cho KD, Lee N. The correlation of comorbidities on the mortality in patients with COVID-19: an observational study based on the Korean National Health Insurance Big Data. J Korean Med Sci 2020;35:e243.
13. Peng M, He J, Xue Y, Yang X, Liu S, Gong Z. Role of hypertension on the severity of COVID-19: a review. J Cardiovasc Pharmacol 2021;78:e648-55.
14. Zhang P, Zhu L, Cai J, Lei F, Qin JJ, Xie J, et al. Association of inpatient use of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers with mortality among patients with hypertension hospitalized with COVID-19. Circ Res 2020;126:1671-81.
15. Korean Society of Hypertension; Hypertension Epidemiology Research Working Group. Korea Hypertension Fact Sheet 2022 [Internet]. Seoul, Korea: Korean Society of Hypertension; 2022 [cited 2023 Sep 10]. Available from: http://www.koreanhypertension.org/reference/guide?mode=read&idno=10079.
16. Agusti A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, et al. Global initiative for chronic obstructive lung disease 2023 report: GOLD executive summary. Eur Respir J 2023;61:2300239.
17. Meza D, Khuder B, Bailey JI, Rosenberg SR, Kalhan R, Reyfman PA. Mortality from COVID-19 in patients with COPD: a US study in the N3C Data Enclave. Int J Chron Obstruct Pulmon Dis 2021;16:2323-6.
18. Dolby T, Nafilyan V, Morgan A, Kallis C, Sheikh A, Quint JK. Relationship between asthma and severe COVID-19: a national cohort study. Thorax 2023;78:120-7.
19. Assaf SM, Tarasevych SP, Diamant Z, Hanania NA. Asthma and severe acute respiratory syndrome coronavirus 2019: current evidence and knowledge gaps. Curr Opin Pulm Med 2021;27:45-53.
20. Kim DK, Rhee CK. Updated view on the treatment of chronic obstructive pulmonary disease in Korea. J Korean Med Assoc 2021;64:225-31.
21. Lee H, Lee JR, Jung H, Lee JY. Power of universal health coverage in the era of COVID-19: a nationwide observational study. Lancet Reg Health West Pac 2021;7:100088.
22. Magesh S, John D, Li WT, Li Y, Mattingly-App A, Jain S, et al. Disparities in COVID-19 outcomes by race, ethnicity, and socioeconomic status: a systematic-review and meta-analysis. JAMA Netw Open 2021;4:e2134147.
23. Byeon KH, Kim DW, Kim J, Choi BY, Choi B, Cho KD. Factors affecting the survival of early COVID-19 patients in South Korea: an observational study based on the Korean National Health Insurance big data. Int J Infect Dis 2021;105:588-94.
24. Health Insurance Review & Assessment Service. 2021 Medical Aid Statistics [Internet]. Wonju, Korea: Health Insurance Review & Assessment Service; 2023 [cited 2023 Sep 10]. Available from: https://www.hira.or.kr/bbsDummy.do?pgmid=HIRAJ030000007001&brdScnBltNo=4&brdBltNo=5&pageIndex=1&pageIndex2=1.
25. Tsai J, Wilson M. COVID-19: a potential public health problem for homeless populations. Lancet Public Health 2020;5:e186-7.
26. Vardavas CI, Nikitara K. COVID-19 and smoking: a systematic review of the evidence. Tob Induc Dis 2020;18:20.
27. Jeong HE, Lee J, Shin HJ, Shin JY. Socioeconomic disparities in Korea by health insurance type during the COVID-19 pandemic: a nationwide study. Epidemiol Health 2021;43:e2021007.
28. Oh TK, Choi JW, Song IA. Socioeconomic disparity and the risk of contracting COVID-19 in South Korea: an NHIS-COVID-19 database cohort study. BMC Public Health 2021;21:144.
29. Jang SN, Kim CO. Care inequality among older adults during the COVID-19 pandemic. Ann Geriatr Med Res 2020;24:229-31.

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The Relationship between Chronic Musculoskeletal Pain and Sarcopenia Risk in Community-Dwelling Older Adults: A Cross-Sectional Study

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Background: This study aimed to better understand the relationship between chronic musculoskeletal pain and the risk of sarcopenia in older adults. **Methods:** The risk of sarcopenia was assessed in 210 older adults using the SARC-F (strength, assistance with walking, rising from a chair, ascending stairs, and falls) questionnaire. Geriatric pain measures were used to assess pain. We also recorded the pain sites (ankles/feet, wrists/hands, upper back, lower back, neck, shoulder, hips, and knees). **Results:** Participant mean age was 72.4±7 years, and 109 (51.9%) of the participants were female. The prevalence rates of sarcopenia and chronic musculoskeletal pain were 60% and 92.9%, respectively. Older adults at risk of sarcopenia had a higher mean age, body mass index (BMI), number of comorbidities and falls, presence of chronic pain, pain intensity, and pain sites. Sarcopenia risk was correlated with chronic pain intensity (current and last 7 days) (r=0.506, p<0.001 and r=0.584, p<0.001, respectively), multisite pain (r=0.442, p<0.001), and Geriatric Pain Measure score (r=0.730; p<0.001). Age (odds ratio [OR]=1.1; 95% confidence interval [CI], 1.0–1.2), BMI (OR=1.1; 95% CI, 1.0–1.2), and geriatric pain (OR=1.1; 95% CI, 1.0–1.1) were associated with sarcopenia risk. **Conclusions:** The risk of sarcopenia is linked to chronic pain, which frequently occurs in geriatric populations. Our study results also showed that higher pain intensity was associated with a higher risk of sarcopenia. Older adults at risk for sarcopenia often experience chronic musculoskeletal pain, which must be better recognized. Moreover, its significance must be noted in the treatment process.

Key Words: Chronic pain, Aged, Sarcopenia, Musculoskeletal pain, Muscular atrophy

INTRODUCTION

Sarcopenia is a progressive and generalized skeletal muscle disorder characterized by accelerated loss of muscle mass and function in older adults.[1] It can lead to abnormal gait, balance disorders, falls, fractures, disability, and death in older adults.[2] The varying reported prevalence rates, from 0.8% to 64.8%, can be attributed to differences in population, lifestyle, age, setting, and culture, as well as the instruments used to diagnose sarcopenia.[3-7]

One of the most prevalent medical conditions in older adults (≥65 years), chronic pain, is also highly disabling. In older adults, chronic pain impairs mobility, is linked to depression and anxiety, and can damage social and familial ties.[8] According to estimates, >50% of older adults experience chronic pain and 70% report experiencing pain at multiple sites.[9] The most common painful conditions affecting older adults are arthritis-related; however, older adults also experience a high incidence of chronic systemic diseases that can cause pain, such as cancer-related, diabetes-related, and post-stroke pain. Additionally, pain may be a stressor that accelerates the decline in health and function as an individual ages. Compared to older adults without pain, those with pain are less physically active, have worse functional mobility, and experience more comorbidities.[10] The consequences of pain, such as those discussed here, may contribute to increased susceptibility to sarcope-

nia and other geriatric syndromes that are prevalent in older adults.

Numerous studies have examined the relationships between pain and specific geriatric syndromes, including falls, depression, cognitive decline, and functional limitations.[11-13] While an increasing number of studies have examined how pain and sarcopenia are connected, so far, the results are inconsistent.[14,15] Data from a prospective study showed that pain was a strong predictor of sarcopenia, except for knee pain.[16] In addition, the risk of sarcopenia may change depending on the nature of the pain being experienced, as pain intensity and location significantly affect functional impairments caused by pain. Therefore, the present study examined the relationship between chronic musculoskeletal pain and the risk of sarcopenia, pain intensity, and pain location in community-dwelling older adults.

MATERIALS AND METHODS

Study Design and Participants

The population for this cross-sectional research consisted of community-dwelling older adults in Teyyaredüzü District in Giresun and Akçaabat-Söğütlü District in Trabzon, Turkey. The populations of Teyyaredüzü district and Söğütlü neighborhood are 15,576 and 23,189, respectively.[17,18] According to the information obtained from the Turkish Statistical Institute (Türkiye İstatistik Kurumu), older adults comprised 9.7% of the population in 2021. Among those, this study included 3,760 older adults.[19] The sample size was calculated using OpenEpi version 3.01 (https://www.openepi.com) considering the prevalence of sarcopenia risk. Erbas Sacar et al.[20] reported a sarcopenia prevalence of 12.7% in Turkey. Therefore, according to this prevalence, a minimum of 164 participants was required, with a margin of error of 5% and a confidence interval of 95%. Based on this prevalence rate, we evaluated 267 community-dwelling older adults for eligibility.

Forty-three older adults did not want to participate in the study, and 14 older adults did not meet the inclusion criteria. Therefore, this study included 210 older adults (Fig. 1). The inclusion criteria were age ≥ 65 years and Mini-Mental State Examination (MMSE) score of ≥ 24.[21] The exclusion criteria were hearing impairments that could limit communication, presence of depression and neuropathic pain, and unwillingness to participate in the study. The 15-item Geriatric Depression Scale (GDS-15) was used to assess depression. No, mild, moderate, and severe depression were defined as scores of 0–4, 5–8, 9–11, and 12–15, respectively.[22] We applied the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain questionnaire to evaluate neuropathic pain. Among the 24 total point, 12 points or more suggest the presence of neuropathic pain.[23]

Ethics Approval and Consent to Participate

The Ethics Committee of Ordu University for Clinical Researches (No. 2022/134) granted permission for this study, which was conducted according to the guidelines of the Declaration of Helsinki. Before the study started, all of the participants provided written permission. This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[24]

Outcome Measures

We recorded participant physical and sociodemographic information, including age, body mass index (BMI, kg/m^2), sex, education (years), number of comorbidities (hypertension, asthma, heart attack, cancer, kidney disease, diabetes, chronic lung disease, congestive heart failure, and arthritis), medications, and falls in the previous year. The MMSE was used to determine whether older adults were cognitively capable of participating in this study. In clinical practice and research, the MMSE is frequently used to assess general cognitive function. The possible MMSE scores range from 0 to 30, with higher scores indicating better cognitive performance.[21]

The responses to the survey question "have you had pain in any part of your body that has lasted for 3 months or more?" were used to determine the presence of chronic musculoskeletal pain.[25] Participants who responded "yes" to this question were considered to have chronic musculoskeletal pain. They were then asked, "in what part(s) of your body do you feel this pain?" which choices among the neck, shoulder, upper back, wrists or hands, lower back, hips, knees, ankles, or feet.

Comprehensive pain was assessed using the Geriatric Pain Measure (GPM), a 24-item scale that is easily applied in geriatric outpatients. This scale consists of five dimensions: pain with movement, withdrawal due to pain, pain intensity, pain with strenuous activities, and pain with other activities. Twenty-two scale items

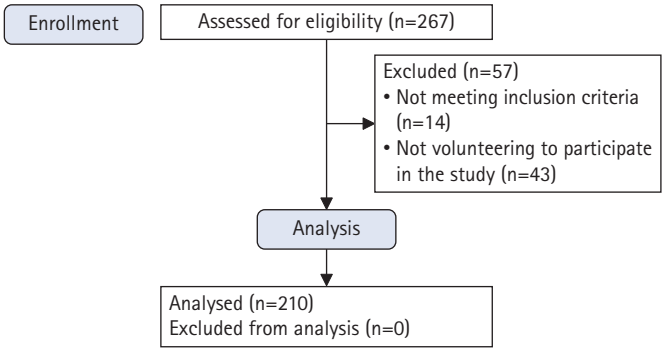

Fig. 1. Flow chart of study participants.

are scored in pairs, while the other two are assigned numeric values between 0 and 10. The sum of the "yes" responses yields a score from 0 to 42. The items on the scale are multiplied by 2.38 to normalize the score from 0–100 to obtain the final GPM score. Total GPM scores of 0–29, 30– 69, and 70 points are categorized as mild, moderate, and severe pain, respectively.[26,27] We recorded pain intensity based on the responses to two questions on the GPM: "If you were to rate your pain on a scale from 0 to 10, with 0 representing no pain and 10 representing the most terrible suffering imaginable, how bad is it right now?" and "How severe was your average pain in the previous 7 days?"

The SARC-F questionnaire consists of five sections: falls (how many times the individual has fallen in the last year), ambulation (the individual's capacity to move about their room), rising from a chair (the individual's capacity to get up from a chair), climbing stairs (the individual's capacity to climb a flight of 10 stairs), and strength (the individual's capacity to lift 2.5 kg). The scores range from 0 to 2 points, with 0 meaning no difficulty, 1 meaning some difficulty, and 2 meaning great difficulty or inability. For falls, score of 0, 1, and 2 correspond to 0, 1–3, and ≥ 4 falls in the last year, respectively. Individuals with summed scores of the five component scores of ≥ 4 points from a possible range of 0–10 points are considered to be at risk for sarcopenia.[28]

Statistical Analyses

We performed the statistical analysis using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA). The normality of the distribution of the variables was checked using the Shapiro–Wilk test. Numbers and percentages were used to represent categorical variables, whereas means and standard deviations were used to represent continuous variables. The chi-square test for categorical variables was used to compare the sarcopenia risk (SARC-F < 4 and ≥ 4) and pain (mild, moderate, and severe) groups. Both independent samples t-test and Mann–Whitney U tests were used to compare continuous variables. The Pearson correlation coefficient was used to calculate the correlations between SARC-F scores and pain assessments (GPM total score, pain intensity today and in the last 7 days, and multisite pain). The correlations were graded as follows: 0.81–1.00, very strong; 0.61–0.80, strong; 0.41–0.60, moderate; and 0.40, weak.[29] We applied multivariate logistic regression analyses to determine the association between chronic musculoskeletal pain and sarcopenia risk (SARC-F). We observed no multicollinearity between the independent variables according to the variance inflation factor (VIF) and correlation coefficient values. Statistical significance was set at $p < 0.05$.

RESULTS

We recruited a total of 210 older adults with a mean age of 72.4 ± 7.0 years. Most of the older adults were women (51.9%) and had chronic pain, multisite pain, and sarcopenia risk (60%). The mean age, BMI, proportion of female sex, comorbidities, presence of chronic pain, pain intensity, pain sites, and number of falls were higher in older adults at risk of sarcopenia. The demographic and clinical details of the participants are presented in Table 1.

In this study, most older adults (48.1%) experienced moderate pain. The subgroup prevalence of SARC-F scores according to pain severity is shown in Table 2. The SARC-F items and total scores differed among the three pain groups. The severe pain subgroup had more difficulty with the SARC-F items. As pain severity increased, the prevalence of sarcopenia also increased.

We observed a significant correlation between sarcopenia risk and chronic pain intensity (today and last 7 days), multisite pain, and total GPM score ($p < 0.001$) (Table 3). Assessment of the distribution of pain sites according to sarcopenia risk showed that older adults at risk of sarcopenia had higher numbers of all pain sites than did those without sarcopenia risk.

As shown in Table 4, the logistic regression model was statistically significant, $\chi^2(3) = 128.534$, $p < 0.001$. The model explained 62.1% (Nagelkerke R^2) of the variance in the risk of sarcopenia. Age, BMI, and GPM were statistically significant variables in the logistic regression model. Increased age, high BMI, and severe pain were associated with increased risks of sarcopenia.

In older adults with and without sarcopenia, the knee, lower back, and upper back were the most common sites of pain (Fig. 2). Older adults at risk for sarcopenia had more chronic musculoskeletal pain than those without sarcopenia. Knee pain, which is the most common site of pain, was found in 75.4% of older adults at risk of sarcopenia, while it was 35.7% in older adults without sarcopenia risk.

DISCUSSION

In face-to-face interviews with community-dwelling older adults, > 50% of the study participants reported having pain for at least three months. In addition, the prevalence of sarcopenia risk, as determined using the SARC-F scale, was 60%. We observed the significant presence and severity of chronic pain in many older adults at risk for sarcopenia. We also demonstrated a significant correlation between chronic pain and the risk of sarcopenia in this cross-sectional study of older adults. As pain severity increased, the prevalence of sarcopenia also increased. Age, BMI, and pain severity increased the risk of sarcopenia. Furthermore, older adults at risk of sarcopenia reported more incidents of knee and multisite pain compared to

Table 1. Demographics and basal clinical features of the participants

	Total (n = 210)	SARC-F ≥ 4 (n = 126)	SARC-F < 4 (n = 84)	p-value
Age (y)	72.4 ± 7.0	73.8 ± 7.6	70.3 ± 5.7	< 0.001*
BMI (kg/m^2)	28.7 ± 6.1	29.7 ± 6.9	27.0 ± 3.9	0.001*
Sex, female	109 (51.9)	80 (63.5)	29 (34.5)	< 0.001*
Education (y)				
No	72 (34.2)	54 (42.9)	18 (21.4)	0.002*
0–5	107 (51)	59 (46.8)	48 (57.1)	
≥ 6	31 (14.8)	13 (10.3)	18 (21.5)	
Number of comorbidity	2 (0–6)	2 (0–6)	1 (0–4)	< 0.001*
Number of medications	2 (0–11)	2 (0–11)	1 (0–9)	< 0.001*
Falls	1 (0–2)	1 (0–2)	0 (0–2)	< 0.001*
Chronic pain, yes	195 (92.9)	125 (99.2)	70 (83.3)	< 0.001*
SARC-F (0–10)	4 (0–10)	6 (4–10)	2 (0–3)	< 0.001*
Geriatric pain measure	62 ± 22.7	73.9 ± 16.0	43.3 ± 18.6	< 0.001*
Pain intensity today (0–10)	6 (0–10)	7 (0–10)	4 (0–10)	< 0.001*
Pain intensity last 7 days (0–10)	6 (0–10)	6 (2–10)	4 (0–10)	< 0.001*
Number of pain sites				< 0.001*
0	15 (7.1)	1 (0.8)	14 (16.7)	
1	46 (21.9)	16 (12.7)	30 (35.7)	
2	51 (24.3)	29 (23)	22 (26.2)	
3	35 (16.7)	25 (19.8)	10 (11.9)	
4$^+$	63 (30)	55 (43.7)	8 (9.6)	

Values are presented as mean±standard deviation or number (%) or median (min–max).
SARC-F, strength, assistance with walking, rising from a chair, ascending stairs, and falls.
*p<0.05.

Table 2. SARC-F: subgroup prevalence and item-response of indicators

SARC-F	Response (%)			p-value
	Mild pain (0–29)	Moderate pain (30–69)	Severe pain (70–100)	
Subgroup prevalence (%)	11.4	48.1	40.5	
Item-response				
Strength-difficulty lifting and carrying 10 lb				< 0.001*
0 (None)	58.3	35.6	9.4	
1 (Some)	41.7	51.5	40.0	
2 (A lot or unable)	0	12.9	50.6	
Climb stairs-difficulty climbing a flight of 10 stairs				< 0.001*
0 (None)	41.7	16.8	2.4	
1 (Some)	58.3	64.4	24.7	
2 (A lot or unable)	0	18.8	72.9	
Assistance in walking-difficulty walking across a room				< 0.001*
0 (None)	83.3	66.3	20.0	
1 (Some)	16.7	32.7	51.8	
2 (A lot, use aids, or unable)	0	1	28.2	
Rise from a chair-difficulty transferring from a chair or bed				< 0.001*
0 (None)	70.8	41.6	3.5	
1 (Some)	29.2	54.5	57.6	
2 (A lot or unable without help)	0	4	38.8	
Falls-times fallen in the past year				0.005*
0 (None)	70.8	52.5	35.3	
1 (1–3 falls)	20.8	36.6	38.8	
2 (≥ 4 falls)	8.3	10.9	25.9	
SARC-F (total) ≥ 4				< 0.001*
No	91.7	55.4	7.1	
Yes	8.3	44.6	92.9	

SARC-F, strength, assistance with walking, rising from a chair, ascending stairs, and falls.
*p<0.05.

Table 3. Correlations among sarcopenia risk and chronic pain intensity, multisite pain, and total score of GPM

	Multisite pain	Pain intensity today	Pain intensity last 7 days	GPM	SARC-F
Multisite pain	-	0.436**	0.493**	0.547**	0.442**
Pain intensity today	0.436**	-	0.727**	0.847**	0.506**
Pain intensity last 7 days	0.493**	0.727**	-	0.833**	0.584**
GPM	0.547**	0.847**	0.833**	-	0.730**
SARC-F	0.442**	0.506**	0.584**	0.730**	-

GPM, Geriatric Pain Measure; SARC-F, strength, assistance with walking, rising from a chair, ascending stairs, and falls.
**p<0.001.

Table 4. Logistic regression analysis between multisite pain, GPM score, and sarcopenia risk status

	B	SE	Wald	df	Sig.	Exp(B)	
						OR	95% CI
Age	0.111	0.036	9.365	1	0.002*	1.117	1.041–1.199
BMI	0.118	0.046	6.526	1	0.011*	1.126	1.028–1.233
GPM	0.101	0.014	49.206	1	< 0.001*	1.106	1.075–1.138
Constant	-16.732	3.428	23.817	1	< 0.001	0.000	-

GPM, Geriatric Pain Measure; BMI, body mass index; SE, standard error; OR, odds ratio; CI, confidence interval.
Omnibus test (χ^2=128.534, df=3, p<0.001), Hosmer–Lemeshow test (p>0.05), Nagelkerke R^2=0.621.
*p<0.05.

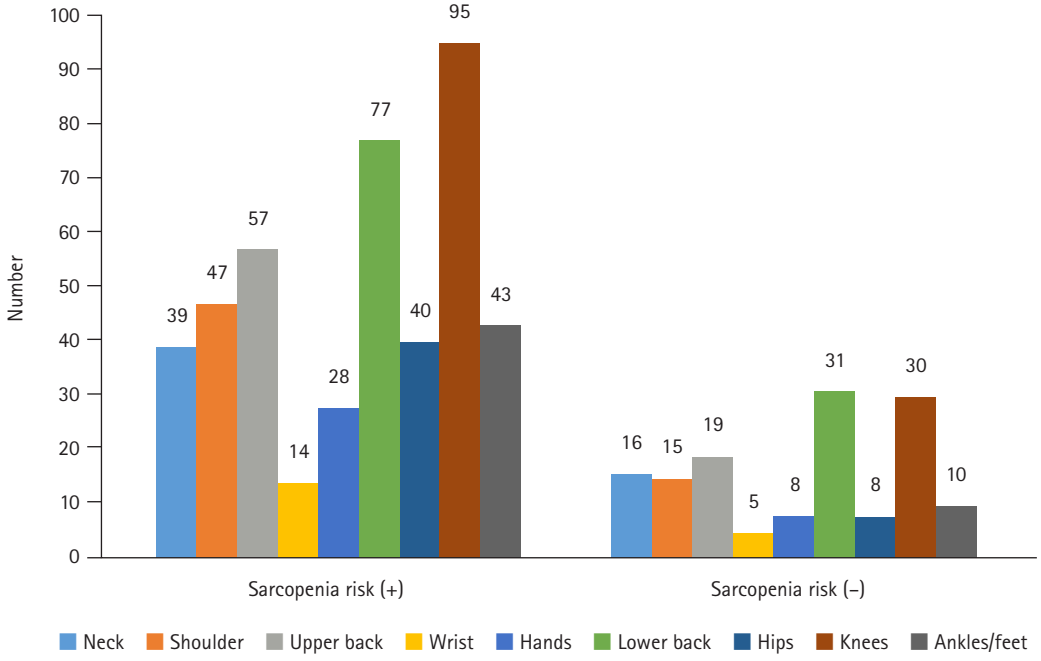

Fig. 2. Distributions of pain site in older adults with and without sarcopenia risk.

those without sarcopenia.

In the present study, the risk of sarcopenia increased with advancing age and high BMI and was more prevalent in women than in men. Additionally, the mean age, BMI, and comorbidities were higher in older adults at risk for sarcopenia, in line with the literature. In previous research among older adults, these factors were also associated with an increased risk of sarcopenia.[30] The possible explanations for these findings may be the significantly higher skeletal muscle mass, physical fitness, and muscle strength in men.[31] In addition, muscle loss starts to increase at 70 years of age.[32] The loss of muscle mass may be linked to a higher rate of disability, lower functional capacity, basal metabolic rate, and bone mineral density, which may have a detrimental impact on sarcopenia.[31] Furthermore, aging and obesity induce fat infiltration into muscles.

Therefore, advanced age and high BMI may cause sarcopenia by impairing muscle quality and function.[31,33] In addition to these factors, comorbidities such as diabetes and end-stage organ diseases are also associated with sarcopenia, as they cause losses of muscle mass and strength.[32] These previous findings support our results related to female sex, age, BMI, and comorbidities.

We observed a prevalence of chronic pain of 92.9%, which is consistent with that reported in a previous study of 873 participants >60 years of age. The previous study reported a prevalence of pain of 41.2% in women and 33.2% in men, with approximately 88% of patients aged 60–75 years of both sexes.[15] In a one-year prospective cohort study, 64 (7.3%) older people who were followed for one year developed sarcopenia. Sarcopenia was more likely to occur in older adults who reported experiencing pain than in those who did not. Women and men with lower back pain, pain in more than one location, joint pain, and moderate-to-severe pain also had higher risks of sarcopenia, consistent with the results of the present study. Our findings regarding the relationship between chronic pain and sarcopenia risk are supported by the findings of previous studies that also reported associations between chronic pain and functional impairment.[34-37] This relationship could be cyclic, where long-lasting pain leads to decreased activity, resulting in muscle weakening, further pain, and reduced activity. However, the exact duration for pain to prompt individuals to cease their physical activity and experience muscle loss remains undetermined; therefore, further research is warranted on this subject.

In this study, participants with severe pain had the highest prevalence of sarcopenia. Additionally, high pain severity was associated with an increased risk of sarcopenia. This could be because participants in the severe pain group were afraid of pain and did not want to perform maximal voluntary contractions. However, arthrogenous muscle inhibition is thought to occur because changes in afferent input from the affected joint cause decreased efferent motor neuron stimulation of nearby skeletal muscles to decrease.[38] Furthermore, the etiology of pain, such as radiculopathy, diabetic polyneuropathy, and knee osteoarthritis, can affect muscular strength and mass.

In the present study, the knee was the most common site of pain. However, we did not collect data on the etiology of pain. In contrast, a previous study reported a significantly increased risk of osteoarthrosis among older adults who were experiencing pain.[15] Additionally, their prospective cohort study investigated the impact of osteoarthritic lower extremity pain on muscle strength and mass in the lower extremity. Scott et al.[38] reported that knee and hip pain as well as more severe knee pain, stiffness, and dysfunction were predictive of a greater decline in lower extremity muscle strength and quality in older women. The primary finding of this study indicates that patient-reported osteoarthritis pain serves as a more accurate predictor of muscle wasting in older adults. This outcome aligns with the findings of a previous study. Foley et al.[39] demonstrated that lower extremity joint pain, stiffness, and dysfunction (but not radiographic osteoarthritis) were associated with declines in muscle parameters over a period of nearly 3 years in women. The association of pain with decreased muscle strength, performance, and quality in these studies may explain the high prevalence of pain in older adults at risk of sarcopenia in our study.

In this study, upper and lower back pain were the most common complaints after knee pain in older adults at risk of sarcopenia. Reduced muscle mass and strength are typical symptoms of age-related skeletal muscle sarcopenia.[1] Alterations in postural alignment often occur to compensate for decreased muscle strength in older adults.[40] An incorrect body position negatively influences muscle function and can cause structural changes in overloaded parts of the spine, leading to pain, especially in older adults.[41] Additionally, back muscle function influences thoracic spinal compressive loading, which may contribute to the development of upper back pain.[42] Moreover, diminished trunk muscle strength and endurance are linked to lower back pain.[43] These possible causes may partially explain the relationship between sarcopenia However, additional studies examining these causal relationships are needed.

This study has several limitations. First, as we used SARC-F to assess sarcopenia risk, our results may differ from those of studies involving other populations using different sarcopenia criteria such as those proposed by the European Working Group on Sarcopenia in Older People.[44] Although SARC-F appears to have limited screening capacity for excluding sarcopenia, it is simple, useful, feasible, and does not require sophisticated equipment; in addition, it has been extensively validated in the scientific literature.[45] Tsuji et al.[1] demonstrated the correlation of SARC-F scores with pain disability assessment scale scores, indicating pain-related disability. Second, the cross-sectional nature of this study made it difficult to establish a timeline for the development of sarcopenia and chronic pain. Further prospective cohort studies examining the association between sarcopenia, pain-related factors, and treatment outcomes in older community-dwelling adults with chronic musculoskeletal pain are required. Third, we did not collect information on the causes of pain or its treatment, which remains a key area for future research. Finally, we only included relatively young older adults. Therefore, further research on the association between pain and sarcopenia in older adults is required.

Our findings of a high rate of chronic pain in the older adult population, which was associated with a high risk of sarcopenia, warrant the development of systematic approaches to proactively identify older adults with these conditions. Many older adults ex-

perience multisite pain, in addition to high levels of chronic pain, making it especially important to consider this population when designing pain management strategies. Further studies are needed to determine the timing of sarcopenia and chronic musculoskeletal pain. The results of this study highlight the need for early pain interventions in the management of sarcopenia and the identification of vulnerable populations that might be experiencing pain.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, UKS; Data curation, UKS, AYŞ; Formal analysis, UKS, AYŞ; Investigation, UKS; Writing-original draft, UKS, AYŞ; Writing-review & editing, UKS, AYŞ.

REFERENCES

1. Tsuji H, Tetsunaga T, Tetsunaga T, Misawa H, Oda Y, Takao S, et al. Evaluation of SARC-F and SARC-CalF for sarcopenia screening in patients with chronic musculoskeletal pain: a prospective cross-sectional study. Medicine (Baltimore) 2022;101:e29568.
2. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis. Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010;39:412-23.
3. Bahat G, Tufan A, Kilic C, Karan MA, Cruz-Jentoft AJ. Prevalence of sarcopenia and its components in community-dwelling outpatient older adults and their relation with functionality. Aging Male 2020;23:424-30.
4. Simsek H, Meseri R, Sahin S, Kilavuz A, Bicakli DH, Uyar M, et al. Prevalence of sarcopenia and related factors in community-dwelling elderly individuals. Saudi Med J 2019;40:568-74.
5. Erkoyun E, Ucku R. The prevalence of sarcopenia risk and associated factors in patients aged 65-79 years living in a district of Izmir province of Turkey. Turk J Phys Med Rehabil 2020;66:10-6.
6. Savas S, Taskiran E, Sarac FZ, Akcicek F. A cross-sectional study on sarcopenia using EWGSOP1 and EWGSOP2 criteria with regional thresholds and different adjustments in a specific geriatric outpatient clinic. Eur Geriatr Med 2020;11:239-46.
7. Ates Bulut E, Soysal P, Isik AT. Frequency and coincidence of geriatric syndromes according to age groups: single-center experience in Turkey between 2013 and 2017. Clin Interv Aging 2018;13:1899-905.
8. Schwan J, Sclafani J, Tawfik VL. Chronic pain management in the elderly. Anesthesiol Clin 2019;37:547-60.
9. Patel KV, Guralnik JM, Dansie EJ, Turk DC. Prevalence and impact of pain among older adults in the United States: findings from the 2011 National Health and Aging Trends Study. Pain 2013;154:2649-57.
10. Perna S, Alalwan TA, Al-Thawadi S, Negro M, Parimbelli M, Cerullo G, et al. Evidence-based role of nutrients and antioxidants for chronic pain management in musculoskeletal frailty and sarcopenia in aging. Geriatrics (Basel) 2020;5:16.
11. Kroenke K, Wu J, Bair MJ, Krebs EE, Damush TM, Tu W. Reciprocal relationship between pain and depression: a 12-month longitudinal analysis in primary care. J Pain 2011;12:964-73.
12. Karp JF, Reynolds CF, Butters MA, Dew MA, Mazumdar S, Begley AE, et al. The relationship between pain and mental flexibility in older adult pain clinic patients. Pain Med 2006;7:444-52.
13. Wilkie R, Peat G, Thomas E, Croft P. Factors associated with participation restriction in community-dwelling adults aged 50 years and over. Qual Life Res 2007;16:1147-56.
14. Scott D, Blyth F, Naganathan V, Le Couteur DG, Handelsman DJ, Seibel MJ, et al. Prospective associations of chronic and intrusive pain with sarcopenia and physical disability amongst older Australian men: the Concord Health and Ageing in Men Project. Exp Gerontol 2021;153:111501.
15. Lin T, Huang X, Guo D, Zhao Y, Song Q, Liang R, et al. Pain as a risk factor for incident sarcopenia in community-dwelling older adults: a 1-year prospective cohort study. J Am Geriatr Soc 2023;71:546-52.
16. Murphy RA, Ip EH, Zhang Q, Boudreau RM, Cawthon PM, Newman AB, et al. Transition to sarcopenia and determinants of transitions in older adults: a population-based study. J Gerontol A Biol Sci Med Sci 2014;69:751-8.
17. Turkiye Provincial District Neighborhood Village Population. General information of Teyyaredüzü Neighborhood population [Internet]. Ankara, Turkey: Türkiye Provincial District Neighborhood Village Population; 2022 [cited 2023 Sep 6]. Available from: https://www.nufusune.com/30722-giresun-merkez-teyyareduzu-mahallesi-nufusu.
18. Turkiye Provincial District Neighborhood Village Population. General information of Söğütlü District population [Internet]. Ankara, Turkey: Türkiye Provincial District Neighborhood Village Population; 2022 [cited 2023 Sep 6]. Available from:

https://www.nufusune.com/156317-trabzon-akcaabat-sogutlu-mahallesi-nufusu.
19. Turkish Statistical Institute. Seniors with statistics, 2021 [Internet]. Ankara, Turkey: Turkish Statistical Institute; 2022 [cited 2023 Sep 6]. Available from: https://data.tuik.gov.tr/Bulten/Index?p=Istatistiklerle-Yaslilar-2021-45636.
20. Erbas Sacar D, Kilic C, Karan MA, Bahat G. Ability of SARC-F to find probable sarcopenia cases in older adults. J Nutr Health Aging 2021;25:757-61.
21. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.
22. Yesavage JA, Sheikh JI. 9/Geriatric depression scale (GDS) recent evidence and development of a shorter version. Clinical Gerontol 1986;5:165-73. https://doi.org/10.1300/J018v05n01_09.
23. Bennett M. The LANSS Pain Scale: the Leeds assessment of neuropathic symptoms and signs. Pain 2001;92:147-57.
24. Noh JH, Jung HW, Ga H, Lim JY. Ethical guidelines for publishing in the Annals of Geriatric Medicine and Research. Ann Geriatr Med Res 2022;26:1-3.
25. Blyth FM, March LM, Brnabic AJ, Jorm LR, Williamson M, Cousins MJ. Chronic pain in Australia: a prevalence study. Pain 2001;89:127-34.
26. Ferrell BA, Stein WM, Beck JC. The Geriatric Pain Measure: validity, reliability and factor analysis. J Am Geriatr Soc 2000;48:1669-73.
27. Dursun G. Validity and reliability of the geriatric pain measure in elderly individuals [master's thesis]. Antalya, Turkey: Akdeniz Üniversitesi; 2013.
28. Malmstrom TK, Miller DK, Simonsick EM, Ferrucci L, Morley JE. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. J Cachexia Sarcopenia Muscle 2016;7:28-36.
29. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-74.
30. Sahin UK, Tozluoglu EY, Durdu H, Korkmaz N, Bahar NT, Yavuz E. Screening for frailty and sarcopenia in community-dwelling older adults: a cross-sectional study from the Eastern Black Sea region of Turkey. Aging Clin Exp Res 2022;34:2047-56.
31. Janssen I, Heymsfield SB, Wang ZM, Ross R. Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. J Appl Physiol (1985) 2000;89:81-8.
32. Cruz-Jentoft AJ, Landi F, Topinkova E, Michel JP. Understanding sarcopenia as a geriatric syndrome. Curr Opin Clin Nutr Metab Care 2010;13:1-7.
33. Batsis JA, Villareal DT. Sarcopenic obesity in older adults: aetiology, epidemiology and treatment strategies. Nat Rev Endocrinol 2018;14:513-37.
34. Hairi NN, Cumming RG, Blyth FM, Naganathan V. Chronic pain, impact of pain and pain severity with physical disability in older people: is there a gender difference? Maturitas 2013;74:68-73.
35. Henchoz Y, Bula C, Guessous I, Rodondi N, Goy R, Demont M, et al. Chronic symptoms in a representative sample of community-dwelling older people: a cross-sectional study in Switzerland. BMJ Open 2017;7:e014485.
36. Raftery MN, Sarma K, Murphy AW, De la Harpe D, Normand C, McGuire BE. Chronic pain in the Republic of Ireland: community prevalence, psychosocial profile and predictors of pain-related disability. Results from the Prevalence, Impact and Cost of Chronic Pain (PRIME) study, part 1. Pain 2011;152:1096-103.
37. Covinsky KE, Lindquist K, Dunlop DD, Yelin E. Pain, functional limitations, and aging. J Am Geriatr Soc 2009;57:1556-61.
38. Scott D, Blizzard L, Fell J, Jones G. Prospective study of self-reported pain, radiographic osteoarthritis, sarcopenia progression, and falls risk in community-dwelling older adults. Arthritis Care Res (Hoboken) 2012;64:30-7.
39. Foley SJ, Lord SR, Srikanth V, Cooley H, Jones G. Falls risk is associated with pain and dysfunction but not radiographic osteoarthritis in older adults: Tasmanian Older Adult Cohort study. Osteoarthritis Cartilage 2006;14:533-9.
40. Kim MJ, Kim TY, Choi YA, Chin JH, Lee SY. A study on the characteristics of standing posture of elderly women with sarcopenia in Korea. J Exerc Rehabil 2018;14:481-8.
41. Cichon D, Ignasiak Z, Fugiel J, Kochan K, Ignasiak T. Efficacy of physiotherapy in reducing back pain and improve joint mobility in older women. Ortop Traumatol Rehabil 2019;21:45-55.
42. Briggs AM, van Dieen JH, Wrigley TV, Greig AM, Phillips B, Lo SK, et al. Thoracic kyphosis affects spinal loads and trunk muscle force. Phys Ther 2007;87:595-607.
43. O'Sullivan P. Diagnosis and classification of chronic low back pain disorders: maladaptive movement and motor control impairments as underlying mechanism. Man Ther 2005;10:242-55.
44. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16-31.
45. Baek JY, Jung HW, Kim KM, Kim M, Park CY, Lee KP, et al. Korean Working Group on Sarcopenia guideline: expert consensus on sarcopenia screening and diagnosis by the Korean Society of Sarcopenia, the Korean Society for Bone and Mineral Research, and the Korean Geriatrics Society. Ann Geriatr Med Res 2023;27:9-21.

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The Triglyceride-Glucose Index is Independently Associated with Chronic Kidney Disease in the Geriatric Population, Regardless of Obesity and Sex

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Background: Insulin resistance (IR) negatively affects several risk factors of chronic kidney disease (CKD). This cross-sectional study investigated whether the triglyceride-glucose (TyG) index, which reflects IR, was independently associated with CKD in a geriatric population, regardless of obesity and sex. **Methods:** The analysis included 7,326 individuals (2,864 males and 4,462 females) aged ≥60 years. Non-obesity or obesity was evaluated using a body mass index cutoff of 25 kg/m^2. The TyG index was calculated as ln [triglyceride concentration (mg/dL)×fasting plasma glucose concentration (mg/dL)]/2. All participants were categorized into three groups according to TyG tertiles. Moderate-to-severe CKD ($_{MS}$CKD) was defined as an estimated glomerular filtration rate (eGFR) of <45.0 mL/min/1.73 m^2. **Results:** In males and females with or without obesity, a trend test showed a decreasing tendency in the eGFR from the lowest to highest TyG tertiles. Males without obesity and females with obesity in the middle and highest tertiles of the TyG index were 2.342 and 2.393, and were 2.313 and 3.516 times more likely to have $_{MS}$CKD, respectively. Those with or without obesity in the highest tertile of the TyG index were 1.736 and 2.374 times more likely to have $_{MS}$CKD, respectively. **Conclusion:** Geriatric populations with an increased TyG index have a high risk of $_{MS}$CKD regardless of obesity and sex. Our findings suggest that increased IR is associated with CKD in the geriatric population independent of obesity and sex.

Key Words: Body mass index, Insulin resistance, Metabolic syndrome, Aged, Renal insufficiency

INTRODUCTION

Chronic kidney disease (CKD) is a common condition in older adults. CKD increases the mortality rate and risk of conditions including myocardial infarction, hypertension, and type 2 diabetes in the geriatric population. From a pathophysiological perspective, these health concerns share a common pathway mediated by insulin resistance (IR).[1-3] In 2017, CKD reportedly led to 1.2 million deaths globally. Owing to the aging of the global population, the prevalence and related mortality rate of CKD are expected to rise, with estimated CKD-related deaths increasing to 2.2 million or 4.0 million by 2040 in the best-case or worst-case scenarios, respectively.[4] Therefore, developing effective strategies for CKD screening, detection, and management is essential to prevent or suppress the development of severe CKD, particularly in the geriatric population.

The association between obesity and CKD has been globally recognized for decades, and studies have evaluated the risk of CKD by broadly using body mass index (BMI) as the obesity index.[5-7] However, Kim et al.[8,9] reported that high fat and low muscle mass are more closely related to CKD than BMI-based obesity evaluation. Additionally, the limitation of BMI is apparent in the early screening and detection of high-risk older adults with CKD. The reason for these findings is that BMI does not precisely re-

flect overall adiposity and does not distinguish visceral fat, which induces the onset of IR.[10,11] IR, rather than BMI-based obesity evaluation, is strongly associated with CKD because IR induces CKD risk factors, including glomerular hyperfiltration, sodium retention, defective tubular reabsorption, tissue inflammation, and fibrosis.[12-14] Therefore, IR is more likely related to CKD than obesity.

The homeostasis model assessment of insulin resistance (HOMA-IR) has been widely used to examine insulin sensitivity for many years.[15] The triglyceride-glucose (TyG) index was strongly related to hyperinsulinemic-euglycemic clamp data collected in Brazil, Mexico, and South Korea.[16-18] Additionally, the TyG index is better than the HOMA-IR index for identifying various IR-related health concerns such as arterial stiffness, hypertension, and non-alcoholic steatohepatitis.[19-21] Therefore, the TyG index is a reliable and valid indicator of IR that is superior to the HOMA-IR.

We hypothesized that IR is associated with CKD independent of obesity and sex and that an increased TyG index can be used for the early screening and detection of high-risk geriatric populations with CKD. Based on this hypothesis, we conducted a population-based cross-sectional study to examine the association of the TyG index with CKD in the geriatric population, regardless of obesity and sex.

MATERIALS AND METHODS

Study Design and Subjects

We analyzed data from a database of South Koreans' general health, nutritional status, and lifestyle data from the Korea National Health and Nutritional Examination Survey (KNHANES) 2014–2018. The analysis included 7,326 participants (2,864 men and 4,462 women) among all participants aged ≥60 years from the 2014–2018 KNHANES. Fig. 1 shows a flowchart of participant recruitment. All participants provided written informed consent, and the study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Institutional Review Board of Silla University (No. 1041449-202203-HR-001).

This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[22]

TyG Index and eGFR

Blood samples were collected in the morning after a fast of at least 8 hours. Circulating glucose and triglyceride concentrations were measured by enzymatic methods using a Hitachi automatic analyzer 7600 (Hitachi, Tokyo, Japan). The TyG index was calculated as follows.[17]

ln [triglyceride concentration (mg/dL) × fasting plasma glucose concentration (mg/dL)]/2.

Creatinine concentrations were analyzed using the Jaffe rate-blanked creatinine assay and compensated at a certified laboratory (Seegene Medical Foundation, Seoul, Korea). The estimated glomerular filtration rate (eGFR) was calculated using the new Japanese-coefficient modified MDRD (Modification of Diet in Renal Disease) study equation as follows.[8,9,23-25]

$$eGFR\ (mL/min/1.73\ m^2) = 194 \times (\text{serum creatinine})^{-1.094} \times (\text{age})^{-0.287}\ (\times 0.739 \text{ for females})$$

All participants were assigned into groups according to TyG tertiles. Moderate-to-severe CKD ($_{MS}$CKD) was defined as an eGFR < 45.0 mL/min/1.73 m^2.[23-25]

Statistical Analysis

All data are shown as mean ± standard deviation. Independent t-test or Mann–Whitney U tests were used to compare male and female variables. A one-way analysis of variance (ANOVA) was used to compare the anthropometric and biochemical characteristics of the three TyG index groups. The Bonferroni post-hoc test was applied when ANOVA showed significant differences ($p < 0.05$). The Mann–Whitney U test was used to analyze differences between groups with non-normal data distributions ($p < 0.05$). The Jonckheere–Terpstra test was used to compare the values between the three groups (two-tailed, $p < 0.05$). The Jonckheere–Terpstra test generates standardized statistics (SS) that point to the strength of tendencies in variables that increase or decline across groups.[26-28] We applied logistic regression to evaluate the obesity- and sex-specific associations between the TyG index

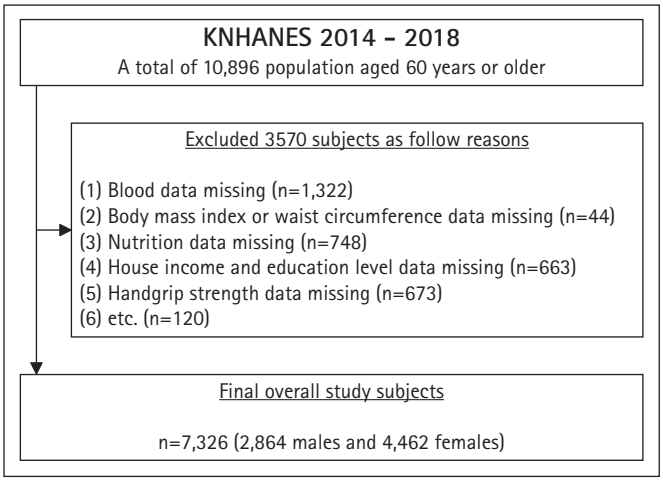

Fig. 1. Flowchart of the subjects. KNHANES, Korea National Health and Nutritional Examination Survey.

and $_{MS}$CKD. The fully adjusted model was adjusted for potential confounders such as education level, household income, smoking, drinking, handgrip strength, moderate-to-vigorous physical activity, total energy intake, and BMI, which are recognized or suspected factors associated with CKD. IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA) was used to perform the statistical analyses. The optimal cutoff values for the TyG index in male and female participants with or without obesity to predict $_{MS}$CKD were derived from receiver operating characteristic (ROC) curve analysis (area under the ROC curve [AUC] values). The sensitivity and specificity were also calculated. We used MedCalc for Windows version 9.1.0.1 (MedCalc, Ostend, Belgium).

RESULTS

Table 1 presents the participants' characteristics. The mean age of the participants was 66.1 ± 10.5 years and was significantly higher in male participants than in females ($p < 0.001$). The mean TyG index and eGFR were 8.6 ± 0.6 and 62.8 ± 13.4 mL/min/1.73m^2, respectively. The eGFR in male participants was significantly lower than that in females ($p < 0.001$). The TyG index did not differ significantly between the sexes. Supplementary Table S1 provides more information on the subjects.

Table 2 displays the obesity- and sex-specific differences and tendencies based on the eGFR tertiles in male subjects. In subjects with and without obesity, the tendency test indicated a significant decrease in eGFR from the lowest to highest TyG tertiles (SS -5.61 and -3.59, respectively; both $p < 0.001$). Post hoc testing revealed that the mean eGFR in the lowest tertile was significantly higher than that in the middle and highest tertile. Similar to the male participants, the eGFR values in female participants with and without obesity are shown in Table 3. Supplementary Tables S2 and S3 provide the results of the analyses of additional variables and several covariates for male and female participants, respectively.

Table 4 compares the obesity- and sex-specific odds ratios for an association between the TyG index and $_{MS}$CKD. Male and female participants with and without obesity were divided into tertiles based on TyG index values. For male participants without obesity, in the unadjusted model, the middle and highest tertiles displayed odds ratios of 2.392 (95% confidence interval [CI], 1.522–3.760) and 2.439 (95% CI, 1.552–3.835), respectively, compared to the lowest tertile in $_{MS}$CKD. In the fully adjusted model, the middle and highest tertiles showed odds ratios of 2.342 (95% CI, 1.464–3.747) and 2.393 (95% CI, 1.498–3.823), respectively, relative to the lowest tertile in $_{MS}$CKD. Regarding female participants without obesity, in the unadjusted model, the highest tertile displayed an odds ratio of 2.123, relative to the lowest tertile (95% CI, 1.411–3.194) in $_{MS}$CKD. In the fully adjusted model, the highest tertile showed an odds ratio of 2.374 relative to the lowest tertile (95% CI, 1.539–3.662) of $_{MS}$CKD. Among male subjects with obesity, in the unadjusted model, the highest tertile displayed an odds ratio of 1.620 relative to the lowest tertile (95% CI, 1.016–2.584) for $_{MS}$CKD. In the fully adjusted model, the highest tertile showed an odds ratio of 1.736 relative to the lowest tertile (95% CI, 1.053–2.863) in $_{MS}$CKD. Regarding obese female subjects, in the unadjusted model, the middle and highest tertiles had odds ratios of 2.216 (95% CI, 1.361–3.606) and 3.141 (95% CI, 1.975–4.974), respectively, relative to the lowest tertile of $_{MS}$CKD. In the fully ad-

Table 1. Characteristics of the subjects

	Overall (n = 7,326)	Male (n = 2,864)	Female (n = 4,462)	p-value
Age (y)	66.1 ± 10.5	69.4 ± 6.1	64.0 ± 12.1	< 0.001[a)]
TyG index	8.6 ± 0.6	8.6 ± 0.5	8.6 ± 0.6	0.148
eGFR (mg/dL)	62.8 ± 13.4	60.6 ± 12.6	64.2 ± 13.7	< 0.001[a)]
Height (cm)	158.9 ± 8.4	166.1 ± 5.8	154.3 ± 6.2	< 0.001[a)]
Body mass (kg)	61.5 ± 9.2	67.4 ± 8.5	57.8 ± 7.4	< 0.001[a)]
Body mass index (kg/m^2)	24.3 ± 2.8	24.4 ± 2.5	24.3 ± 2.9	< 0.001[a)]
Waist circumference (cm)	84.7 ± 8.7	88.1 ± 7.6	82.6 ± 8.7	< 0.001[a)]
FPG (mg/dL)	100.3 ± 20.2	100.3 ± 19.9	100.4 ± 20.3	0.868
HbA1c (%)	5.7 ± 0.7	5.7 ± 0.7	5.7 ± 0.7	0.385
Triglyceride (mg/dL)	124.5 ± 66.8	125.2 ± 65.0	124.0 ± 67.9	0.465
Creatinine (mg/dL)	0.85 ± 0.28	0.82 ± 0.29	0.85 ± 0.28	< 0.001[a)]
Obesity status				< 0.01
Non-obese subjects	4,670 (63.7)	1,766 (61.7)	2,904 (65.1)	
Obese subjects	2,656 (36.2)	1,098 (38.3)	1,558 (34.9)	

Values are presented as mean±standard deviation or number (%).
eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; TyG index, triglyceride-glucose index.
[a)]The Mann–Whitney U test was applied to assess differences between groups.

Table 2. Anthropometric data, the TyG index, and eGFR-related biochemical characteristics and trends according to TyG index tertiles in male subjects

	Male non-obese subjects						Male obese subjects					
	A (n = 604)	B (n = 590)	C (n = 593)	Post-hoc	ss[b]	p-value[b]	A (n = 359)	B (n = 362)	C (n = 356)	Post-hoc	ss[b]	p-value[b]
TyG index	8.00 ± 0.24	8.59 ± 0.15	9.22 ± 0.27	A < B < C	44.82	< 0.001	8.01 ± 0.25	8.61 ± 0.15	9.23 ± 0.25	A < B < C	34.79	< 0.001
eGFR (mg/dL)	64.0 ± 12.4	60.6 ± 12.6	60.0 ± 12.2	A > B, C	-5.61	< 0.001	61.1 ± 13.1	58.4 ± 12.1	57.7 ± 12.4	A > B, C	-3.59	< 0.001
Body mass index (kg/m^2)	22.9 ± 1.3	22.8 ± 1.3	22.8 ± 1.4	ns	-0.59	0.553	26.9 ± 1.7	27.0 ± 1.9	27.0 ± 1.7	ns	0.31	0.756
Age (y)	69.8 ± 6.2	69.8 ± 6.3	70.0 ± 6.3	ns	0.58	0.564	68.0 ± 5.6	69.0 ± 5.9	69.2 ± 6.0	A < B, C	2.69	< 0.01[a]
Height (cm)	166.0 ± 5.8	165.9 ± 5.8	165.9 ± 5.7	ns	-0.44	0.66	166.3 ± 5.9	166.6 ± 5.7	166.0 ± 5.8	ns	-0.49	0.625
Body mass (kg)	63.1 ± 5.7	62.8 ± 5.9	62.9 ± 5.9	ns	-0.31	0.756	74.5 ± 7.2	75.0 ± 7.1	74.5 ± 7.2	ns	0.05	0.960
Waist circumference (cm)	84.5 ± 5.6	84.2 ± 5.3	84.3 ± 5.8	ns	-0.49	0.625	94.0 ± 6.2	94.5 ± 6.4	94.4 ± 6.0	ns	1.18	0.238
FPG (mg/dL)	92.0 ± 9.9	99.3 ± 15.8	108.6 ± 24.5	A < B < C	17.23	< 0.001[a]	92.8 ± 10.6	99.2 ± 13.7	110.9 ± 30.0	A < B < C	13.84	< 0.001[a]
Triglyceride (mg/dL)	67.0 ± 15.1	111.8 ± 20.9	198.0 ± 59.7	A < B < C	42.49	< 0.001[a]	67.5 ± 15.4	113.3 ± 21.0	195.2 ± 54.8	A < B < C	32.94	< 0.001[a]
Creatinine (mg/dL)	0.82 ± 0.16	0.86 ± 0.18	0.88 ± 0.18	A < B, C	6.16	< 0.001[a]	0.83 ± 0.15	0.88 ± 0.48	0.90 ± 0.17	A < B, C	5.15	< 0.001

Values are presented as mean±standard deviation.

A group is lowest tertile; B, middle tertile; and C, highest tertile.

TyG index, triglyceride-glucose index; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; ss, standardized statistics; ns, not significant.

[a]The Mann–Whitney U test was applied to assess differences between the three groups.

[b]The Jonckheere–Terpstra test was used to assess the trend among the three groups.

Table 3. Anthropometric data, the TyG index, and eGFR-related biochemical characteristics and trends according to TyG index tertiles in female subjects

	Female non-obese subjects						Female obese subjects					
	A (n = 973)	B (n = 988)	C (n = 973)	Post-hoc	ss[b]	p-value[b]	A (n = 505)	B (n = 510)	C (n = 513)	Post-hoc	ss[b]	p-value[b]
TyG index	7.95 ± 0.25	8.57 ± 0.15	9.22 ± 0.28	A < B < C	57.44	< 0.001	7.97 ± 0.25	8.60 ± 0.15	9.24 ± 0.28	A < B < C	41.45	< 0.001
eGFR (mg/dL)	68.2 ± 13.9	65.6 ± 12.9	64.0 ± 13.5	A > B > C	-6.18	< 0.001[a]	63.6 ± 13.4	60.4 ± 13.3	59.1 ± 13.3	A > B, C	-4.54	< 0.001
Body mass index (kg/m^2)	22.6 ± 1.4	22.6 ± 1.3	22.6 ± 1.4	ns	0.41	0.686[a]	27.5 ± 2.3	27.6 ± 2.3	27.7 ± 2.3	ns	1.37	0.170
Age (y)	60.4 ± 13.5	61.4 ± 12.9	61.5 ± 13.6	ns	1.79	0.074[a]	69.4 ± 6.3	69.4 ± 6.4	70.3 ± 6.2	ns	2.22	< 0.05
Height (cm)	155.3 ± 6.5	155.4 ± 6.5	155.0 ± 6.3	ns	-1.07	0.286	152.7 ± 5.4	152.5 ± 5.7	152.1 ± 5.1	ns	-1.51	0.131
Body mass (kg)	54.6 ± 5.2	54.6 ± 5.3	54.4 ± 5.4	ns	-0.71	0.478	64.2 ± 6.7	64.1 ± 7.0	64.1 ± 7.0	ns	-0.95	0.34
Waist circumference (cm)	78.2 ± 6.0	78.5 ± 6.0	78.1 ± 6.0	ns	-0.31	0.758	90.7 ± 6.8	90.5 ± 6.9	91.1 ± 7.0	ns	1.32	0.187
FPG (mg/dL)	91.8 ± 8.9	98.5 ± 14.2	109.4 ± 26.1	A < B < C	22.93	< 0.001[a]	92.4 ± 10.1	99.9 ± 15.2	111.5 ± 30.8	A < B < C	16.91	< 0.001[a]
Triglyceride (mg/dL)	63.9 ± 15.0	110.2 ± 19.4	197.5 ± 64.7	A < B < C	54.58	< 0.001[a]	64.9 ± 14.9	109.4 ± 19.4	198.4 ± 61.0	A < B < C	39.42	< 0.001[a]
Creatinine (mg/dL)	0.80 ± 0.45	0.83 ± 0.28	0.88 ± 0.27	A, B < C	10.99	< 0.001	0.82 ± 0.14	0.84 ± 0.17	0.88 ± 0.22	A < B < C	5.47	< 0.001[a]

Values are presented as mean±standard deviation.

A group is lowest tertile; B, middle tertile; and C, highest tertile.

TyG index, triglyceride-glucose index; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; ss, standardized statistics; ns, not significant.

[a]The Mann–Whitney U test was applied to assess differences between the three groups.

[b]The Jonckheere–Terpstra test was used to assess the trend among the three groups.

Table 4. Obesity- and sex-specific odds ratios for the relationship between the triglyceride-glucose index and moderate-to-severe chronic kidney disease

	Unadjusted model	Fully adjusted model
Male non-obese subjects		
A (n = 593)	2.439 (1.552–3.835)***	2.393 (1.498–3.823)***
B (n = 590)	2.392 (1.522–3.760)***	2.342 (1.464–3.747)***
C (n = 604)	Reference	Reference
Male obese subjects		
A (n = 356)	1.620 (1.016–2.584)*	1.736 (1.053–2.863)*
B (n = 362)	1.355 (0.841–2.185)	1.485 (0.895–2.463)
C (n = 359)	Reference	Reference
Female non-obese subjects		
A (n = 973)	2.123 (1.411–3.194)***	2.374 (1.539–3.662)***
B (n = 988)	1.388 (0.900–2.141)	1.499 (0.952–2.360)
C (n = 973)	Reference	Reference
Female obese subjects		
A (n = 513)	3.141 (1.975–4.974)***	3.516 (2.164–5.713)***
B (n = 510)	2.216 (1.361–3.606)**	2.313 (1.397–3.828)**
C (n = 505)	Reference	Reference

Values are presented as odds ratio (95% confidence interval).
A group is highest tertile; B, middle tertile; and C, lowest tertile. The fully adjusted model was adjusted for education level, house income, medication, smoking, drinking, hand-grip strength, moderate to vigorous physical activity, total energy intake and body mass index.
*p<0.05, **p<0.01, ***p<0.001.

justed model, the middle and highest tertiles showed odds ratios of 2.313 (95% CI, 1.397–3.828) and 3.516 (95% CI, 2.164–5.713), respectively, relative to the lowest tertile in $_{MS}$CKD.

DISCUSSION

This study investigated whether the TyG index, which reflects IR, is associated with CKD in a geriatric population, independent of obesity and sex. The results showed that the TyG index was associated with CKD in the geriatric population, regardless of obesity. Additionally, the relationship between the TyG index and CKD was significant in both male and female participants. These findings suggested that IR is associated with CKD in the geriatric population independent of obesity and sex.

The long-standing consensus is that aging and obesity trigger a decline in kidney function. The effect of aging on CKD is undeniable due to the high global prevalence of CKD in the geriatric population. However, the association between obesity and CKD is increasing, mainly owing to the limitations of BMI. BMI is not an accurate indicator of overall adiposity and visceral fat, which induces the onset of IR.[10,11] Recent studies published in 2019, 2020, and 2021 reported that IR was strongly related to a decline in kidney function rather than obesity per se.[29-31] Our findings on IR also support these recent reports. In the present study, both male and female participants (Tables 2, 3) showed a stronger decreasing trend in eGFR in subjects without obesity than in those with obesity as the TyG index increased. If obesity causes a decline in kidney function, the decreasing trend in eGFR should be more pronounced in subjects with obesity than in those without. This suggests that the effect of IR on CKD is more significant than that on obesity.

We also found that male participants without obesity in the middle and highest tertiles of the TyG index were 2.342 and 2.393 times more likely to have $_{MS}$CKD, respectively. Similarly, female participants without obesity in the highest tertile were 2.374 times more likely to develop $_{MS}$CKD (Table 4). Male participants with obesity in the highest tertile of the TyG index were 1.736 times more likely to develop $_{MS}$CKD. Additionally, female subjects with obesity in the middle and highest tertiles of the TyG index were 2.313 and 3.516 times more likely to have $_{MS}$CKD, respectively (Table 4). These findings suggest that increased IR is an independent risk factor for CKD in both men and women, regardless of obesity status. Therefore, IR is a primary pathophysiology that may be independently associated with CKD in geriatric populations regardless of obesity.

Several studies have reported a relationship between IR and CKD.[32,33] Animal and human studies have reported that hyperinsulinemia leads to kidney vasodilatation, enhances sodium reabsorption, stimulates the renin-angiotensin system, and causes glomerular hyperfiltration, which increases the GFR.[34-36] Increased filtration per nephron causes nephron loss and leads to glomerular hypertension, which causes glomerular sclerosis and a subsequent

decline in kidney function.[37] In addition, clinical studies have shown pre-existing IR in individuals with a mild decline in kidney function.[38,39] The relationship between IR and CKD can be explained via biological mechanisms such as inflammation, oxidative stress, and metabolic acidosis.

Studies have demonstrated the good performance of the TyG index in predicting or discriminating IR-related health concerns. However, specific cutoff values have not been confirmed, and few studies have suggested the potential value of the TyG index. Shin[40] studied 4,415 Korean adults aged 20–80 years and showed that a TyG index cutoff value of ≥ 8.81 discriminated individuals with IR with AUC of 0.894, sensitivity of 86.7%, and specificity of 80.1%. Endukuru et al.[41] studied 150 Indian adults aged 18–65 years and found that a TyG index cutoff value for IR of ≥ 9.88 showed AUC of 0.836, sensitivity of 76.0%, and specificity of 88.0%. The value suggested by Endukuru et al.[41] was derived from only 150 adults, and the AUC was relatively low compared with that suggested by Shin.[40] In the present study, the potential cutoff value of the TyG index to distinguish individuals with $_{MS}$CKD, was > 8.62 (AUC 0.584; sensitivity 59.34%; specificity 53.26%) (Supplementary Fig. S1). Considering the differences in population age, race, and number, the potential cutoff value in the present study cannot be directly compared with those obtained in the two previous studies. Additionally, the relatively low AUC, sensitivity, and specificity of the potential TyG index cutoff value in the present study suggest the need for re-examination using another sample of the geriatric population. However, as a geriatric population-specific cutoff value to distinguish CKD in high-risk individuals in the early stages, the potential TyG index cutoff value identified in the present study may be appropriate for clinical practice.

Previous studies in the Korean population have provided TyG index cutoff values to discriminate high-risk individuals with several health concerns. Kim et al.[27] found that TyG index values of ≥ 8.72 and 8.67, respectively, were risk factors for sarcopenic obesity in men and women aged ≥ 60 years with health issues such as hypertension and hyperlipidemia. Kang et al.[42] reported a TyG index value of ≥ 8.83 as a cutoff value for obstructive sleep apnea in men and women with health issues aged ≥ 55 years. Park et al.[43] showed that a TyG index value of ≥ 8.44 was a cutoff value of coronary artery disease in men and women aged ≥ 65 years without health issues. Differences in age distribution, inconsistency in sex-specific populations, and differences in basic health status make comparing and determining a precise TyG index cutoff value for all health concerns in the Korean population difficult. However, these reports suggest that late middle-aged and older adults with health issues and a TyG index value of ≥ 8.6 require careful monitoring to suppress the progression of health concerns. In healthy geriatric populations, a TyG index value of ≥ 8.44 may be applied as a cutoff for early-stage prevention of health concerns.

The present study had several strengths and limitations. This study's strength was the adjustment for potential covariates, such as demographic parameters and lifestyle factors that might affect the relationship between the TyG index and CKD. However, the study subjects were older Korean adults; thus, whether the findings of the present study can be applied to other ethnicities or nations is unclear. Further investigations in different races are needed to confirm the association between the TyG index and CKD.

In conclusion, the geriatric population with an increased TyG index has a high risk of CKD regardless of obesity and sex. This finding suggests that increased IR is associated with CKD in the geriatric population independent of obesity and sex.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, BK, SO; Data curation, BK, GK; Funding acquisition, BK, NM; Investigation, BK, SO, KH; Methodology, NM, KT; Project administration, BK, KH; Supervision, BK, GK; Writing-original draft, BK; Writing-review & editing, BK, SO.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.23.0096.

REFERENCES

1. Schefold JC, Filippatos G, Hasenfuss G, Anker SD, von Haehling S. Heart failure and kidney dysfunction: epidemiology, mechanisms and management. Nat Rev Nephrol 2016;12:610-23.
2. Mukai H, Ming P, Lindholm B, Heimburger O, Barany P, Stenvinkel P, et al. Lung dysfunction and mortality in patients with

chronic kidney disease. Kidney Blood Press Res 2018;43:522-35.
3. Kalantar-Zadeh K, Jafar TH, Nitsch D, Neuen BL, Perkovic V. Chronic kidney disease. Lancet 2021;398:786-802.
4. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2020;395:709-33.
5. Tsujimoto T, Sairenchi T, Iso H, Irie F, Yamagishi K, Watanabe H, et al. The dose-response relationship between body mass index and the risk of incident stage ≥ 3 chronic kidney disease in a general Japanese population: the Ibaraki prefectural health study (IPHS). J Epidemiol 2014;24:444-51.
6. Lu JL, Molnar MZ, Naseer A, Mikkelsen MK, Kalantar-Zadeh K, Kovesdy CP. Association of age and BMI with kidney function and mortality: a cohort study. Lancet Diabetes Endocrinol 2015;3:704-14.
7. Chang TJ, Zheng CM, Wu MY, Chen TT, Wu YC, Wu YL, et al. Relationship between body mass index and renal function deterioration among the Taiwanese chronic kidney disease population. Sci Rep 2018;8:6908.
8. Kim B, Kim G, Kim E, Park J, Isobe T, Sakae T, et al. The A Body Shape Index Might Be a Stronger Predictor of Chronic Kidney Disease Than BMI in a Senior Population. Int J Environ Res Public Health 2021;18:12874.
9. Kim B, Park H, Kim G, Isobe T, Sakae T, Oh S. Relationships of fat and muscle mass with chronic kidney disease in older adults: a cross-sectional pilot study. Int J Environ Res Public Health 2020;17:9124.
10. de Mutsert R, Gast K, Widya R, de Koning E, Jazet I, Lamb H, et al. Associations of abdominal subcutaneous and visceral fat with insulin resistance and secretion differ between men and women: the Netherlands epidemiology of obesity study. Metab Syndr Relat Disord 2018;16:54-63.
11. Rothman KJ. BMI-related errors in the measurement of obesity. Int J Obes (Lond) 2008;32 Suppl 3:S56-9.
12. Moon JH, Kim JS. The cutoff value in body fat percentage for increased risk of metabolic syndrome in elderly people with normal body weight. J Korean Geriatr Soc 2015;19:16-24.
13. Whaley-Connell A, Sowers JR. Insulin resistance in kidney disease: is there a distinct role separate from that of diabetes or obesity? Cardiorenal Med 2017;8:41-9.
14. Artunc F, Schleicher E, Weigert C, Fritsche A, Stefan N, Haring HU. The impact of insulin resistance on the kidney and vasculature. Nat Rev Nephrol 2016;12:721-37.
15. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-9.
16. Lee S, Choi S, Kim HJ, Chung YS, Lee KW, Lee HC, et al. Cutoff values of surrogate measures of insulin resistance for metabolic syndrome in Korean non-diabetic adults. J Korean Med Sci 2006;21:695-700.
17. Simental-Mendia LE, Rodriguez-Moran M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. Metab Syndr Relat Disord 2008;6:299-304.
18. Vasques AC, Novaes FS, de Oliveira Mda S, Souza JR, Yamanaka A, Pareja JC, et al. TyG index performs better than HOMA in a Brazilian population: a hyperglycemic clamp validated study. Diabetes Res Clin Pract 2011;93:e98-100.
19. Wang Y, Yang W, Jiang X. Association between triglyceride-glucose index and hypertension: a meta-analysis. Front Cardiovasc Med 2021;8:644035.
20. Riviere B, Jaussent A, Macioce V, Faure S, Builles N, Lefebvre P, et al. The triglycerides and glucose (TyG) index: a new marker associated with nonalcoholic steatohepatitis (NASH) in obese patients. Diabetes Metab 2022;48:101345.
21. Wu S, Xu L, Wu M, Chen S, Wang Y, Tian Y. Association between triglyceride-glucose index and risk of arterial stiffness: a cohort study. Cardiovasc Diabetol 2021;20:146.
22. Noh JH, Jung HW, Ga H, Lim JY. Ethical guidelines for publishing in the Annals of Geriatric Medicine and Research. Ann Geriatr Med Res 2022;26:1-3.
23. Matsuo S, Imai E, Horio M, Yasuda Y, Tomita K, Nitta K, et al. Revised equations for estimated GFR from serum creatinine in Japan. Am J Kidney Dis 2009;53:982-92.
24. Kim B, Kim GM, Oh S. Use of the visceral adiposity index as an indicator of chronic kidney disease in older adults: comparison with body mass index. J Clin Med 2022;11:6297.
25. Lee S, Shimada H, Park H, Makizako H, Lee S, Doi T, et al. The association between kidney function and cognitive decline in community-dwelling, elderly Japanese people. J Am Med Dir Assoc 2015;16:349.
26. Kim B, Ku M, Kiyoji T, Isobe T, Sakae T, Oh S. Cardiorespiratory fitness is strongly linked to metabolic syndrome among physical fitness components: a retrospective cross-sectional study. J Physiol Anthropol 2020;39:30.
27. Kim B, Kim G, Lee Y, Taniguchi K, Isobe T, Oh S. Triglyceride-glucose index as a potential indicator of sarcopenic obesity in older people. Nutrients 2023;15:555.
28. Nakanishi Y, Tsugihashi Y, Akahane M, Noda T, Nishioka Y, Myojin T, et al. Comparison of Japanese centenarians' and non-centenarians' medical expenditures in the last year of life. JAMA

Netw Open 2021;4:e2131884.
29. Chen HY, Lu FH, Chang CJ, Wang RS, Yang YC, Chang YF, et al. Metabolic abnormalities, but not obesity per se, associated with chronic kidney disease in a Taiwanese population. Nutr Metab Cardiovasc Dis 2020;30:418-25.
30. Fritz J, Brozek W, Concin H, Nagel G, Kerschbaum J, Lhotta K, et al. The triglyceride-glucose index and obesity-related risk of end-stage kidney disease in Austrian adults. JAMA Netw Open 2021;4:e212612.
31. Kawamoto R, Akase T, Ninomiya D, Kumagi T, Kikuchi A. Metabolic syndrome is a predictor of decreased renal function among community-dwelling middle-aged and elderly Japanese. Int Urol Nephrol 2019;51:2285-94.
32. Kobayashi H, Tokudome G, Hara Y, Sugano N, Endo S, Suetsugu Y, et al. Insulin resistance is a risk factor for the progression of chronic kidney disease. Clin Nephrol 2009;71:643-51.
33. Kobayashi S, Maesato K, Moriya H, Ohtake T, Ikeda T. Insulin resistance in patients with chronic kidney disease. Am J Kidney Dis 2005;45:275-80.
34. Esteghamati A, Ashraf H, Nakhjavani M, Najafian B, Hamidi S, Abbasi M. Insulin resistance is an independent correlate of increased urine albumin excretion: a cross-sectional study in Iranian Type 2 diabetic patients. Diabet Med 2009;26:177-81.
35. Tucker BJ, Anderson CM, Thies RS, Collins RC, Blantz RC. Glomerular hemodynamic alterations during acute hyperinsulinemia in normal and diabetic rats. Kidney Int 1992;42:1160-8.
36. Dengel DR, Goldberg AP, Mayuga RS, Kairis GM, Weir MR. Insulin resistance, elevated glomerular filtration fraction, and renal injury. Hypertension 1996;28:127-32.
37. Helal I, Fick-Brosnahan GM, Reed-Gitomer B, Schrier RW. Glomerular hyperfiltration: definitions, mechanisms and clinical implications. Nat Rev Nephrol 2012;8:293-300.
38. Kato Y, Hayashi M, Ohno Y, Suzawa T, Sasaki T, Saruta T. Mild renal dysfunction is associated with insulin resistance in chronic glomerulonephritis. Clin Nephrol 2000;54:366-73.
39. Chen J, Muntner P, Hamm LL, Fonseca V, Batuman V, Whelton PK, et al. Insulin resistance and risk of chronic kidney disease in nondiabetic US adults. J Am Soc Nephrol 2003;14:469-77.
40. Shin KA. Triglyceride and glucose (TyG) index is a clinical surrogate marker for the diagnosis of metabolic syndrome. Biomed Sci Lett 2017;23:348-54.
41. Endukuru CK, Gaur GS, Yerrabelli D, Sahoo J, Vairappan B. Cut-off values and clinical utility of surrogate markers for insulin resistance and beta-cell function to identify metabolic syndrome and its components among Southern Indian adults. J Obes Metab Syndr 2020;29:281-91.
42. Kang HH, Kim SW, Lee SH. Association between triglyceride glucose index and obstructive sleep apnea risk in Korean adults: a cross-sectional cohort study. Lipids Health Dis 2020;19:182.
43. Park GM, Cho YR, Won KB, Yang YJ, Park S, Ann SH, et al. Triglyceride glucose index is a useful marker for predicting subclinical coronary artery disease in the absence of traditional risk factors. Lipids Health Dis 2020;19:7.

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Mucous Membrane Pemphigoid in a Nonagenarian: A Case Report

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Mucous membrane pemphigoid is a rare autoimmune blistering disease characterized by post-bullous erosion of mucous membranes. Herein, we present a case of a nonagenarian man who was referred to our department of dermatology presenting with painful erosion of the buccal mucosa. Physical examination revealed palate erosion associated with erosion of the buccal mucosa. A diagnosis of mucous membrane pemphigoid was confirmed, and the patient was successfully treated with topical corticosteroids.

Key Words: Autoimmune blistering disease, Geriatric, Mucous membrane pemphigoid

INTRODUCTION

Mucous membrane pemphigoids are a group of chronic autoimmune blistering diseases of the chorioepithelial or dermoepidermal junction, which are characterized by predominant or exclusive mucosal involvement.[1)] Mucous membrane pemphigoids primarily affect older patients, typically those aged 60–80 years.[2)] Mucosal involvement includes the oral, nasopharyngeal, laryngopharyngeal, genital, esophageal, tracheal, anal, and ocular mucosal membranes. Additionally, skin lesions may also be present, although they are typically mild and are observed in approximately 30% of patients.[2)] Mucous membrane pemphigoids are characterized by scarring resulting from initial inflammation, leading to significant morbidity, including pain, malnutrition, and corneal blindness. In nonagenarians, the management of mucous membrane pemphigoid becomes more complex owing to the age-related physiological changes, comorbidities, and potential polypharmacy interactions. Herein, we report a case of an old patient who presented with painful buccal erosions and was diagnosed with mucous membrane pemphigoid that was successfully treated with topical corticosteroids.

CASE REPORT

A 92-year-old male patient presented with a 6-month history of oral erosion that had resulted in feeding disorders and subsequent weight loss. His medical history included hypertension, atrial fibrillation, and dyslipidemia. Clinical examination revealed post-blistering erosions of the left buccal mucosa associated with palatal erosion (Fig. 1). The patient did not present any other mucosal or skin lesions. A skin biopsy revealed a cleavage between the epidermis and dermis with a few interstitial eosinophils present (Fig. 2). Direct cutaneous immunofluorescence of the biopsy revealed linear immunoglobulin G (IgG) and C3 deposits along the basement membrane. Laboratory test results were negative for antibodies against BP180, BP230, type VII collagen, and laminin 332. Immunoblotting studies of the skin extract and indirect immunofluorescence of salt-split skin yielded negative results. Clinical, histological, and immunological findings were consistent with a diagnosis of mild mucous membrane pemphigoid because the clinical involvement was limited to one site. As the Consensus Conference[1)] indicates that topical treatments can be introduced initially, the patient was prescribed clobetasol propionate cream. The lesions healed completely within 3 months of daily applica-

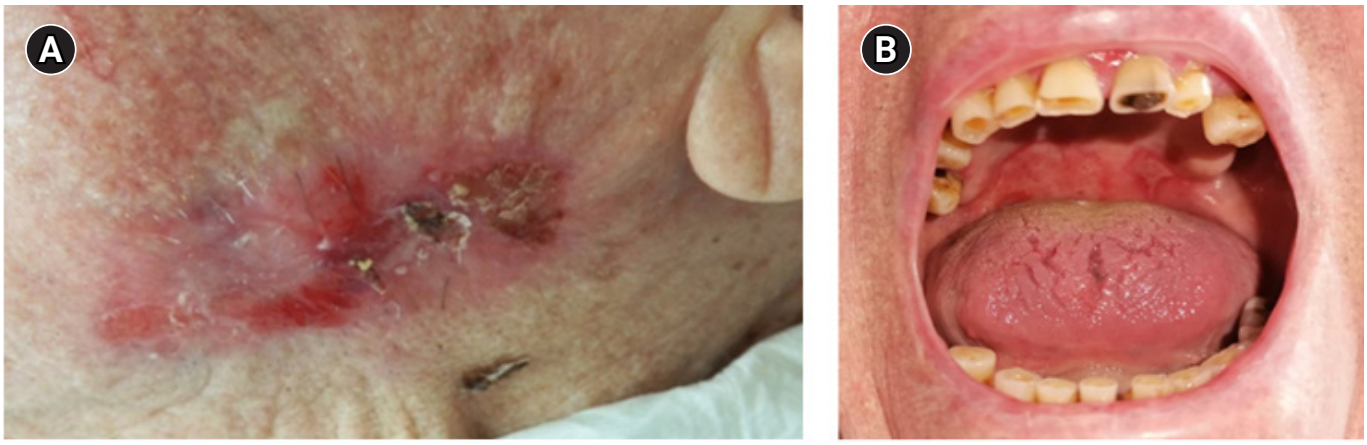

Fig. 1. Clinical presentation: (A) atrophic plaque on the left cheek, with a post-blister erosion in the center associated with painful erosion located on the palate (B).

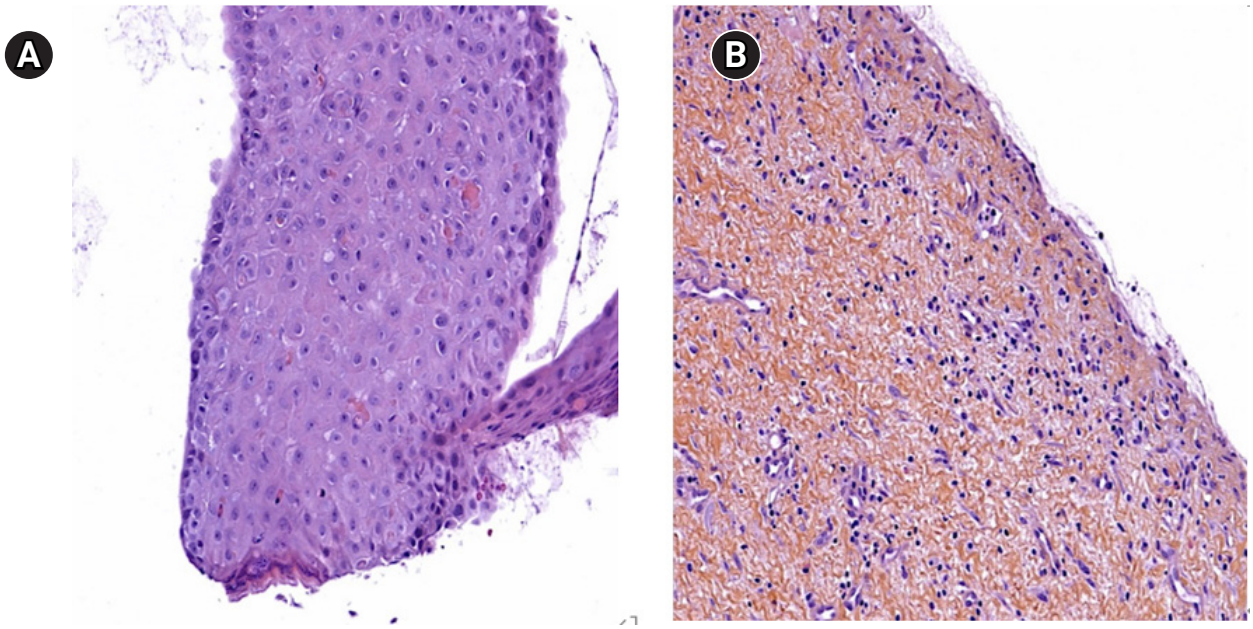

Fig. 2. The skin biopsy revealed a cleavage between the epidermis (A) and dermis with a few interstitial eosinophils (B) (hematoxylin-eosin saffron staining, original magnification ×20).

tion, allowing the resolution of pain and recovery of optimal oral feeding. No recurrence was observed after 1 year of follow-up.

DISCUSSION

The symptoms and complications of mucous membrane pemphigoid can substantially impact the quality of life of patients living with the disease and can cause difficulties in eating, ultimately leading to malnutrition in some cases, as observed in our patient. Scar formation is a characteristic feature of mucous membrane pemphigoid, which can result in major disabilities (e.g., blindness and esophageal, anal, and vaginal stenosis) and life-threatening situations (e.g., laryngeal stenosis leading to respiratory failure).

Mucous membrane pemphigoid is characterized by autoantibodies directed against various antigens of the dermoepidermal junction (i.e., BP180, laminin 332, type VII collagen, α6β4 integrin).[2] Despite the recognition of multiple antigens targeted by autoantibodies and the use of various detection techniques (e.g., enzyme-linked immunosorbent assay [ELISA], immunoblot studies of skin extract, salt-split skin indirect immunofluorescence, and biochip technology), approximately one-third of the patients with mucous membrane pemphigoid do not have detectable autoanti-

bodies, as in our patient.[3,4] According to the Consensus Conference,[1] a diagnosis of mucous membrane pemphigoid is established based on the clinical presentation along with the detection of anti-dermoepidermal junction autoantibodies on direct immunofluorescence, direct immunoelectron microscopy, or serological tests (e.g., ELISA, immunoblotting).[2,5] Direct immunofluorescence is the major diagnostic test, which has the highest sensitivity for the diagnosis of mucous membrane pemphigoid.[5]

For mild/moderate mucous membrane pemphigoid, dapsone, methotrexate, tetracyclines, and/or topical corticosteroids are recommended as the first-line treatment.[5] Considering the advanced age and potential frailty of our patient, we opted for a topical treatment. High-potency topical corticosteroids led to complete remission in our patient within 3 months, indicating that less invasive treatments can be more beneficial in geriatric patients with mild/moderate mucous membrane pemphigoid. Such a strategy limits the risk of potentially life-threatening adverse events associated with systemic therapies in patients of advanced age.

In conclusion, mucous membrane pemphigoid is a rare autoimmune disease that predominantly affects the mucous membrane and frequently affects the oral mucosa. Recognizing this condition is crucial due to its potential to reduce the quality of life (e.g., oral pain), especially among older patients.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, OBDL, BT; Data curation, OBDL, PC, MC, LC, PC, BT; Investigation, OBDL, PC, MC, LC, PC, BT; Methodology, OBDL, PC, MC, LC, PC, BT; Supervision, PC, BT; Writing-original draft, OBDL, PC, BT; Writing-review & editing, OBDL, BT.

REFERENCES

1. Chan LS, Ahmed AR, Anhalt GJ, Bernauer W, Cooper KD, Elder MJ, et al. The first international consensus on mucous membrane pemphigoid: definition, diagnostic criteria, pathogenic factors, medical treatment, and prognostic indicators. Arch Dermatol 2002;138:370-9.
2. Rashid H, Lamberts A, Borradori L, Alberti-Violetti S, Barry RJ, Caproni M, et al. European guidelines (S3) on diagnosis and management of mucous membrane pemphigoid, initiated by the European Academy of Dermatology and Venereology: Part I. J Eur Acad Dermatol Venereol 2021;35:1750-64.
3. Hayakawa T, Furumura M, Fukano H, Li X, Ishii N, Hamada T, et al. Diagnosis of oral mucous membrane pemphigoid by means of combined serologic testing. Oral Surg Oral Med Oral Pathol Oral Radiol 2014;117:483-96.
4. Bernard P, Antonicelli F, Bedane C, Joly P, Le Roux-Villet C, Duvert-Lehembre S, et al. Prevalence and clinical significance of anti-laminin 332 autoantibodies detected by a novel enzyme-linked immunosorbent assay in mucous membrane pemphigoid. JAMA Dermatol 2013;149:533-40.
5. Schmidt E, Rashid H, Marzano AV, Lamberts A, Di Zenzo G, Diercks GF, et al. European Guidelines (S3) on diagnosis and management of mucous membrane pemphigoid, initiated by the European Academy of Dermatology and Venereology: Part II. J Eur Acad Dermatol Venereol 2021;35:1926-48.

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Clostridium tetani Infection in a Geriatric Patient: Do Not Let Your Guard Off!

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Tetanus is an infectious disease caused by *Clostridium tetani* toxin. Although easily preventable through vaccination, over 73,000 new infections and 35,000 deaths due to tetanus occurred worldwide in 2019, with higher rates in countries with healthcare barriers. Here, we present a clinical case of *C. tetani* infection in an 85-year-old patient. Patient robustness and high functional reserve before infection are favorable predictors of survival for an otherwise fatal disease. However, the patient did not experience any severe complications. Therefore, this report is a strong call for tetanus vaccination.

Key Words: *Clostridium tetani*, Tetanus, Rehabilitation, Aged, Cognitive dysfunction, Quadriplegia, Cross infection, Frailty, Sarcopenia

INTRODUCTION

Tetanus is a non-communicable disease caused by the tetanospasmin neurotoxin produced by the gram-positive bacterium *Clostridium tetani*. The condition presents as spastic paralysis that spreads from the head and neck to the trunk and limbs.[1)] Global incidence and mortality depend on the barriers to care and availability of vaccines; however, even with proper care, mortality is up to 50% in adults.[1)] Herein, we describe the tetanus sequelae in an 85-year-old survivor. Written informed consent was obtained from the patient for publishing this case report.

CASE REPORT

An 85-year-old man was transferred from the geriatric medicine unit of our tertiary hospital to our rehabilitation unit and underwent intensive treatment for the sequelae of *C. tetani* infection. He is a farmer leading an active lifestyle. His past medical history included atrial fibrillation (AF) and benign prostatic hypertrophy.

Two months prior, he was admitted to a local hospital because of trismus and hypertonia after injuring his leg while working on his farm. Since the clinical findings and medical history were strongly suggestive of *C. tetani* infection, he began immediate treatment with immunoglobulins, tetanus vaccination, and metronidazole for ten days (Fig. 1). He was transferred to our intensive care unit (ICU), where he underwent tracheostomy, mechanical ventilation, and vasoactive support owing to respiratory failure. The seizures were treated with baclofen, midazolam, and diazepam. Electroencephalography revealed severely slow cerebral activity. Due to worsening respiratory function, opacity on chest radiography, and peripheral leukocytosis due to possible ventilator-associated pneumonia (VAP), blood cultures and tracheal secretion samples were sent for laboratory analysis. The tracheal secretions tested positive for *Klebsiella pneumoniae* and methicillin-sensitive *Staphylococcus aureus* (MSSA); therefore, antibiotic therapy with piperacillin-tazobactam was prescribed (Fig. 1).

The patient was later moved to a geriatric unit in a coma and breathed spontaneously on 4 L/min of supplemental oxygen via a tracheal cannula. After three days, the antibiotic therapy was switched to linezolid (14 days) due to VAP exacerbation, and combined treatment with meropenem for 17 days was prescribed after septic shock occurred (Fig. 1). The patient gradually awoke, and the feeding tube was removed. He developed cholestasis and acute edematous pancreatitis; however, the endoscopic treatment got postponed due to spontaneous recovery. Urinary tract infection caused by the multidrug-resistant organisms (MDROs) *K. pneumoniae*, *Acinetobacter baumannii*, and *Enterococcus faecalis* was treated with colistin and amoxicillin-clavulanate for 1 week (Fig. 1). Eventually, his clinical condition improved, and he was considered eligible for rehabilitation.

In our unit, the patient was placed in MDRO isolation. He still required tracheal supplemental oxygen (1 L/min) and a bladder catheter and developed pressure ulcers on the right (unstageable) and left (stage II) heels, sacrum (stage II), and right elbow (stage III). He was sarcopenic and had low handgrip strength (9.9 kg) and appendicular skeletal mass (ASM, 16.9 kg). The rehabilitative evaluations are presented in Table 1.

On the first day, the patient underwent rehabilitation with good compliance. However, *Clostridioides difficile* infection occurred, and oral vancomycin was prescribed for 10 days. After 3 days, he presented with AF with a third-degree atrioventricular block (heart rate, 30 beats/min) without secondary bradyarrhythmia. The patient was transferred to our hospital's cardiac ICU to undergo single-chamber pacemaker implantation and presented with hyperkinetic delirium during the postoperative course. Two days later, the patient was transferred to our hospital. A *Pseudomonas aeruginosa* bloodstream infection was treated with ceftazidime-avibactam and amikacin for 1 week (Fig. 1). Meanwhile, on a routine nasopharyngeal swab, the patient tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The patient was treated with remdesivir for 3 days and placed on droplet isolation. The following day, a second recurrence of *C. difficile* occurred; therefore, he was transferred to a geriatric medicine unit. The infection was successfully treated with fidaxomicin for ten days.

Two days after completing treatment for the recurrence of *C. difficile*, he presented with bloodstream infection due to *Candida parapsilosis* (fluconazole-resistant), MSSA, and *Candida tropicalis* originating from the intravenous catheter; after replacing the infected catheter, it was treated with caspofungin and cefazolin for 17 days. After 10 days, the patient presented with a bloodstream infection caused by *P. aeruginosa*. Antibiotic treatment with piperacillin-tazobactam was prescribed and eventually shifted to aztreonam and ceftazidime-avibactam owing to evidence of antibiotic resistance from the antibiogram. After 4 days, owing to the improvement in clinical condition, the antibiotic was shifted to cefepime for 10 additional days (Fig. 1).

During the last months of hospitalization, tracheostomy closure was performed by an ear, nose, and throat (ENT) specialist and pulmonologist. Throughout the hospitalization, nutritional supplementation was prescribed to manage malnutrition and sarcope-

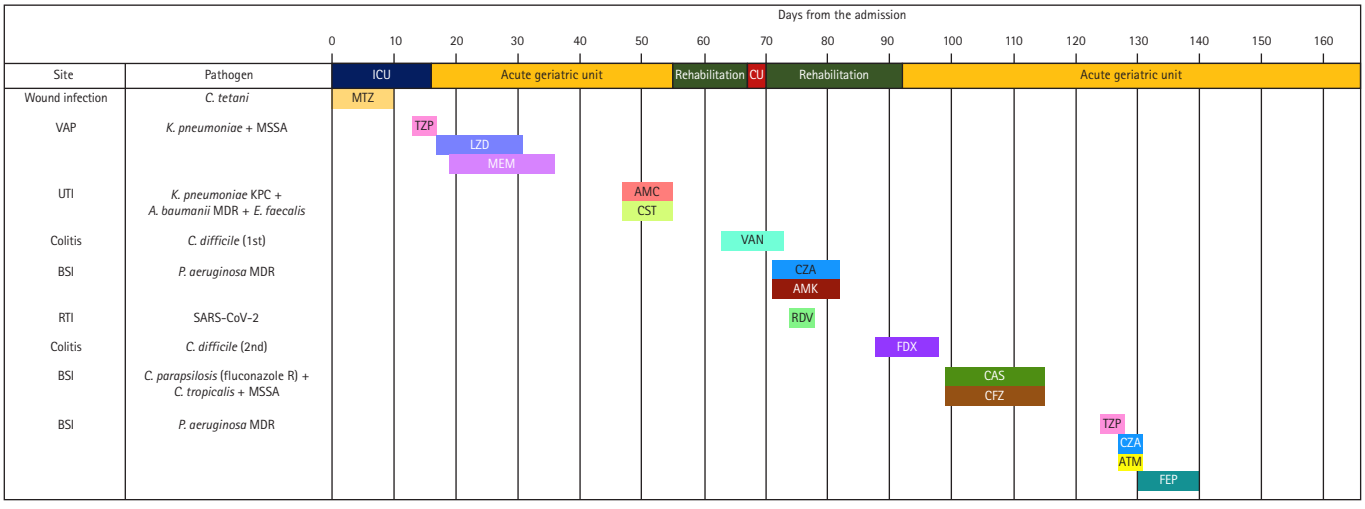

Fig. 1. Timeline of infections and duration of antibiotic treatments. AMC, amoxicillin-clavulanic acid; AMK, amikacin; ATM, aztreonam; BSI, bloodstream infection; CAS, caspofungin; CFZ, cefazolin; CST, colistin; CZA, ceftazidime-avibactam; CU, cardiac intensive care unit/cardiology unit; FDX, fidaxomicin; FEP, cefepime; ICU, intensive care unit; KPC, *Klebsiella pneumoniae carbapenemase*; LZD, linezolid; MDR, multidrug resistant; MEM, meropenem; MSSA, methicillin-sensitive *Staphylococcus aureus*; MTZ, metronidazole; R, resistant; RTI, respiratory tract infection; TZP, piperacillin-tazobactam; UTI, urinary tract infection; VAN, vancomycin; VAP, ventilator-associated pneumonia.

Table 1. Rehabilitative evaluation and objectives

Physical evaluation	Logopedic evaluation	Functional evaluation	Short-term objectives	Mid-term objectives	Long-term objectives
Performs isometric pelvic contraction and weak hip raising in supine position; Sits for a few minutes supported by upper limbs; No alterations in tactile, thermic, and pain sensitivity. Upper limbs - ROM preserved and pain-free beyond the middle degrees; GMS MRC 3/5. Lower limbs - PROM preserved until final degrees, pain on mobilization of left hip and knee; GMS MRC 2/5 on activating muscles of hip and knee and MRC 3/5 on activating muscles of tibiotarsus.	Cognitive - Not oriented in space, time, and self; - Impairment in executive functions, problem solving, working and episodic memory; - Ideomotor and buccofacial apraxia; - Successfully executes simple orders but fails to comprehend extended sentences due to early decline in working memory. Speech - Poor oral motor excursions; - Poor verbal communication; - Hypophonia (due to O_2-therapy). Dysphagia - Able to consume pureed foods; - Inhales water; - Raclage allows the patient to expectorate.	Requires maximum assistance with dressing and personal hygiene; Requires modest help for posture changes; Requires bilateral support for bed-to-wheelchair transfers.	Discontinuing oxygen therapy; Closing the tracheostomy; Recovering swallowing, phonation, sitting, autonomy in postural transitions and transfers, and upright standing.	Improvement of functional independence in walking, balance, and ADL.	Recovering independence in ADL e IADL.

ROM, active range of motion; PROM, passive range of motion; GMS, global muscle strength; MRC, Medical Research Council scale; ADL, activities of daily living; IADL, instrumental activities of daily living.

nia. From the motor point of view, although intensive rehabilitation was compromised due to the large number of infectious (Fig. 1) and non-infectious complications, the patient continued to undergo short physiotherapy sessions according to the changes in his clinical condition.

At discharge, the patient was able to perform postural transition with assistance. Motor and respiratory reconditioning continued at discharge. From a motor point of view, posture transition training and aided transfers, axial stability, and balance improvement exercises, with the primary goal of achieving a standing position, were prescribed. From a respiratory perspective, breath-movement coordination exercises, thoracic expansion and girdle opening exercises, and inhalation-exhalation exercises were recommended. Wheelchairs and walkers were recommended for the current mobility deficit on short and medium trips and to facilitate safe postural transitions. Rehabilitation, ENT, and geriatric follow-up evaluations were recommended.

DISCUSSION

This report describes the sequelae of tetanus in a geriatric patient. Tetanus is an often-fatal disease accompanied by several complications and is even more severe in geriatric patients.[2,3] Our patient developed respiratory failure, coma, VAP, septic shock, healthcare-associated infections (HAI), acute sarcopenia, life-threatening bradyarrhythmia, and pressure ulcers. The electroencephalogram and cognitive function assessment results (Table 1) raised the possibility of incident dementia, likely with vascular or mixed etiology. AF also plays a role in cognitive decline,[4] and ICU admission may increase the risk of dementia.[5,6] However, as no specific examinations were performed, this diagnosis cannot be validated. Furthermore, HAI, delirium, and sarcopenia were associated with adverse outcomes in hospitalized patients.[7-11]

This case demonstrates the catastrophic effects of an otherwise preventable disease. In 2019, more than 73,000 new infections and 35,000 deaths due to tetanus occurred worldwide, with the highest incidence rates reported in Nepal, Eritrea, Pakistan, and Afghanistan.[12,13]

Maternal and neonatal tetanus are public health concerns in developing countries[12]; in higher-income countries, aged individuals are susceptible to both cases and death.[1] Although vaccination does not affect the environmental distribution,[14] serum antibody levels decrease with aging.[15,16] Furthermore, the possibility that older adults may not have completed their primary vaccination cycle should not be overlooked.[17] Vaccines have reduced tetanus incidence and mortality by up to 89% in the last century.[12] After the primary cycle,[1] periodic booster shots are recommended for adults.[13] The current state-of-the-art tetanus vaccination involves three vaccine doses at the 3rd, 5th, and 11th months of life; booster doses at 7 and 14 years of age; further booster doses every ten years.[18] Diagnosis of *C. tetani* infection is based on clinical examination, medical history, and epidemiology. The differential diagnosis of trismus includes local oral or pharyngeal conditions, and the differential diagnosis of muscular spasms includes strychnine poisoning and iatrogenic causes.[18] In the event of a risk of *C. tetani* infection, the procedure envisages the administration of a vaccine dose plus the simultaneous administration of immunoglobulins if the vaccine status is absent or uncertain or if 10 years have elapsed since the last booster vaccine was administered. If the last dose of vaccine was administered < 5 years prior, no further booster vaccine is required; on the contrary, after the 5th year of administration, a booster dose is recommended without simultaneous administration of immunoglobulins. Other steps for infection management include endotracheal intubation and early tracheostomy for airway protection, diazepam or midazolam administration to eliminate reflex spasms, surgical debridement of infected tissues, and antibiotic therapy with metronidazole or benzylpenicillin for 7–10 days.[18,19]

The SARS-CoV-2 pandemic has deeply affected people's lifestyles, especially those of older and frailer individuals.[20-22] The coronavirus disease 2019 (COVID-19) has caused a dramatic decrease in compulsory vaccination among children.[23-25] Although no studies have been conducted on vaccination shifts in older individuals, the effect of the pandemic on health service accessibility in older persons has been widely documented.[26,27]

Therefore, this study is intended to be a strong call for tetanus vaccination, especially in geriatric patients. In addition, we hope that health can become a universal right.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, SC, LG, EDA; Methodology, LG, LM; Validation, EDA, FI; Investigation, AP, FA, SC, RR, FI, FMP; Supervision: LG, LM, FL; Writing-original draft, AP, SC; Writing-review & editing, SC, EDA; Visualization, AP, SC.

REFERENCES

1. Hall E, Patricia Wodi A, Hamborsky J, Morelli V, Schilie S. Epidemiology and prevention of vaccine-preventable diseases. 14th ed. Washington, DC: US Centers for Disease Control and Prevention; 2021.
2. Udwadia FE, Lall A, Udwadia ZF, Sekhar M, Vora A. Tetanus and its complications: intensive care and management experience in 150 Indian patients. Epidemiol Infect 1987;99:675-84.
3. Kaushik R, Ferrante LE. Long-term recovery after critical illness in older adults. Curr Opin Crit Care 2022;28:572-80.
4. Papanastasiou CA, Theochari CA, Zareifopoulos N, Arfaras-Melainis A, Giannakoulas G, Karamitsos TD, et al. Atrial fibrillation is associated with cognitive impairment, all-cause dementia, vascular dementia, and Alzheimer's disease: a systematic review and meta-analysis. J Gen Intern Med 2021;36:3122-35.
5. James BD, Grodstein F, Barnes LL, Marquez DX, Bennett DA. ICU hospitalization and incident dementia in community-based cohorts of older adults. Alzheimers Dement 2022;18(S11):e067719.
6. Ahmad MH, Teo SP. Post-intensive care syndrome. Ann Geriatr Med Res 2021;25:72-8.
7. De Spiegeleer A, Kahya H, Sanchez-Rodriguez D, Piotrowicz K, Surquin M, Marco E, et al. Acute sarcopenia changes following hospitalization: influence of pre-admission care dependency level. Age Ageing 2021;50:2140-6.
8. Kennedy R, Freeman H, Martin R, Whittington C, Osborne J, Markland A, et al. Hospital-associated disability associated with

delirium among older adults. Innov Aging 2021;5(Supplement_1):581-582.
9. Bordino V, Vicentini C, D'Ambrosio A, Quattrocolo F; Collaborating Group, Zotti CM. Burden of healthcare-associated infections in Italy: incidence, attributable mortality and disability-adjusted life years (DALYs) from a nationwide study, 2016. J Hosp Infect 2021;113:164-71.
10. Cacciatore S, Marzetti E. Sarcopenia and physical function: proxies of overall health and predictors of mortality in older adults. Arch Gerontol Geriatr 2023;112:105037.
11. Kwak MJ. Delirium in frail older adults. Ann Geriatr Med Res 2021;25:150-9.
12. Behrens H, Ochmann S, Dadonaite B, Roser M. Tetanus [Online]. London, UK: Our World in Data; 2019 [cited 2023 Aug 1]. Available from: https://ourworldindata.org/tetanus.
13. European Centre for Disease Prevention and Control. Tetanus [Internet]. Solna, Sweden: European Centre for Disease Prevention and Control; c2023 [cited 2023 Aug 1]. Available from: https://www.ecdc.europa.eu/en/tetanus.
14. Kyu HH, Mumford JE, Stanaway JD, Barber RM, Hancock JR, Vos T, et al. Mortality from tetanus between 1990 and 2015: findings from the global burden of disease study 2015. BMC Public Health 2017;17:179.
15. Burke M, Rowe T. Vaccinations in older adults. Clin Geriatr Med 2018;34:131-43.
16. Shin JH, Park CJ, Kim JJ, Cho JS, Lee SC, Ryu JH, et al. A multicenter study on the tetanus antibody titers of elderly Koreans. J Korean Geriatr Soc 2011;15:20-8.
17. Richardson JP, Knight AL. The prevention of tetanus in the elderly. Arch Intern Med 1991;151:1712-7.
18. Yen LM, Thwaites CL. Tetanus. Lancet 2019;393:1657-68.
19. Rodrigo C, Fernando D, Rajapakse S. Pharmacological management of tetanus: an evidence-based review. Crit Care 2014;18:217.
20. Aravindhan K, Morgan K, Mat S, Hamid TA, Ibrahim R, Saedon NI, et al. Effects of the COVID-19 pandemic on psychological status and quality of life among participants of the Malaysian elders longitudinal research (MELoR) study. Ann Geriatr Med Res 2022;26:354-62.
21. Tosato M, Ciciarello F, Zazzara MB, Janiri D, Pais C, Cacciatore S, et al. Lifestyle changes and psychological well-being in older adults during COVID-19 pandemic. Clin Geriatr Med 2022;38:449-59.
22. Lekamwasam R, Lekamwasam S. Effects of COVID-19 pandemic on health and wellbeing of older people: a comprehensive review. Ann Geriatr Med Res 2020;24:166-72.
23. Causey K, Fullman N, Sorensen RJD, Galles NC, Zheng P, Aravkin A, et al. Estimating global and regional disruptions to routine childhood vaccine coverage during the COVID-19 pandemic in 2020: a modelling study. Lancet 2021;398:522-34.
24. Guglielmi G. Pandemic drives largest drop in childhood vaccinations in 30 years. Nature 2022;608:253.
25. Bastani P, Mohammadpour M, Samadbeik M, Bastani M, Rossi-Fedele G, Balasubramanian M. Factors influencing access and utilization of health services among older people during the COVID-19 pandemic: a scoping review. Arch Public Health 2021;79:190.
26. von Humboldt S, Low G, Leal I. Health service accessibility, mental health, and changes in behavior during the COVID-19 pandemic: a qualitative study of older adults. Int J Environ Res Public Health 2022;19:4277.
27. Ftouni R, AlJardali B, Hamdanieh M, Ftouni L, Salem N. Challenges of Telemedicine during the COVID-19 pandemic: a systematic review. BMC Med Inform Decis Mak 2022;22:207.

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Association between Support after Dementia Diagnosis and Subsequent Decrease in Social Participation

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Dear Editor,

We are writing this letter to accelerate research and discussion on the nature of post-diagnostic support for dementia. Accurate diagnosis of dementia provides a gateway to care and support for people living with dementia and their relatives.[1)] The reasons for recommending early diagnosis is that cognitive rehabilitation in the milder stages of dementia was suggested to be effective in preventing further impairment.[2)] National plans focused on early diagnosis of dementia have been initiated in many countries.[3)] However, the stigma and anxiety associated with diagnosis of dementia without care and support may reduce social participation.[4)] Also, post-diagnostic support is supposed to moderate the negative impact, but little is known about the delivery and effectiveness of the support. Therefore, we have analyzed the association between post-diagnosis support and subsequent changes in social participation using data from an online survey.

In this survey conducted in December 2021, the respondents were family caregivers of people living at home with early phase dementia and were recruited from a commercial panel.[5)] Family caregivers of those diagnosed with dementia or mild cognitive impairment for more than three months prior to the survey were included. The outcome variable was the number of categories of social participation that decreased after diagnosis (range 0–3) measured retrospectively. Social participation was categorized into three groups based on Levasseur et al.'s taxonomy[6)]: (1) activities with others around but not including a specific activity with them; (2) activities in collaboration with others to reach a common goal; and (3) activities helping others or contributing to the community. For example, walking, shopping, and eating out were examples of the first group; visiting friends' homes, peer meetings, and group exercises were examples of the second group; and doing volunteer work and involving in community organization activities would be categorized in the third group. In addition, social participation was stratified as people living with dementia alone (unaccompanied) and those with living with family members (accompanied). As an independent variable, the respondents were asked to choose the sources of support they consulted immediately after the diagnosis of dementia. The sources of support included the informal sector (family members/relatives, friends, other people living with dementia), the medical sector (primary care physician, memory clinic, medical center for dementia), and the long-term care sector (care manager, long-term care facility, community general support center). These sources were multiple-response items, and participants selecting each item were compared with those who did not. Adult day service users (n = 171) were excluded from the analysis because it was not a social participation that was focused in this study.

Finally, 355 respondents were included in the analysis. The mean age of care recipients was 77.2 ± 12.0 years and the mean score of the Dementia Assessment Sheet for Community-based Integrated Care System 8-item (DASC-8)[7)] was 12.8 ± 2.7. Majority of them (n = 309; 87.0%) lived with their family members and 197 participants (55.5%) had a level of care need certification. For the respondents of family caregivers, the mean age was 50.0 ± 12.9 years. Of the respondents, 161 (45.4%) were children of the participants, 63 (17.7%) were spouses, 120 (59.7%) lived with the participants.

Primary care doctors were the most common post-diagnosis source of support (35.8%), followed by family members/relatives (20.0%) and care managers (15.2%). Moreover, 93 participants (14.6%) did not receive any support. After diagnosis, unaccompanied social participation decreased by 0.95 ± 1.11, while accompa-

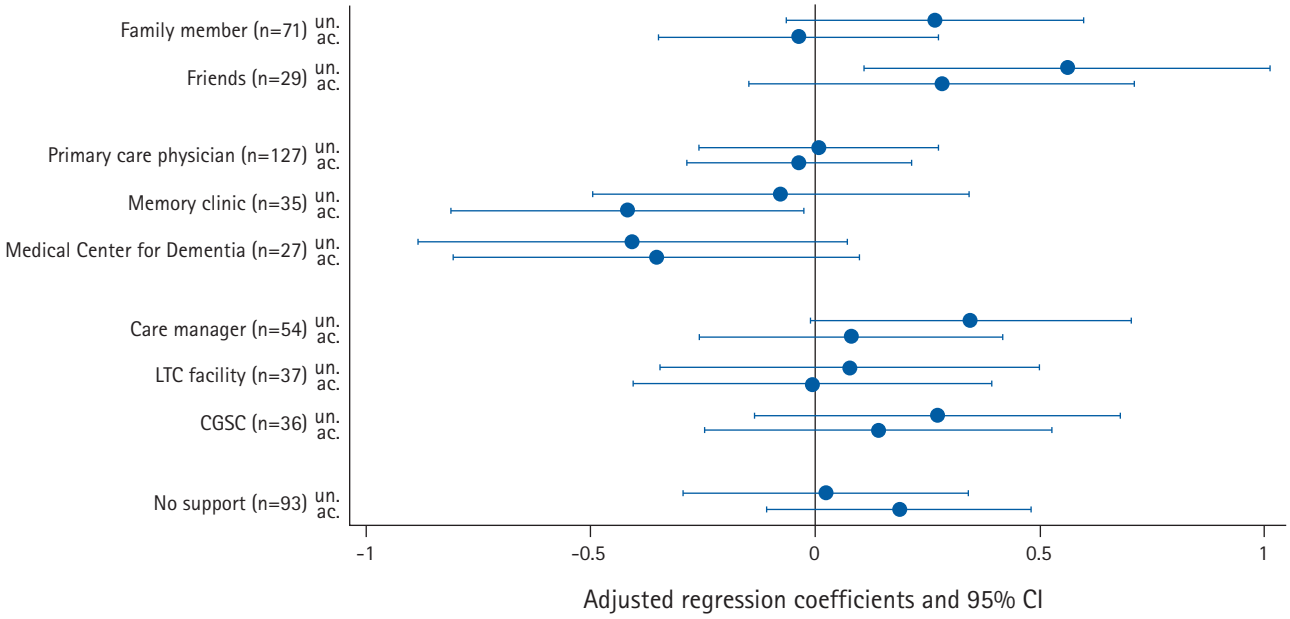

Fig. 1. Decreased number of social participations after dementia diagnosis by source of support. LTC, long-term care; CGSC, community general support center; un., unaccompanied; ac., accompanied; CI, confidence interval. Adjusted for age, sex, ling arrangement, months from diagnosis, DASC8 (Dementia Assessment Sheet for Community-based Integrated Care System 8-item) score, care needs level.

nied social participation decreased by 0.78 ± 1.06.

Fig. 1 presents a summary of linear regression analyses with the source of support as the independent variable, the decreased number of social participations as the dependent variable, and age, sex, DASC-8 score, living arrangement, and care needs level as the adjusted variables. Positive regression coefficients indicate a greater decrease in social participation. Support from the informal sector tended to be associated with a decrease in social participation, while support from the medical sector resulted in an opposite trend. In particular, support from friends was significantly associated with greater decrease in social participation (unaccompanied: $\beta = 0.561$, $p = 0.015$). Support from memory clinic (accompanied: $\beta = -0.417$, $p = 0.038$) and dementia medical centers was associated with a smaller decrease (unaccompanied: $\beta = -0.406$, $p = 0.096$). Support from care managers was associated with decreased social participation (unaccompanied: $\beta = 0.346$, $p = 0.057$). Absence of support was not significantly associated with changes in social participation.

Although the present survey is limited by its retrospective nature and small sample size, the implications of the findings are important. The study suggested that social participation decrease depends on the source of support rather than its presence or absence of support. Support from the medical sector, especially memory clinic and Medical Centers for Dementia, had a protective effect against a decline in social participation. It is specified that Medical Centers for Dementia are to be staffed by professionals, including mental health social workers,[8] and a previous study reported that 72.6% of the centers offered post-consultation support and 21.5% offered peer support.[9] This study suggested the importance of assigning personnel to provide post-diagnostic support to medical institutions that play a central role in dementia in the community.

The association between support from friends and decreased social participation might be due to negative or overprotective attitudes toward social participation of people with dementia. Stigma and misinformation on dementia among the general public have been extensively reported.[10] Although support from care managers was common, it was associated with a decrease in social participation. Participants supported by care managers may have already had problems related to social participation and sought support for access to long-term care insurance services.[11] In addition, unaccompanied social participation tended to be affected more by support than accompanied participation.

Future research should investigate the kind of support received by people diagnosed with dementia. The present survey did not identify the detailed nature of this support. Even if unintentional, an overprotectiveness implies restrictions on the activities of people with dementia. Improving the quality of post-diagnostic support will contribute to a better living with dementia.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The authors claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization: STsuda, STakehara, TY, SH; Formal analysis: HM, STsuda; Funding acquisition: SH; Supervision: SH, STsuda; Writing-original draft: HM; Writing-review & editing: HM, STsuda, STakehara, TY, SH.

REFERENCES

1. Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet 2020;396:413-46.
2. Park J, Im JJ, Song IU, Kang Y. A comparison of memory beliefs, cognitive activity, and depression among healthy older adults, amnestic mild cognitive impairment, and patient with Alzheimer's disease. Ann Geriatr Med Res 2019;23:16-9.
3. Hampel H, Vergallo A, Iwatsubo T, Cho M, Kurokawa K, Wang H, et al. Evaluation of major national dementia policies and health-care system preparedness for early medical action and implementation. Alzheimers Dement 2022;18:1993-2002.
4. Maki Y, Yamaguchi H. Early detection of dementia in the community under a community-based integrated care system. Geriatr Gerontol Int 2014;14 Suppl 2:2-10.
5. Tsuda S, Matsumoto H, Takehara S, Yabuki T, Hotta S. Family caregiver's concerns and anxiety about unaccompanied out-of-home activities of persons with cognitive impairment. BMC Geriatr 2023;23:396.
6. Levasseur M, Richard L, Gauvin L, Raymond E. Inventory and analysis of definitions of social participation found in the aging literature: proposed taxonomy of social activities. Soc Sci Med 2010;71:2141-9.
7. Toyoshima K, Araki A, Tamura Y, Ishikawa J, Kodera R, Oba K, et al. Use of Dementia Assessment Sheet for Community-based Integrated Care System 8-items (DASC-8) for the screening of frailty and components of comprehensive geriatric assessment. Geriatr Gerontol Int 2020;20:1157-63.
8. Awata S. Current activities of medical centers for dementia in Japan. Geriatr Gerontol Int 2014;14 Suppl 2:23-7.
9. Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology. Report on the evaluation of the operation of the Medical Centers for Dementia [Internet]. Tokyo, Japan: Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology; 2022 [cited 2023 Sep 20]. Available from: https://www.tmghig.jp/research/info/archives/014345/.
10. Nguyen T, Li X. Understanding public-stigma and self-stigma in the context of dementia: a systematic review of the global literature. Dementia (London) 2020;19:148-81.
11. Yamada M, Arai H. Long-term care system in Japan. Ann Geriatr Med Res 2020;24:174-80.

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1. Oh TJ, Song Y, Moon JH, Choi SH, Jang HC. Diabetic peripheral neuropathy as a risk factor for sarcopenia. Ann Geriatr Med Res 2019;23:170-5.

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2. Fillit H, Rockwood K, Woodhouse K, Young JB. Brocklehurst's textbook of geriatric medicine and gerontology. 8th ed. Philadelphia, PA: Elsevier; 2016.
3. Korea National Statistical Office. Annual report on the cause of death statistics, 2015. Daejeon: Korea National Statistical Office; 2016.

- Book chapter:

4. Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh

JH, Brenner BM, editors. Hypertension pathophysiology, diagnosis, and management. 2nd ed. New York, NY: Raven Press; 1995. p. 465-78.
- Website:
5. AMA: helping doctors help patients [Internet]. Chicago, IL: American Medical Association; c2019 [cited 2019 Dec 22]. Available from: http://www.ama-assn.org.

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