Original Articles
- Associations of Death at Home with Medical Resources and Medical Activities in Cancer Patients: A Nationwide Study Using Japanese National Database
- Comparative Study of the Accuracy of At-Point Clinical Frailty Scale and Morse Fall Scale in Identifying High-Risk Fall Patients among Hospitalized Adults
- Domains of the Kihon Checklist Associated with Prefrailty among Community-Dwelling Older Adults
- Assessing Medication Use Quality in Older Outpatients Using the Beers Criteria: Findings from a Single-Center Retrospective Study
- Mortality-Related Risk Factors in Geriatric Patients with Hip Fracture
- The Mediating Role of Social Participation in Motoric Cognitive Risk and its Relation to Depression and Loneliness in Older Adults
- Integrated Effects of Thai Essential Oil and Balance Exercise on Parameters associated with Falls in Older Adults at Risk of Falling: A Randomized Controlled Study
- Matrix Metalloproteinases/Tissue Inhibitors of Metalloproteinases Ratio: A Biomarker of Bone Resorption in Geriatric Osteoporosis?
- A Multiple Case Study of Older Adults’ Internal Resiliency and Quality of Life during the COVID-19 Health Emergency

Case Reports
- An Uncommon Case of Weight Loss in a Nonagenarian
- Very Late-Onset Schizophrenia-Like Psychosis: A Case Report and Critical Literature Review

Letter to the Editor
- Does Denosumab Really Improve Muscle Strength? Current Evidence Is Weak
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: 2208-1239). 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, KoreaCID, KCI, DOAJ Crossref, and Google Scholar. It is accessible without barrier from Korea Citation Index (https://www.kci.go.kr) or National Library of Korea (http://nl.go.kr) in the event a journal is no longer published.

Subscription Information

For subscription and all other information visit our website available from: http://www.e-agmr.org. To subscribe to this journal or renew your current subscription, please contact us through Fax (+82-2-2269-1040) or E-mail (agmr.editorial@gmail.com). The printed journal also can be ordered by contacting our Editorial Office.

Revenue Source

AGMR is mainly funded by the Korean Geriatrics Society. The journal is also financed by receiving an article processing charge (reprinting cost) paid by the authors, advertising and academic/corporate sponsors. This Journal is supported by the Korean Federation of Science and Technology Societies (KOFST) Grant funded by the Korean Government.

Open Access

This is an open-access journal distributed under the term of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.
# Editorial Board

## Editor-in-Chief
- Jae-Young Lim  
  Seoul National University, Korea

## Deputy Editor-in-Chief
- Hyuk Ga  
  Incheon Eun-Hye Convalescent Hospital, Korea
- Hee-Won Jung  
  University of Ulsan, Korea

## Emeritus Editors
- Chang Won Won  
  Kyung Hee University, Korea
- Jun Hyun Yoo  
  Sungkyunkwan University, Korea

## Executive Editor
- Hee-Won Jung  
  University of Ulsan, Korea

## Associate Editors
- Tung Wai Auyeung  
  The Chinese University of Hong Kong, Hong Kong
- Jae Kyung Choi  
  Kunkook University, Korea
- Jongkyoung Choi  
  National Medical Center, Korea
- Milan Chang Gudjonsson  
  University of Iceland, Iceland

## Editors
- Hidenori Arai  
  National Center for Geriatrics and Gerontology, Japan
- Prasert Assantachai  
  Mahidol University, Thailand
- Ji Yeon Baek  
  University of Ulsan, Korea
- Ramanarayana Boyapati  
  Sibor Institute of Dental Sciences, India
- Ian Cameron  
  The University of Sydney, Australia
- Matteo Cesari  
  University of Milan, Italy
- Liang-Kung Chen  
  Taipei Veterans General Hospital, Taiwan
- Han Sung Choi  
  Kyung Hee University, Korea
- Ming-Yueh Chou  
  Kaohsiung Veterans General Hospital, Taiwan
- Walter Frontera  
  University of Puerto Rico School of Medicine, USA
- Emiel Hoogendijk  
  Longitudinal Aging Study Amsterdam, Netherlands
- Der-Sheng Han  
  National Taiwan University, Taiwan
- Eun Seong Hwang  
  University of Seoul, Korea
- Soong-Nang Jang  
  Chung Ang University, Korea
- Il-Young Jang  
  Asan Medical Center, Korea
- Kyong Yeun Jung  
  Eulji General Hospital, Korea
- Dae Hyun Kim  
  Harvard Medical School, USA
- Sun Young Kim  
  Kyung Hee University, Korea
- Ki-Sun Kwon  
  Korea Research Institute of Bioscience and Biotechnology, Korea

## Statistical Editor
- Rockli Kim  
  Korea University, Korea

## Journal Management Team
- Na Ri Jung  
  The Korean Geriatrics Society, Korea
- Hee-Won Jung  
  University of Ulsan, Korea
- Jee-Hyun Noh  
  Seoul National University, Korea
- Ji Hye Kim  
  Infolumi, Korea
- In A Park  
  M2PI, Korea
- Minyoung Choi  
  M2PI, Korea
Original Articles

91 Associations of Death at Home with Medical Resources and Medical Activities in Cancer Patients: A Nationwide Study Using Japanese National Database
Kunio Tarasawa, Kenji Fujimori, Tomoaki Ogata, Hiroki Chiba

99 Comparative Study of the Accuracy of At-Point Clinical Frailty Scale and Morse Fall Scale in Identifying High-Risk Fall Patients among Hospitalized Adults
Sungwhan Ji, Hee-Won Jung, Jeounghee Kim, Younghye Kwon, Yeonmi Seo, Semin Choi, Hyoun Jin Oh, Ji Yeon Baek, II-Young Jang, Eunju Lee, for the Asan Multidisciplinary Committee for Seniors (AMCS)

106 Domains of the Kihon Checklist Associated with Prefrailty among Community-Dwelling Older Adults
Taishiro Kamazaki, Hiroshi Otao, Mizuki Hachiya, Atsuko Kubo, Hiroyuki Okawa, Kazuhiko Fujiwara, Asuka Sakamoto, Suguru Shimokihara, Michio Maruta, Gwanghee Han, Takayuki Tabira

116 Assessing Medication Use Quality in Older Outpatients Using the Beers Criteria: Findings from a Single-Center Retrospective Study
Kittipak Jenghua, Kanchira Wutthi, Chanisorn Wannakrachang, Sitanan Chathongyos, Panadda Ngamsom

126 Mortality-Related Risk Factors in Geriatric Patients with Hip Fracture
Rıdvan Gonul, Pınar Tosun Tasar, Kutsi Tuncer, Omer Karasahin, Dogan Nasır Binici, Can Sevinc, Mustafa Turgut, Sevnaz Sahin

134 The Mediating Role of Social Participation in Motoric Cognitive Risk and its Relation to Depression and Loneliness in Older Adults
Ji Hyeun Park, Sangmi Park, Jae Hyu Jung, Suyeong Bae, Sohyeon Yun, Anastassiya Khan, Ickpyo Hong, Ji-Hyuk Park

141 Integrated Effects of Thai Essential Oil and Balance Exercise on Parameters associated with Falls in Older Adults at Risk of Falling: A Randomized Controlled Study
Pattanasin Areeudomwong, Thidarat Duangyod, Chatchada Sutalahkla, Vitsarut Buttagat

151 Matrix Metalloproteinases/Tissue Inhibitors of Metalloproteinases Ratio: A Biomarker of Bone Resorption in Geriatric Osteoporosis?
Bahar Bektan Kanat, Gulru Ulugger Avci, Osman Faruk Bayramlar, Damla Unal, Ozge Sonmez, Ibrahim Murat Bolayiri, Alper Doventas, Deniz Suna Erdincli, Hakan Yavuzer

158 A Multiple Case Study of Older Adults’ Internal Resiliency and Quality of Life during the COVID-19 Health Emergency
Case Reports

172  An Uncommon Case of Weight Loss in a Nonagenarian
    Gurinderjit Kaur Sidhu, Goh Kiat Sern, Htet Htet Khine

175  Very Late-Onset Schizophrenia-Like Psychosis: A Case Report and Critical Literature Review
    Joana Regala, Francisco Moniz-Pereira

Letter to the Editor

179  Does Denosumab Really Improve Muscle Strength? Current Evidence Is Weak
    Belinda R. Beck, David Scott, Robin M. Daly, Jakub Mesinovic
Associations of Death at Home with Medical Resources and Medical Activities in Cancer Patients: A Nationwide Study Using Japanese National Database

Kunio Tarasawa¹, Kenji Fujimori¹, Tomoaki Ogata², Hiroki Chiba³

¹Department of Health Administration and Policy, Graduate School of Medicine, Tohoku University, Sendai, Japan
²Division of Health Policy and Management, Faculty of Medicine, Tohoku Medical and Pharmaceutical University, Sendai, Japan
³Department of Medical Education, School of Medicine, Kitasato University, Sagamihara, Japan

Background: Over half of the Japanese population hope to spend their last days at home; however, 73.0% die in hospitals. The proportion of deaths due to cancer in hospitals is even higher, at 82.4%, and is also high globally. Therefore, there is an urgent need to establish conditions that fulfill the hopes of patients, especially those with cancer, who hope to spend their last days at home. This study aimed to clarify medical resources and activities that are related to proportion of death at home among cancer patients.

Methods: We used data from the Japanese National Database and public data. Japan’s Ministry of Health, Labour, and Welfare provides national data on medical services to applicants for research purposes. Using the data, we calculated the proportion of deaths at home in each prefecture. We also collected information on medical resources and activities from public data and conducted multiple regression analyses to investigate factors associated with the proportion of death at home. Results: In total, 51,874 eligible patients were identified. The maximum and minimum proportions of death at home based on prefectures differed by approximately three-fold (14.8%–41.6%). We also identified scheduled home-visit medical care (coefficient=0.580) and acute and long-term care beds (coefficient=-0.317 and -0.245) as factors that increased and decreased the proportion of death at home, respectively.

Conclusion: To fulfill the hopes of cancer patients to spend their last days at home, we recommend that the government develop policies to increase home visits by physicians and optimize hospital acute and long-term care beds.

Key Words: Database, Home care agencies, Health resources, Mortality, Neoplasms

INTRODUCTION

Japan is currently the most aged country worldwide. The population aged 65 years and older is approximately 36.4 million, and the percentage of older people has reached 29.1%. This shows that aging is progressing at an unprecedented speed worldwide. In addition, Japan’s total population is declining, with births falling below 900,000 and deaths exceeding 1.3 million. The estimated death toll in 2030 is 1.6 million. Therefore, Japan is a super-aging and multi-death society.

According to a survey by the Cabinet Office of Japan, over half of the population (approximately 55.0%) hope to spend their last days at home. However, only approximately 10% die at home, and 73% die in a hospital. In particular, the proportion of hospital deaths due to cancer, which is the leading cause of death, is even higher at 82.4% and is also high globally. These findings suggest possible discrepancies between the people's hope and their actual places of death. A high percentage of people dying at home and low percentage of people being admitted to and dying in hospitals are considered indicators of appropriate care at the end of life.
Therefore, there is an urgent need to establish conditions for fulfilling the hopes of patients to die at home, especially cancer patients.

Previous studies demonstrated that a high level of physician home visit activity is associated with patient deaths at home. Another contributing factor is the provision of home visits to end-stage cancer patients and bedridden patients without cancer at home-care support clinics. A previous survey on visiting nurse agencies revealed additional contributing factors to the patient home death rate, including the patient’s lack of attachment to the hospital, a contractual relationship with a home-care support clinic, and two-way information exchange by telephone or face-to-face communication with the attending physician. These findings on medical activity provide valuable insights into death at home in Japan. However, these studies were often limited to small regions or groups, and large-scale studies investigating factors that influence the proportion of deaths at home are lacking. An association between death at home and the density of home-care resources has also been reported by a study using public data from Japan. However, because the report included suicides and homicides as deaths at home, the accuracy of the proportion of deaths at home calculated in the study remains an issue.

Therefore, it is essential to fulfil the people’s hopes by identifying differences between areas with high and low death at home rates and defining significant characteristics such as medical resources and activities related to death at home through large-scale and highly accurate survey data. In other words, understanding the actual conditions and factors associated with death at home in detail is crucial. Clarifying the factors associated with death at home in Japan, which is an aging country, is also expected to inform other countries that are also aging. Therefore, this study aimed to clarify the actual proportions and factors associated with death at home in cancer patients by analyzing the Japanese National Database (NDB).

MATERIALS AND METHODS

Data Source
We analyzed three datasets in this study, including the NDB; public data from the Ministry of Health, Labor, and Welfare; and the standardized claim data ratio (SCR) published by the Cabinet Office. Japan’s Ministry of Health, Labour and Welfare provides applicants with the NDB, which is a big data related to medical services for research purposes. The NDB is a highly universal database that contains health insurance claim and specific health checkup data from all over Japan and stores > 90% of the total information. Several studies with useful results using the NDB have been reported. The present study used the NDB to collect large-scale and accurate data on deaths at home among cancer patients. The NDB extraction period was from April 2017 to March 2018. The Ministry of Health, Labour, and Welfare extracted the NDB data using the following extraction flow and provided it to the authors in an aggregated format. First, the data on cancer patients were extracted based on their disease names. This extraction excluded “cases with suspicion” and “cases with the curative outcome.” Next, “patients with registered deaths in the outcome” or “patients with medical fees received by physicians when the patient died at home” were extracted. The patients were then restricted to those aged 65 years and older according to the definition of geriatric population applied in this study. Finally, the extracted patients were classified as “hospitalized patients,” “outpatients with medical fees for home death,” and “other outpatients.” The data were provided in a format that could be aggregated by prefecture. We calculated the proportion of deaths at home as the ratio of outpatients with medical fees for deaths at home to the total number of deaths. To determine the proportion of deaths at home and extract the data on outpatients whose outcome were death, we devised ways to improve the accuracy by extracting cases for which medical fees related to death at home were calculated. By examining cases in which physicians were involved in patients who died at home, the proportion of patients who died at home was calculated.

We collected public data and SCR to examine medical resources and activities. The public data included resident information, medical resources, and medical activities provided online by the Ministry of Health, Labour, and Welfare and the Cabinet Office of Japan. We collected these data to investigate factors associated with the proportion of death at home.

The resident information included the number of people per household, percentage of households with older adult couples, percentage of older adults in single-person households, and national medical expenses per person.

The medical resources included the number of home-care support clinics, home-care support hospitals, visiting nursing stations, acute care beds, and long-term care beds. These data were collected in numbers per 100,000 people in the prefectures.

The medical activities included the frequency of medical fee data for acute care hospitalization, chronic care hospitalization, unscheduled home-visit medical care, scheduled home-visit medical care, and home-visit nursing care. These were extracted from the SCR published by the Cabinet Office of Japan. The SCR shows sex/age-adjusted regional differences in medical practice based on medical claims information. An SCR of 100 is consistent with the national average.
medical care are items billed when a physician provides medical care in the patient’s home. Unscheduled and scheduled home-visit medical care did not include home nursing or rehabilitation.

We did not obtain ethical approval as we only used existing data that were aggregated by the prefecture.

Database Construction
All data collected in this study were aggregated by prefecture, and a database was constructed. Since there are 47 prefectures in Japan, the analysis included 47 subjects.

Statistical Analysis
Three types of analyses were performed. First, we calculated and graphed the statistics of the proportions of death at home by prefecture. Second, we classified the 47 prefectures into two groups according to the median proportion of deaths at home (high and low) and compared the associated factors according to these groups. Third, we performed a multiple regression analysis using the forward-backward stepwise selection method to estimate the factors affecting the proportions of deaths at home. This analysis was performed after confirming the normal distributions of the objective variables.

We report the means and standard deviations and compared the groups using the Welch’s t-test. To accommodate multicollinearity, we performed a multiple regression analysis, excluding duplicate variables if the correlation between the explanatory variables was > 0.7. All p-values were two-tailed, and statistical significance was set at p < 0.05. All statistical analyses were conducted using IBM SPSS Statistics for Windows, version 28.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Patients
During the 12-month study period, we extracted data from 181,453 patients aged 65 years and older. Additionally, we identified 51,874 patients who died at home (outpatient with medical fees for death at home) (Fig. 1). The patients included were 28,557 males and 23,317 females.

The Proportion of Deaths at Home by Prefecture
Fig. 2 shows the proportions of deaths at home by prefecture. The mean proportion of deaths at home across all prefectures was 26.1% ± 6.0%, ranging from 14.8% (Akita) to 41.6% (Kanagawa). A three-fold difference was observed between the minimum and maximum values.

Comparison of the Proportions of Deaths at Home according to High and Low Groups
Table 1 compares the factors associated with high and low proportions of death at home. Among the 47 prefectures, 24 and 23 were assigned to the high and low proportions of death at home groups, respectively. Nine items differed significantly between the two groups. The high group demonstrated significantly higher SCR for unscheduled and scheduled home-visit medical care and home-visit nursing care than the low group. Conversely, the low group showed significantly higher national medical expenses per person, number of home-care support hospitals and acute and long-term care beds, and SCR for acute and chronic care hospitalization than the high group.

Factors Associated with the Proportions of Deaths at Home
Table 2 presents the factors affecting the proportion of death at home. Due to multicollinearity, we excluded national medical expenses per person and SCR for chronic care hospitalization and unscheduled home visits from the explanatory variables. The multiple regression analysis identified three items that significantly affected the proportion of death at home. Among the items, the SCR for scheduled home-visit medical care (β = 0.580) was a factor that was related to increased proportions of death at home, where-as the number of acute (β = -0.317) and long-term care beds (β = -0.245) were associated with reduced proportions of death at
The mean proportion of 47 prefectures (26.1%)

Fig. 2. The proportion of deaths at home by prefecture. The bar graph shows the proportion of deaths at home in 47 prefectures in Japan. The horizontal line in the graph shows the mean proportion of deaths at home in 47 prefectures.

Table 1. Comparison of the factors associated with high and low groups of death at home

<table>
<thead>
<tr>
<th>Variable</th>
<th>High group (n = 24)</th>
<th>Low group (n = 23)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of people per household</td>
<td>2.3 ± 0.1</td>
<td>2.3 ± 0.2</td>
<td>0.509</td>
</tr>
<tr>
<td>Elderly couple households (%)</td>
<td>12.3 ± 1.6</td>
<td>12.2 ± 1.6</td>
<td>0.793</td>
</tr>
<tr>
<td>Elderly single-person households (%)</td>
<td>11.2 ± 1.7</td>
<td>11.9 ± 2.0</td>
<td>0.227</td>
</tr>
<tr>
<td>The national medical expenses per person (Japanese thousand yen)</td>
<td>338.1 ± 29.9</td>
<td>370.8 ± 38.4</td>
<td>0.002**</td>
</tr>
<tr>
<td>Number of home care support clinics (/100,000 population)</td>
<td>11.1 ± 3.6</td>
<td>10.8 ± 5.4</td>
<td>0.822</td>
</tr>
<tr>
<td>Number of home care support hospitals (/100,000 population)</td>
<td>0.9 ± 0.4</td>
<td>1.4 ± 0.9</td>
<td>0.023*</td>
</tr>
<tr>
<td>Number of visiting nursing stations (/100,000 population)</td>
<td>7.7 ± 2.0</td>
<td>7.6 ± 1.5</td>
<td>0.873</td>
</tr>
<tr>
<td>Number of acute care beds (/100,000 population)</td>
<td>473.6 ± 71.7</td>
<td>536.6 ± 57.7</td>
<td>0.002**</td>
</tr>
<tr>
<td>Number of long-term care beds (/100,000 population)</td>
<td>236.2 ± 62.8</td>
<td>376.9 ± 187.4</td>
<td>0.002**</td>
</tr>
<tr>
<td>SCR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For acute care hospitalization</td>
<td>98.1 ± 14.8</td>
<td>112 ± 15.9</td>
<td>0.003**</td>
</tr>
<tr>
<td>For chronic care hospitalization</td>
<td>85.6 ± 19.9</td>
<td>127.3 ± 55.8</td>
<td>0.002**</td>
</tr>
<tr>
<td>For unscheduled home-visit medical care</td>
<td>106.8 ± 24.2</td>
<td>74.8 ± 22.2</td>
<td>0.001***</td>
</tr>
<tr>
<td>For scheduled home-visit medical care</td>
<td>97.9 ± 25.9</td>
<td>74.6 ± 20.9</td>
<td>0.001**</td>
</tr>
<tr>
<td>For home-visit nursing care</td>
<td>103.2 ± 32.7</td>
<td>74.6 ± 21.6</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

Each prefecture was divided into two groups according to the median high and low proportion of death at home. Values are presented as mean±standard deviation. SCR, standardized claim data ratio.

*p<0.05, **p<0.01, ***p<0.001, derived from the Welch’s t-test.
Table 2. Associated factors for the proportion of deaths at home by multiple regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Standardized coefficient (β)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of acute care beds (/100,000 population)</td>
<td>-0.317</td>
<td>0.004**</td>
</tr>
<tr>
<td>Number of long-term care beds (/100,000 population)</td>
<td>-0.245</td>
<td>0.023*</td>
</tr>
<tr>
<td>SCR for scheduled home-visit medical care</td>
<td>0.580</td>
<td>0.001***</td>
</tr>
</tbody>
</table>

Objective variable is the proportion of deaths at home. Variable input method is the forward-backward stepwise selection method. Adjusted R²=0.627.

SCR, standardized claim data ratio.
*p<0.05, **p<0.01, ***p<0.001.

home. The adjusted R2 value for the multiple regression model was 0.627.

**DISCUSSION**

In this study, we used the Japanese NDB, public data, and SCR to clarify the medical resources and activities that affect the proportion of death at home for cancer patients.

This study had two advantages. The first was clarifying the actual proportion of death at home using large-scale nationwide data. In particular, the widespread use of the NDB is expected to elucidate the current state of home medical care in Japan. Second, we extracted the data on patients who died at home with high accuracy by calculating medical fees related to deaths at home, including cases visited by physicians and confirmed deaths at home. We believe that these advantages allowed us to clarify the actual proportion of deaths at home in Japan.

The analysis revealed specific differences by prefecture in the proportions of deaths at home of cancer patients; we found an approximately three-fold difference between the maximum and minimum values. Moreover, we found that physicians’ activities in home-visit medical care substantially increased the proportion of deaths at home. By contrast, the number of acute and long-term care beds significantly decreased the proportion of deaths at home.

To our knowledge, this is the first study to use large-scale and highly accurate data. As the findings were obtained by verifying the NDB, public data, and SCR throughout Japan, our results indicated a universal tendency regarding death at home in Japan. In addition, these findings could provide valuable suggestions for the challenges regarding death at home in other countries with aging populations, as in Japan.

The proportion of deaths at home was highest (41.6%) in Kanagawa. Kanagawa had the highest SCR for home-visit medical care in Japan (153.7), supporting the results of multiple regression analysis. Moreover, the prefecture’s number of acute beds corrected by population was the second lowest in Japan (362.3 beds per 100,000 population). Hence, we determined that the proportion of deaths at home was high in Kanagawa owing to the increased home-visit medical care and lack of hospital beds in the acute phase. In contrast, the proportion of deaths at home in Akita was the lowest (14.8%). In Akita, the SCR for home-visit medical care and nursing were the second lowest in Japan (SCR = 43.9 and 47.6, respectively). Contrarily, the number of acute beds corrected by population in the prefecture was the fifth highest in Japan (594.0 beds per 100,000 population). Thus, we determined that the proportion of deaths at home in Akita was low because of a lack of home-visit medical and nursing care combined with access to acute care hospital beds. The average age of the population by prefecture was higher in Akita than in Kanagawa (53.2 vs. 46.8 years).

This difference indicates different levels of care in these areas, which could affect whether the patients can receive home medical care. In an aging area such as Akita, inpatient care may be preferred because of the burden of care; thus, the proportion of deaths at home might be lower. In addition, the number of long-term care beds reduced the proportion of deaths at home. The SCR for chronic care hospitalization was significantly lower in the group with a high proportion of deaths at home. Therefore, more long-term care beds and improved long-term care also led to a low proportion of deaths at home.

These results demonstrated the need to improve home-visit medical care activities to increase the proportion of cancer patients who die at home. Therefore, physicians should be trained to provide home-visit medical care, and home-visit medical fees must be increased. Chiba et al. reported that compared to cases in hospitals, home-visiting physicians more frequently explained the meaning of death at home and its process, available insurance systems, and financial information.

Therefore, it is particularly important to train home-visiting physicians to explain this information. Enhancing home-visit medical care activities may improve home-based palliative care and establish a system that enables cancer patients to fulfill their hope of spending their last days at home. Simultaneously, the optimization of medical resources allocation in acute and long-term care beds, which affects the proportion of deaths at home, is another issue to be resolved.
Although the present study had significant findings, it also had some limitations. First, regarding death at home, it is important that the patient has hope for spending their last days at home and have family members who could care for the patient. However, this information could not be obtained from the NDB or public records. Additional large-scale qualitative studies are required to verify these findings. Second, it was impossible to clarify the death status of other outpatients. The deaths of other outpatients included lonely deaths without family members, sudden deaths due to sudden illness, and deaths at home, which did not meet our study criteria. On the other hand, other outpatients might have died at home but did not meet the requirements of this study. Therefore, we might have underestimated the proportion of deaths at home in this study. Third, since we analyzed data that had already been aggregated, we could not ascertain underlying diseases other than cancer. The target patients might have included those who died of diseases other than cancer. Since older individuals tend to have many comorbidities, the results of this study should be carefully interpreted.

In conclusion, using the Japanese NDB, public data, and SCR, we clarified the medical resources and activities that affect proportion of death at home for cancer patients. Physicians’ home-visit medical care activities significantly increased the proportion of deaths at home. Conversely, the number of acute and long-term care beds significantly decreased the proportion of deaths at home. In Japan, which faces a super-aging and multi-death society, the government should consider optimizing medical resources and activities to enable cancer patients to fulfill their hopes of spending their last days at home.

ACKNOWLEDGMENTS

We thank Dr. Jimpei Misawa and Dr. Yukinori Moriya for providing helpful advice for this study.

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

This work was supported by the Japan Society for the Promotion of Science Grant-in-Aid for Scientific Research (C) (Grant No. JP19K10550). The funders had no role in the study design, data collection, analysis, the decision to publish, or the preparation of the manuscript.

AUTHOR CONTRIBUTIONS

Conceptualization, KT, KF, TO, HC; Data curation, KT, KF; Funding acquisition, KT; Investigation, KT; Methodology, KT; Project administration, KT; Supervision, KF; Writing-original draft, KT; Writing-review & editing, KT, KF, TO, HC.

REFERENCES


27. Portal Site of Official Statistics of Japan. Prefecture, gender population and population sex ratio-total population, Japanese population, 2015 [Internet]. Tokyo, Japan: Portal Site of Official Statistics of Japan; 2015 [cited 2023 Jun 10]. Available from: https://www.e-stat.go.jp/stat-search/files?page=1&query=%E4%BA%BA%E5%8F%A3%E6%8E%A8%E8%A8%88%E3%80%80%E9%83%BD%E9%81%93%E5%BA%9C%E7%9C%8C%E3%80%80%E5%B9%B3%E6%88%9029&layout=datalist&stat_infid=000031690317.


INTRODUCTION

Falls are a major concern in hospitalized patients, particularly in older adults and those with frailty. Falls can result in a range of negative outcomes, including fractures and head injuries, leading to longer hospital stays and significant morbidity and mortality. Moreover, falls can cause psychological distress, fear of falling, and a loss of confidence in one's ability to move safely. Falls also create a significant burden on healthcare systems by increasing healthcare costs and diverting resources from other areas of care. Therefore, it is crucial to screen patients who are at high risk of falling and implement preventive measures in a hospital setting.

The Morse Fall Scale (MFS), developed in 1986, is a widely used tool in healthcare settings to assess a patient's risk of falling. It considers six factors: history of falling, current medications, mobility, mental status, presence of equipment (such as intravenous
lines or catheters), and age. Each factor is assigned a score, and the total scores determine a patient’s overall fall risk. The MFS is one of the most commonly used screening tools for high fall risk in hospitalized patients; however, the optimal cutoff value remains controversial.\(^6\)\(^7\) Furthermore, studies have shown that the screening value of MFS might be insufficient.\(^8\)

Falls are considered a geriatric syndrome, a condition closely related to frailty,\(^9\) which is a state of increased vulnerability and reduced physiological reserves due to the accumulation of aging processes in older adults.\(^11\)\(^12\) Numerous studies have demonstrated a higher risk of falls among hospitalized patients with frailty.\(^13\)\(^14\) Consequently, it may be logical to screen patients for frailty to more effectively predict and prevent falls. Indeed, the MFS itself includes items reflecting the spectrum of frailty, such as a history of falls, mobility, mental status, and age.

Among the tools to assess frailty, the Clinical Frailty Scale (CFS), with scores ranging from 1 (very fit) to 9 (terminally ill), has been widely used in various clinical settings.\(^15\) In acute medical conditions, the CFS is generally applied to assess a patient’s baseline functional status 2 weeks before they fall ill.\(^16\) Meanwhile, the at-point CFS, which incorporates the baseline functional status and severity of an acute illness, can assess the health status of patients at the time of evaluation.\(^16\)\(^17\) A previous study showed that at-point CFS predicted various adverse health outcomes, such as falls, in hospitalized patients aged > 65 years.\(^17\) However, despite the general applicability of frailty in younger and middle-aged adults,\(^18\)\(^19\) no study has established the efficacy of the CFS as a screening tool for falls in this population. Hence, we aimed to assess the screening ability of the at-point CFS and MFS in identifying hospitalized adults aged > 18 years at high risk for falls.

**MATERIALS AND METHODS**

**Study Design and Population**

This retrospective cohort study was conducted at the Asan Medical Center, a tertiary hospital in Seoul, Korea. The study included a total of 2,028 patients, consisting of 1,016 patients aged ≥ 65 years who were admitted to the general ward between May 1 and September 30, 2021 and 1,012 patients aged ≥ 18 years who were admitted to the emergency room between February and March 2022. Although the at-point CFS was measured for all patients who visited the emergency room since August 2021, the most recent data from February and March 2022 were used to increase the accuracy of the study, considering the proficiency of the emergency medical staff in CFS measurements. Patients who did not undergo at-point CFS measurements were excluded. The study protocol was approved by the Institutional Review Board of Asan Medical Center (No. 2022-0722). Written informed consent was waived as the evaluation of the general health status of patients at admission is a routine practice and no harm was expected.

This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.\(^20\)

**MFS**

The MFS is used to assess a patient’s risk of falling by evaluating the presence or absence of various risk factors.\(^21\) It comprises six items: fall history, secondary diagnosis, use of ambulatory aids, intravenous therapy or heparin cap use, gait, and cognitive status related to gait. Each item was scored, with a maximum total score of 125 points. Patients with a score < 45 points were considered to have a low risk of falling, whereas those with a score ≥ 45 were considered to be at high risk. The fall risk assessment using the MFS was performed at the time of admission, once daily during hospitalization, and when the patient’s condition changed. The results of the fall risk assessments were included in electronic medical records.

**At-Point CFS**

The at-point CFS measurement for inpatients was performed by experienced geriatric nurses on the day after admission to the geriatric department. In the emergency room, the at-point CFS was measured by emergency room nurses. We used the Korean-translated version of the CFS 2.0 and a classification tree with established construct validity in the Korean geriatric outpatients\(^22\) and accuracy for predicting adverse outcomes in hospitalized older patients.\(^23\) The Korean-translated version of the CFS 2.0 and classification tree are described in Supplementary Figs. S1 and S2, respectively.

**Outcome Measures**

The fall incidence was obtained from mandatory fall reports for all falls that occurred in the hospital. This comprehensive data collection approach aimed to accurately capture and analyze the frequency and causes of falls in a hospital setting as a standard patient safety measure. Each report contained pertinent details, such as the patient’s demographics, fall location, circumstances leading to the incident, and sustained injuries.

**Statistical Analysis**

The data in this study were analyzed using the SPSS version 21.0 and R software version 3.6.3. The baseline characteristics of the fall and non-fall groups, including frequency, percentage, mean, and standard deviation, were described using descriptive statistics. The t-tests and chi-square tests were used to compare the two groups.
The score distributions of the at-point CFS and MFS among the patients were described. We compared and analyzed the predictive ability of each tool in terms of sensitivity, specificity, and positive and negative predictive values (PPV and NPV, respectively). The area under the receiver operating characteristic (ROC) curve (AUC) was analyzed to compare the diagnostic accuracy of predicting falls and non-falls based on each tool’s evaluation score. We determined the cutoff score for distinguishing between the fall and non-fall groups by adding the sensitivity and specificity scores in each score range and selecting the maximum value. The significance of the AUC difference between the fall risk assessment tools was analyzed using the DeLong test.

RESULTS

Baseline Participant Characteristics

Table 1 presents the baseline characteristics of the study participants categorized according to fall events. Of the 2,028 total patients, 25 (1.23%) experienced falls during hospitalization, whereas 2,003 (99.75%) did not. Participants in the non-fall group were younger than those in the fall group; however, the difference was not statistically significant. The average length of hospitalization was significantly longer in participants with falls than in those without falls (21.12 ± 15.13 vs. 9.30 ± 10.32 days; *p* < 0.001). The mean at-point CFS score was significantly higher in participants with falls than in those without falls (5.56 ± 1.56 vs. 4.52 ± 1.59; *p* < 0.001). The mean MFS score did not differ significantly between the two groups (45.00 ± 19.26 vs. 38.55 ± 16.76 for those with and without falls, respectively; *p* = 0.056).

Distributions of At-Point CFS and MFS Scores

Tables 2 and 3 show the distributions of the at-point CFS and MFS scores. The at-point CFS scores with the highest frequency of falls were 6 points with six falls (24.0%), followed by 7 points with six falls (24.0%), and 5 points with five falls (20.0%). In the fall group, the MFS scores with the highest frequency of falls were

### Table 1. Baseline characteristics of the participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 2,028)</th>
<th>Non-fall (n = 2,003)</th>
<th>Fall (n = 25)</th>
<th>X²/t</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1,195 (58.9)</td>
<td>1,183 (59.1)</td>
<td>12 (48.0)</td>
<td>1.25</td>
<td>0.308</td>
</tr>
<tr>
<td>Female</td>
<td>833 (41.1)</td>
<td>820 (40.9)</td>
<td>13 (52.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>68.33 ± 12.74</td>
<td>68.29 ± 12.77</td>
<td>71.92 ± 9.55</td>
<td>-1.42</td>
<td>0.157</td>
</tr>
<tr>
<td>≤ 40</td>
<td>98 (4.8)</td>
<td>98 (4.9)</td>
<td>0 (0)</td>
<td>2.77</td>
<td>0.0736</td>
</tr>
<tr>
<td>41–50</td>
<td>88 (4.3)</td>
<td>87 (4.3)</td>
<td>1 (4.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>51–60</td>
<td>175 (8.6)</td>
<td>174 (8.7)</td>
<td>1 (4.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>61–70</td>
<td>706 (34.8)</td>
<td>698 (34.8)</td>
<td>8 (32.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71–80</td>
<td>706 (34.8)</td>
<td>695 (34.7)</td>
<td>11 (44.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 81</td>
<td>255 (12.6)</td>
<td>251 (12.5)</td>
<td>4 (16.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of stay (day)</td>
<td>9.45 ± 10.47</td>
<td>9.30 ± 10.32</td>
<td>21.12 ± 15.13</td>
<td>-3.89</td>
<td>0.001</td>
</tr>
<tr>
<td>At-point CFS</td>
<td>4.53 ± 1.59</td>
<td>4.52 ± 1.59</td>
<td>5.56 ± 1.56</td>
<td>-3.25</td>
<td>0.001</td>
</tr>
<tr>
<td>MFS</td>
<td>38.63 ± 16.81</td>
<td>38.55 ± 16.76</td>
<td>45.00 ± 19.26</td>
<td>-1.91</td>
<td>0.056</td>
</tr>
</tbody>
</table>

Values are presented as number (%) or mean ± standard deviation.
CFS, Clinical Frailty Scale; MFS, Morse Fall Scale.

### Table 2. At-point CFS score distribution of the participants

<table>
<thead>
<tr>
<th>CFS point</th>
<th>n (%)</th>
<th>Age (y)</th>
<th>Non-fall (n = 2,003)</th>
<th>Fall (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12 (0.6)</td>
<td>52.50 ± 13.95</td>
<td>12 (0.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>2</td>
<td>64 (3.2)</td>
<td>53.39 ± 15.19</td>
<td>64 (3.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>3</td>
<td>636 (31.4)</td>
<td>67.17 ± 11.03</td>
<td>632 (31.6)</td>
<td>4 (16.0)</td>
</tr>
<tr>
<td>4</td>
<td>376 (18.5)</td>
<td>67.21 ± 12.88</td>
<td>37 (18.7)</td>
<td>2 (8.0)</td>
</tr>
<tr>
<td>5</td>
<td>369 (18.2)</td>
<td>68.89 ± 11.88</td>
<td>364 (14.4)</td>
<td>5 (20.0)</td>
</tr>
<tr>
<td>6</td>
<td>294 (14.5)</td>
<td>72.46 ± 11.17</td>
<td>288 (10.6)</td>
<td>6 (24.0)</td>
</tr>
<tr>
<td>7</td>
<td>199 (9.8)</td>
<td>70.95 ± 14.41</td>
<td>193 (7.9)</td>
<td>6 (24.0)</td>
</tr>
<tr>
<td>8</td>
<td>62 (3.1)</td>
<td>72.21 ± 13.47</td>
<td>60 (3.0)</td>
<td>2 (8.0)</td>
</tr>
<tr>
<td>9</td>
<td>16 (0.8)</td>
<td>76.63 ± 17.95</td>
<td>16 (0.8)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Values are presented as number (%) or mean ± standard deviation.
CFS, Clinical Frailty Scale.
41–50 points with 10 falls (40.0%), followed by 31–40 points with six falls (24.0%), and ≤ 20 points with three falls (12.0%). Using a cutoff score of 45 points, 17 patients (68.0% of the total subjects with fall events) had a score of ≤ 45 points.

Sensitivity, Specificity, PPV, and NPV according to the Screening Tools

For the at-point CFS, the sensitivity, specificity, PPV, and NPV were 84.0%, 35.4%, 1.6%, and 99.4% at a cutoff score of 4 and 76.0%, 54.0%, 2.0%, and 99.4% at a cutoff score of 5, respectively. Based on the optimal cutoff score determined by the sum of sensitivity and specificity presented in the ROC analysis, the optimal cutoff score for the at-point CFS was 5. For the MFS, the cutoff score of 45 points proposed by the original author during tool development showed a sensitivity of 60.0%, specificity of 68.1%, PPV of 2.2%, and NPV of 99.4%; thus, the optimal cutoff score in this study was retained at 45 points (Table 4).

ROC according to the Screening Tools

The optimal cutoff points, which were determined by the maximal points of the sums of sensitivity and specificity, for the at-point CFS and MFS were 5 and 45, respectively. The AUC value of at-point CFS was higher than that of MFS (0.68 and 0.63, respectively), although not statistically significant (p = 0.31) (Fig. 1). After excluding participants aged < 60 years, the AUC value of the at-point CFS was still higher than that of the MFS (0.65 and 0.61, respectively), although also without statistical significance (p = 0.52) (Supplementary Fig. S3). Considering the potential impact of measurement reliability on the results, we conducted subgroup analyses based on the groups measured by emergency room nurses and experienced geriatric nurses. The AUC values for at-point CFS and MFS in the group measured by emergency room nurses, were 0.62 and 0.54, respectively, whereas in the group measured by experienced geriatric nurses, the AUC values were 0.76 and 0.77, respectively. Supplementary Fig. S4 shows the corresponding ROC curves for reference.

Construct Validity of the At-Point CFS

We observed a significant association between the at-point CFS and MFS. The standardized beta coefficient was 2.76, indicating a strong positive relationship between the two variables (p < 0.001). Additionally, the R² value was 0.17. Fig. 2 presents a point plot and linear regression depicting this association.

DISCUSSION

In this comparative study, we aimed to assess the screening ability of the at-point CFS and MFS to identify hospitalized adults with high risk of falls. We found optimal cutoff points of 5 and 45 for the at-point CFS and MFS, respectively. Although the at-point CFS had higher explanatory power than the MFS, the AUC values did not differ significantly between the two tools. To our knowledge, this is the first study to compare the screening values of the at-point CFS and MFS in an acute-care hospital.

In this study, we used the at-point CFS, which is different from the original CFS that reflect baseline health status. However, our findings are consistent with those of previous studies that reported the optimal cutoff point for CFS in determining frailty status. Our current observations are also concordant with our previous report showing that a cutoff point of 5 for the at-point CFS can predict various geriatric adverse events such as pressure ulcers, delirium, longer duration of hospitalization, unexpected emergency department visits after discharge, and institutionalization after discharge in hospitalized patients aged ≥ 65 years. This consistency lends further credibility to our results and suggests that the at-point CFS may serve as a useful tool for predicting fall risk among hospitalized adults.

Falls are the result of a complex system failure rather than a sin-
Frailty is a common and important geriatric syndrome that is closely associated with falls. Physical frailty, characterized by a decline in physical function and muscle strength, can lead to a loss of balance and increased risk of falls. Furthermore, falls are often a consequence of the inability to perform multiple tasks due to cognitive decline and inability to integrate sensory inputs. Polypharmacy, another phenotype that reflects deficits in systemic integrity, is also an important risk factor for falls. Various studies have demonstrated that frailty is an important risk factor for falls among different populations. Hence, falls result from a systemic failure, a concept that may be applicable not only to older adults but also to younger populations.

The CFS is a simple and rapid tool for assessing frailty and has shown promising results in predicting falls. Church et al. showed the predictive ability of CFS in 71% of fall cases in a scoping review. Hatcher et al. demonstrated that the CFS score at admission predicted readmission for falls after trauma-related injuries. The Center for Effective Practice recommends the CFS as a screening tool to evaluate the risk of falls in community-dwelling adults. Jung et al. showed that an at-point CFS ≥ 5 was associated with an increased risk of falls, with an odds ratio of 1.74 in older hospitalized patients. However, none of the studies utilized the at-point CFS in acute medical conditions in populations including young adults.

The MFS is a tool commonly used to assess fall risk among hospitalized patients; however, it has several limitations compared to those of the CFS. One major advantage of the CFS is because it
was initially developed to evaluate frailty, it can predict a wide range of geriatric syndromes other than falls, including outcomes such as delirium and pressure ulcers.\(^{17,23,32}\) In contrast, the MFS measures only the risk of falls, although some of its components include a range of frailties, such as a history of falls and cognitive function. Another limitation of the MFS is the burden to ask six questions to every individual, whereas the CFS requires only one question. Furthermore, the accuracy and cutoff score of the MFS are controversial, as previous studies have shown mixed results.\(^{3,9}\)

One of the key strengths of this study was its comparative approach, which allowed for a more comprehensive assessment of the at-point CFS and MFS to identify hospitalized adults with a high risk of falls. To our knowledge, this is the first study to compare the screening values of the two assessment tools in an acute-care hospital setting, making the result an important contribution to the existing literature. Furthermore, our findings are consistent with previous research on the optimal CFS cutoff points for determining frailty status, providing further support for the at-point CFS as a valuable screening tool for fall risk. Additionally, our study builds on prior research by demonstrating the ability of the at-point CFS to predict various geriatric adverse events, further highlighting its potential clinical utility.

Despite its strengths, our study had several limitations. First, this study was conducted in a single acute-care hospital, which might limit the generalizability of our results to other healthcare settings and patient populations. Second, although we found no significant differences in AUC values between the assessment tools, the sample size might not have been sufficient to detect subtle differences in their predictive abilities. Third, our study did not evaluate other potentially relevant risk factors of fall such as clinical, environmental, or situational factors, which could have provided additional insights into the most effective strategies for fall prevention and intervention. Fourth, only two participants aged < 60 years experienced falls, which might appear insufficient. However, as younger patients are less prone to falls, this situation was unavoidable. As shown in Supplementary Fig. S3, the exclusion of younger participants from the analysis did not affect the overall results. Finally, the inclusion of two distinct groups assessed by emergency room nurses and experienced geriatric nurses could potentially affect the reliability of the at-point CFS measurement. However, the results of the subgroup analysis comparing these two groups showed that this factor did not significantly affect the main results. Nonetheless, further investigations are needed in future studies.

In conclusion, the results of our study demonstrated that the at-point CFS is an effective tool for identifying fall risk among hospitalized adults, with a performance comparable to that of the MFS. Therefore, the at-point CFS may be a valid screening tool for fall risk in hospitalized adults.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

We thank the Asan Multidisciplinary Committee for Seniors (AMCS) and Ministry of Health and Welfare (Research-driven Hospitals, HR20C0026) for their support and funding throughout this research project. The members of the AMCS are listed in Supplementary Table S1.

AUTHOR CONTRIBUTIONS

Conceptualization, HWJ, JK; Methodology, JYB, IYJ; Formal analysis, JK, SJ; Funding acquisition, IYJ, EL; Investigation, HWJ, JK, EL; Resources, IVJ, EL; Data curation, SJ, YK, YS, JYB; Writing-original draft, SJ, HWJ, JYB; Writing-review & editing, JK, YK, SC, HJO.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.23.0057.

REFERENCES

7. Schwendimann R, De Geest S, Milisen K. Evaluation of the Morse Fall Scale in hospitalised patients. Age Ageing 2006;35:


Domains of the Kihon Checklist Associated with Prefrailty among Community-Dwelling Older Adults

Taishiro Kamasaki1,2, Hiroshi Otao1, Mizuki Hachiya1, Atsuko Kubo1, Hiroyuki Okawa1, Kazuhiko Fujiiwara1, Asuka Sakamoto1, Suguru Shimokihara2, Michio Maruta3,4, Gwanghee Han4,5, Takayuki Tabira6

1Department of Rehabilitation Sciences, Faculty of Rehabilitation Sciences, Nishikyushu University, Kanzaki, Japan
2Doctoral Program of Clinical Neuropsychiatry, Graduate School of Health Sciences, Kagoshima University, Kagoshima, Japan
3Department of Occupational Therapy, Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, Japan
4Faculty of Medicine, Kagoshima University, Kagoshima, Japan
5Department of Occupational Therapy, School of Health Sciences at Fukuoka, International University of Health and Welfare, Otawara, Japan
6Graduate School of Health Sciences, Kagoshima University, Kagoshima, Japan

Background: Various functions are involved in prefrailty. However, no studies have examined more relevant functions. Therefore, this study examined the domains of the Kihon Checklist (KCL) associated with prefrailty by comparing them to robustness measures, using the KCL to comprehensively assess life-related functions in community-dwelling older adults.

Methods: The 194 (mean age, 75 ± 6 years) participants were community-dwelling older adults. Their robustness and preferences were assessed using the Japanese Cardiovascular Health Study criteria. Comprehensive life-related functions were assessed using the KCL, and each physical function was measured.

Results: The main KCL characteristics associated with robustness and prefrailty were physical function (odds ratio [OR]=1.83; 95% confidence interval [CI], 1.17–2.88), nutritional status (OR=8.16; 95% CI, 2.96–22.48), and depressed mood (OR=3.46; 95% CI, 1.76–6.79). In particular, older adults had difficulty moving, including climbing stairs and getting up from a chair, which suggested a strong fear of falling. The participants also reported psychological characteristics such as low life fulfillment, a low sense of self-usefulness, and a strong sense of boredom.

Conclusions: Prefrail individuals were characterized by poor physical function and nutritional status, as well as depressive mood. Prefrailty may be prevented or improved by approaches to improve physical function and fear of falling in addition to psychological interventions that encourage activity and a sense of self-usefulness.

Key Words: Older adults, Depressive mood, Kihon Checklist, Physical function, Frailty

INTRODUCTION

Frailty, a risk factor in older adults requiring long-term care,1) is defined as a biological syndrome characterized by a decline in physiological reserves with age.3) Frailty is characterized by reversibility; therefore, early detection and intervention in frail older adults may help restore their vigor.3)

The Cardiovascular Health Study (CHS) criteria are widely used in Europe and the United States.6,7) Japan uses a revised version of the CHS (J-CHS), which comprises five questions. Scores of ≥ 3 and 1–2 indicated frailty or prefrailty, respectively. A Japanese study of community-dwelling older adults reported a 56.9% prevalence of prefrailty as assessed by the J-CHS; that is, more than half of the population falls under this category.6) Prefrail people are at a higher risk of facing impairments in activities of daily living (ADL) and instrumental activities of daily living (IADL) compared to robust people.7) Additionally, the risk of needing long-term care after 2 years is significantly higher than that in
healthy adults. Thus, prefrailty in older adults is a significant risk factor that merits as much attention as frailty. Although most studies have focused on high-risk frailty, literature on the various aspects of prefrailty is scarce. To avoid the need for long-term care and extend healthy life expectancy in older adults, interventions must begin from the prefrailty stage to reduce the overall cost of healthcare and shorten the intervention time.

In Japan, the Kihon Checklist (KCL) is widely used to determine the need for long-term care prevention. The KCL comprehensively and multidimensionally assesses function in older adults. Using this tool, it is easy to ascertain which functions are deteriorating, and which must be targeted for prevention and intervention. As mentioned above, only a limited number of studies have evaluated prefrailty in community-dwelling older adults, and only one study has examined the association between prefrailty and the KCL. Furthermore, after the revision of the J-CHS in 2020, no studies have assessed this association according to the revised criteria. Therefore, this study examined and characterized the association between prefrailty, as determined by the revised J-CHS, and comprehensive functioning, as assessed by the KCL. Identifying the KCL domains associated with prefrailty will contribute to focused rehabilitation interventions for improvement from prefrailty to robustness.

MATERIALS AND METHODS

Participants
This cross-sectional study included community participants who underwent a physical fitness assessment. Participants were recruited through calls from health promotion class staff and posters. The participants were community-dwelling middle-aged and older adults who visited the measurement site independently. Those who were determined to be frail according to the J-CHS, showed deficiency in the primary endpoints, and were aged ≤ 64 years were excluded from the study. All participants in the physical fitness evaluation sessions were fully informed of the content and purpose of the study, and their consent and cooperation were obtained after gaining their understanding. Voluntary participation in the study was explained to the participants, and the physical fitness measurements were performed even if they refused to participate without any disadvantages or consequences. The study protocol was approved by the Ethical Review Committee of Nishikyushu University (No. 21VBC35). Also this study complied the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research.

Prefrailty
The J-CHS assesses five items: weight loss, muscle weakness, fatigue, decreased walking speed, and decreased physical activity. For weight loss, participants were asked whether they had an unintentional weight loss of ≥ 2 kg over a 6-month period, with one point added for “yes” responses. Grip strength was measured using a Smedley-type digital grip strength meter (T.K.K. 5401; Takei Scientific Instruments, Niigata, Japan); points were added for grip strengths of < 28 and < 18 kg in males and females, respectively. Fatigue was assessed by asking the participant whether they had felt tired for any reason in the last 2 weeks; a point was added if the answer was “yes.” To determine the walking speed component, the participants were asked to walk at a normal pace along an 11-m walking path. Their walking speed was calculated for the middle 5 m. A point was added if the walking speed was < 1.0 m/s. Physical activity was assessed by two questions: (1) whether the respondents engaged in light exercise or gymnastics and (2) whether they engaged in regular exercise or sports. Points were added if the respondent answered “not even once a week” to either question. Prefrailty was ascertained when one or two of the five items were scored.

KCL
The KCL is recommended for determining the need for preventive care services and certifying the need for long-term care. The KCL is used to assess functions closely related to daily life from multiple perspectives. The questionnaire was developed by the Ministry of Health, Labor, and Welfare in Japan and has been used in various countries because of its usefulness. It contains 25 questions addressing seven life-related domains: IADLs (questions #1–5), physical function (questions #6–10), nutritional status (questions #11–12), oral function (questions #13–15), social isolation (questions #16–17), cognitive function (questions #18–20), and depressive mood (questions #21–25). Each question consists of a “yes” and “no” two-case system, with one point awarded for each applicable answer. The total score for each of these functions was used as a representative value to provide a comprehensive assessment of the functions of older adults. The KCL items are listed in Supplementary Table S1.

Physical and Cognitive Functioning
Grip strength was measured using a Smedley-type digital grip strength meter (T.K.K. 5401). While standing, the participants were asked to extend their elbow joint, and the proximal interphalangeal joint of the index finger was adjusted to 90°. During the measurements, the examiner ensured that the upper limbs did not
touch the lower limbs or trunk. All measurements were taken twice, alternately on the left and right sides, and the total of the left and right sides divided by the body weight was used as the grip strength.

Knee extension strength was measured using a Locomo Scan-II (Model 20691; ALCARE, Tokyo, Japan) lower-limb muscle strength-measuring device with a training function. Locomo Scan was developed based on a training method for quadriceps exercises. Muscle force measurement data were sampled at 100 m/s, with minimum and maximum measurements of 1 and 1,500 N, respectively. Since the Locomo Scan uses the quadriceps setting exercise method of measurement, this method may induce less pain compared to the conventional method using a hand-held dynamometer. All participants performed isometric knee extension exercises in a long sitting position, and the pressure applied on the Locomo Scan was recorded. The measurements were taken twice, alternately on the left and right sides, with the sum of the left and right sides divided by the body weight used as the knee extensor muscle strength.

The 30-second chair stand test (CS-30) was performed using a chair with a seat height of 40 cm and a digital stopwatch. With their upper limbs crossed in front of their chest, the participants were asked to stand up and sit down repeatedly as fast as possible for 30 seconds, and the number of repetitions was recorded. Because the CS-30 is challenging for older adults, only one measurement was taken, taking fatigue into consideration.

Timed up and go (TUG) tests were performed using a digital stopwatch. The participants were instructed to get up from the chair, go to a landmark located 3 m in front of them, and sit down again. The time required for a series of movements was measured. Measurements were taken once for leftward rotation and once for rightward rotation, and the fastest value was used.

The maximum walking speed was measured using a digital stopwatch. The participants were asked to walk 11 m on level ground as quickly as possible. The time required to cover the middle 5 m distance was recorded. The test was performed twice, and the fastest value was used for analysis.

To assess cognitive function, a face-to-face evaluation was conducted using the Mini-Mental State Examination (MMSE). The MMSE is reported to have intra-rater reliability and is widely used worldwide. The exam consists of 11 items, in which a higher score on a 30-point scale indicates higher cognitive function and a score ≤ 23 indicates cognitive impairment.

Statistical Analysis
To confirm the characteristics of those participants indicated as prefrail, the sex distribution was compared using the chi-square test; age, height, weight, body mass index (BMI), and physical function were compared using Student t-test; and cognitive function and KCL were compared using the Mann–Whitney U test. Next, a binomial logistic regression analysis was conducted to examine the KCL domains associated with robustness and prefrailty, with robustness and prefrailty as dependent variables and each function of the KCL as an independent variable. Sex and age, which were considered covariates, were adjusted for in Model 2. In addition, the characteristics were analyzed in detail by comparing the percentage of respondents falling under the sub-items of each of the KCL that showed significant associations in the binomial logistic analysis between robustness and prefrailty. For effect size, the t-test was confirmed by Cohen’s d, Mann–Whitney U test by r, chi-square test by ϕ coefficient, and Fisher exact probability test by Cramer’s V. Furthermore, as the sample size could not be calculated a priori, power was determined as an a posteriori test. The statistical significance level was set at 5% (p < 0.05). IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA) was used for the analyses.

RESULTS
Study Participants
This study included 218 community-dwelling middle-aged and older adults who participated in community physical fitness sessions between 2019 and 2021. Of these, 24 participants were excluded: those determined to be frail by J-CHS (n = 3), those with missing primary endpoints (n = 2), and those aged < 64 years (n = 19). Therefore, the final analysis included 194 participants (mean age of 75 ± 6 years, 74% female) (Fig. 1).

Comparison of Robustness and Prefrailty
Of the participants, 72% (n = 140) and 28% (n = 54) were designated as robust and prefrail, respectively. We compared the demographic attributes, physical function, cognitive function, and KCL between these groups to identify the characteristics of participants deemed prefrail. Regarding physical function, robust participants had better grip strength (p = 0.002), CS-30 (p = 0.007), TUG (p = 0.001), and maximum walking speed (p < 0.001) than prefrail adults. In addition, robust participants had significantly higher MMSE scores than the prefrail participants (p = 0.016). Similarly, in the KCL, the points for physical function (p < 0.001), nutritional status (p < 0.001), oral function (p = 0.005), and depressive mood (p < 0.001) were significantly higher in robust adults compared to those who were prefrail. We observed no significant differences in other demographic attributes, physical function, or KCL scores (Table 1).
KCL Domains Associated with Robustness and Prefrailty
The KCL domains significantly associated with robustness and prefrailty in this study were physical function (p = 0.003; odds ratio [OR] = 1.94; 95% confidence interval [CI], 1.26–2.99), nutritional status (p < 0.001; OR = 7.47; 95% CI, 2.77–20.14), and depressive mood (p < 0.001; OR = 3.57; 95% CI, 1.84–6.93). After adjusting for gender and age as covariates, the KCL domains of physical function (p = 0.009; OR = 1.83; 95% CI, 1.17–2.88), nutritional status (p < 0.001; OR = 8.16; 95% CI, 2.96–22.48), and depressive mood (p < 0.001; OR = 3.46; 95% CI, 1.76–6.79) were significantly associated with robustness and prefrailty. The same items also showed significant associations in Model 2; the model χ² test was significant (p < 0.001), and the p-value for the Hosmer–Lemeshow test was 0.767. No independent variables had a variance inflation factor (VIF) ≥ 5 (Table 2, Fig. 2).

Comparison of KCL Domain Subitems Associated with Robustness and Prefrailty
We compared the percentages of respondents who fell into the subitems of the KCL domains that showed significant associations with robustness and prefrailty. The results showed significant differences for the following physical functions: “Do you normally climb stairs without using a handrail or wall for support?” (p < 0.001), “Do you normally stand up from a chair without any aids?” (p = 0.007), and “Do you have a fear of falling while walking?” (p = 0.008). We also observed a significant difference in the nutritional status-related question, “Have you lost 2 kg or more in the past 6 months?” (p < 0.001). Finally, regarding depressed mood, we observed significant differences for the questions “In the last 2 weeks, did you feel unfulfilled in your daily life?” (p = 0.012),

Table 1. Participants characteristics

<table>
<thead>
<tr>
<th>Overall (n = 194)</th>
<th>Robustness (n = 140)</th>
<th>Prefrailty (n = 54)</th>
<th>p-value</th>
<th>Effect size</th>
<th>95% CI</th>
<th>Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, female</td>
<td>140 (74)</td>
<td>107 (76)</td>
<td>43 (80)</td>
<td>0.633</td>
<td>0.34</td>
<td>-0.10</td>
</tr>
<tr>
<td>Age (y)</td>
<td>75 ± 6</td>
<td>74 ± 6</td>
<td>77 ± 7</td>
<td>0.003</td>
<td>-0.48</td>
<td>-0.79</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>153.7 ± 6.9</td>
<td>154.1 ± 6.8</td>
<td>152.5 ± 7</td>
<td>0.135</td>
<td>0.24</td>
<td>-0.08</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>54.1 ± 8.8</td>
<td>54.6 ± 8.6</td>
<td>52.9 ± 9.2</td>
<td>0.234</td>
<td>0.19</td>
<td>-0.13</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.9 ± 3.1</td>
<td>22.9 ± 3.1</td>
<td>22.7 ± 3.3</td>
<td>0.605</td>
<td>0.08</td>
<td>-0.23</td>
</tr>
<tr>
<td>Grip (kg/kg)</td>
<td>0.93 ± 0.20</td>
<td>0.95 ± 0.19</td>
<td>0.85 ± 0.21</td>
<td>0.002</td>
<td>0.51</td>
<td>0.19</td>
</tr>
<tr>
<td>Knee extension strength (N/kg)</td>
<td>12.97 ± 3.95</td>
<td>13.21 ± 3.82</td>
<td>12.33 ± 4.22</td>
<td>0.169</td>
<td>0.22</td>
<td>-0.10</td>
</tr>
<tr>
<td>CS-30 (stands)</td>
<td>22 ± 7</td>
<td>23 ± 7</td>
<td>20 ± 7</td>
<td>0.007</td>
<td>0.44</td>
<td>0.12</td>
</tr>
<tr>
<td>TUG (s)</td>
<td>5.7 ± 1.4</td>
<td>5.4 ± 0.9</td>
<td>6.5 ± 2.0</td>
<td>0.001</td>
<td>-0.78</td>
<td>-1.12</td>
</tr>
<tr>
<td>Maximum walking speed (m/s)</td>
<td>1.9 ± 0.4</td>
<td>2.0 ± 0.4</td>
<td>1.7 ± 0.3</td>
<td>&lt;0.001</td>
<td>0.68</td>
<td>0.36</td>
</tr>
<tr>
<td>MMSE</td>
<td>29 (28–30)</td>
<td>30 (28–30)</td>
<td>29 (27–30)</td>
<td>0.016</td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>J-CHS total points</td>
<td>0 (0–1)</td>
<td>0 (0–0)</td>
<td>1 (1–1)</td>
<td>&lt;0.001</td>
<td>0.99</td>
<td></td>
</tr>
<tr>
<td>KCLd</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0.981</td>
<td>0.00</td>
<td>0.06</td>
</tr>
<tr>
<td>IADL</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>&lt;0.001</td>
<td>0.32</td>
<td>0.99</td>
</tr>
<tr>
<td>Physical function</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>1 (0–1)</td>
<td>&lt;0.001</td>
<td>0.28</td>
<td>0.98</td>
</tr>
<tr>
<td>Nutritional status</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>&lt;0.001</td>
<td>0.20</td>
<td>0.84</td>
</tr>
<tr>
<td>Orual function</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0.296</td>
<td>0.08</td>
<td>0.23</td>
</tr>
<tr>
<td>Social isolation</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0.856</td>
<td>0.01</td>
<td>0.05</td>
</tr>
<tr>
<td>Cognitive function</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>&lt;0.001</td>
<td>0.39</td>
<td>1.00</td>
</tr>
<tr>
<td>Depressive mood</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>1 (0–1)</td>
<td>&lt;0.001</td>
<td>0.38</td>
<td>0.64</td>
</tr>
<tr>
<td>Total points</td>
<td>2 (1–3)</td>
<td>1 (1–3)</td>
<td>3 (2–6)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as number (%) or mean±standard deviation or median (1st quartile–3rd quartile).
BMI, body mass index; CS-30, 30-seconds chair stand test; TUG, Timed up and go test; MMSE, Mini-Mental State Examination; J-CHS, Japanese version of the Cardiovascular Health Study; KCL, Kihon Checklist; IADL, instrumental activities of daily living; CI, confidence interval.
*a-test, *b-Mann-Whitney U test, *c-chi-square test. *Highest point of KCL: IADL 5 points, Physical function 5 points, Nutritional status 2 points, Oral function 3 points, Social isolation 2 points, Cognitive function 3 points, and Depressive mood 5 points.
In each model, robustness and prefrailty are set as the dependent variables. Model 2: adjusted for age, sex.

KCL, Kihon Checklist; IADL, instrumental activities of daily living; OR, odds ratio; CI, confidence interval; VIF, variance inflation factor.

**DISCUSSION**

This study examined the KCL domains associated with robustness and prefrailty. Our results showed associations with physical function, nutritional status, and depressed mood. In particular, prefrail participants showed difficulty climbing stairs and getting up from a chair, and a strong fear of falling. Furthermore, these participants also expressed low life fulfillment, a low sense of self-usefulness, and a strong sense of boredom.

Moreover, 28% of the current study participants belonged to the prefrail category, a rate considerably lower than those previously
Table 3. Characteristics of life-related domains associated with robust and prefrailty

<table>
<thead>
<tr>
<th>Domain</th>
<th>KCL questions</th>
<th>Answer</th>
<th>Robust (n = 140)</th>
<th>Prevality (n = 54)</th>
<th>p-value</th>
<th>Effect size</th>
<th>95% CI</th>
<th>Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical function</td>
<td>6. Do you normally climb stairs without using handrail or wall for support?</td>
<td>No</td>
<td>14 (9)</td>
<td>19 (35)</td>
<td>&lt;0.001</td>
<td>0.30</td>
<td>0.13</td>
<td>0.45</td>
</tr>
<tr>
<td></td>
<td>7. Do you normally stand up from a chair without any aids?</td>
<td>No</td>
<td>6 (4)</td>
<td>9 (16)</td>
<td>0.007</td>
<td>0.21</td>
<td>0.04</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td>8. Do you normally walk continuously for 15 minutes?</td>
<td>No</td>
<td>1 (1)</td>
<td>1 (2)</td>
<td>0.480</td>
<td>0.05</td>
<td>0.01</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>9. Have you experienced a fall in the past year?</td>
<td>Yes</td>
<td>13 (9)</td>
<td>9 (17)</td>
<td>0.146</td>
<td>0.10</td>
<td>-0.01</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>10. Do you have a fear of falling while walking?</td>
<td>Yes</td>
<td>15 (11)</td>
<td>14 (26)</td>
<td>0.008</td>
<td>0.19</td>
<td>0.04</td>
<td>0.35</td>
</tr>
<tr>
<td>Nutritional status</td>
<td>11. Have you lost 2 kg or more in the past 6 months?</td>
<td>Yes</td>
<td>1 (1)</td>
<td>13 (24)</td>
<td>&lt;0.001</td>
<td>0.41</td>
<td>0.26</td>
<td>0.53</td>
</tr>
<tr>
<td></td>
<td>12. Height: cm, weight: kg, BMI: kg/m²</td>
<td>Yes</td>
<td>10 (7)</td>
<td>4 (7)</td>
<td>1.00</td>
<td>0.01</td>
<td>0.00</td>
<td>0.17</td>
</tr>
<tr>
<td>Depressive mood</td>
<td>21. In the last 2 weeks have you felt a lack of fulfillment in your daily life?</td>
<td>Yes</td>
<td>4 (3)</td>
<td>7 (13)</td>
<td>0.017</td>
<td>0.20</td>
<td>0.04</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>22. In the last 2 weeks have you felt a lack of joy when doing the things you used to enjoy?</td>
<td>Yes</td>
<td>3 (2)</td>
<td>4 (7)</td>
<td>0.096</td>
<td>0.13</td>
<td>0.01</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td>23. In the last 2 weeks have you felt difficulty in doing what you could do easily before?</td>
<td>Yes</td>
<td>15 (11)</td>
<td>21 (37)</td>
<td>&lt;0.001</td>
<td>0.31</td>
<td>0.16</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>24. In the last 2 weeks have you felt helpless?</td>
<td>Yes</td>
<td>2 (1)</td>
<td>5 (9)</td>
<td>0.019</td>
<td>0.19</td>
<td>0.03</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>25. In the last 2 weeks have you felt tired without a reason?</td>
<td>Yes</td>
<td>1 (1)</td>
<td>13 (24)</td>
<td>&lt;0.001</td>
<td>0.41</td>
<td>0.27</td>
<td>0.53</td>
</tr>
</tbody>
</table>

Values are presented as number (%).
KCL, Kihon Checklist; CI, confidence interval.
*Chi-square test, †Fisher exact probability test.

reported among community-dwelling older adults (42%–45%).22,23 This difference may have occurred because the study participants were already actively engaged in rehabilitation interventions (exercise classes and home exercise programs) to prevent long-term care and to extend their healthy life expectancies. The physical and cognitive functions of the participants in the analysis exceeded the cutoff values for those at risk of important adverse events such as falls.24,26

We compared the attributes, physical function, cognitive function, and KCL to determine the characteristics of prefrail adults. The results revealed significant differences in grip strength, CS-30, TUG, maximum walking speed, MMSE, and four KCL domains (physical function, nutritional status, oral function, and depressed mood). The J-CHS evaluation items included decreased grip strength and gait speed.27 Therefore, the findings of the current study in terms of significant differences between robust and prefrail individuals in grip strength and maximal walking speed are reasonable. In addition, the differences in KCL physical function likely occurred because prefraility is mainly associated with a decline in physical function.27,28 Nutritional status is considered a key contributor to the frailty cycle.29 Additionally, poor oral function worsens nutritional status.30 The results of the current study further corroborate these findings and show that prefrail patients tend to have poorer oral function and nutritional status. Furthermore, depressive mood is also reportedly associated with frailty prevalence and progression11; similar characteristics were shown by the prefrail participants in the present study. These results confirm the possibility that the KCL can be used to identify prefrailty.31,32,33

The results of the binomial logistic regression analysis with robustness and prefrailty as dependent variables showed that physical function, nutritional status, and depressed mood were significantly associated with robustness and prefrailty in Model 2, which was adjusted for sex and age. A previous study examining the characteristics of prefraility in community-dwelling older adults, as determined by the pre-revised J-CHS using the KCL, reported that physical functioning and depressed mood were characteristics of prefrailty, similar to the results of the present study.11 Physical
function in the KCL consists of five items: activities related to mobility such as stair climbing, standing up, walking, history of falls, and fear of falling. Frailty is also associated with mobility impairments. The present study focused on prefrailty; the relationship between mobility impairment and prefrailty suggests the need to address mobility from the prefrailty stage. In addition, prefrailty in community-dwelling older adults is a major risk factor for falls, which further supports the results of the current study and the need to address the risk of falls even in the prefrailty stage. In addition, several studies have reported a relationship between nutritional status and reduced physical function, consistent with the findings of the current study that worsening nutritional status was associated with decreased physical function and increased fatigue. In addition, a significant relationship was noted between depressive mood and reduced physical functioning. The association between frailty and depression in community-dwelling older adults has been reported; these individuals are approximately four times more likely to develop frailty, which may be attributed to depression leading to reduced activity and social frailty. Therefore, additional psychological interventions are required during the prefrailty stage.

We also compared the percentages of respondents falling under the sub-items of the KCL associated with prefrailty and robustness. The results revealed that prefrail individuals had greater difficulty climbing stairs and standing than walking. Interestingly, although we observed no significant difference in the history of falls, the fear of falling differed significantly \((p = 0.008)\). Older age and a strong fear of falling can be important factors in accelerating frailty by limiting physical activity. These characteristics indicate the need to enhance physical activity, focusing specifically on stair climbing and standing movements, to improve mobility-related movement from the prefrailty period. Our results also highlighted the need for an approach to prevent decreased activity due to the fear of falling. Regarding nutritional status, the only significant difference was in the question, “Have you lost 2 kg or more in the last 6 months?” This difference may be related to J-CHS, which contains many similar questions. Regarding depressive mood, the results showed that although the participants felt that their lives were relatively enjoyable, they experienced a lack of fulfillment, hesitancy to engage in activities, a low sense of self-usefulness, and a strong sense of fatigue. As individuals with prefrailty have a significant decline in physical function, not unexpectedly, a larger percentage of these individuals answered “yes” to the question “In the last 2 weeks, have you felt difficulty in doing what you could do easily before?” These findings indicate that prefrail older adults have a lower sense of fulfillment in daily life, which was supported by a previous study reporting that mobility was related to feelings of fulfillment in life in older adults. This study is limited due to its cross-sectional design, which prevented the identification of causal relationships; however, the results demonstrated that community-dwelling older adults with prefrailty may have a reduced sense of fulfillment in their lives due to impaired mobility. Our results suggest that prefrail older adults need to maintain activity levels and improve their sense of fulfillment in their lives while receiving environmental adjustment and social support in addition to interventions for physical function. Furthermore, decreased self-usefulness is a predictor of disability and mortality, and volunteer work and employment activities effectively improve the sense of self-usefulness. Thus, rehabilitation interventions aim to increase a sense of self-usefulness. The strength of this study is that it evaluated the functions associated with prefrailty using the KCL, which allowed for the identification of detailed segmented characteristics. This was also the first study to examine the association between the revised J-CHS and KCL.

This study has several limitations. First, the small sample size limits the generalizability of the results. It may also be necessary to collect more frail participants and classify them into three groups (robustness, prefrailty, and frailty). Second, the study population comprised older adults who routinely engaged in long-term care prevention and health promotion. Future studies should include a wider range of participants with longer follow-up periods. Third, because this was a cross-sectional study, it was not possible to establish causal relationships. Therefore, future longitudinal studies should be conducted. Finally, similar items were found in the revised J-CHS, with which prefrailty and robustness were determined in this study, and in the KCL questions. Future studies are needed to verify whether similar results to the present study can be obtained if prefrailty and robustness are determined using other assessment methods that do not have items similar to the KCL.

In conclusion, the results of this study revealed that physical functioning and depressed mood were associated with prefrailty among community-dwelling older adults, as determined by the revised CHS criteria. Furthermore, a detailed analysis of the sub-items showed particular difficulty in climbing stairs and getting up from a chair and a strong fear of falling. In addition to a lack of sense of fulfillment in their lives, the participants also demonstrated an aversion to activities and a low sense of self-usefulness. Furthermore, the results suggested that psychological approaches to reduce the fear of falling, encourage activity, and enhance self-usefulness may be important for improving prefrailty to robustness, in

www.e-agmr.org
addition to physical function alone. Additional studies are needed to examine whether a multidimensional approach to fear of falling and a psychological approach to depressed mood, can improve physical function and prefrailty.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST
The researchers claim no conflicts of interest.

FUNDING
None.

AUTHOR CONTRIBUTIONS
Conceptualization, TK, HOT, TT; Data curation, TK, HOT, MH, AK, TT; Formal analysis, TK, SS, MM; Investigation, TK, HOT, MH, AK, TT; Methodology, TK, MH, MM; Project administration, SS, MM; Supervision, HOT, TT; Validation, HOK, KG, AS, GH; Writing-original draft, TK; Writing-review & editing, HOK, KG, AS, GH.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.23.0019.

REFERENCES


Assessing Medication Use Quality in Older Outpatients Using the Beers Criteria: Findings from a Single-Center Retrospective Study

Kittipak Jenghua1,2, Kanchira Wutthi1, Chanisorn Wannakrachang1, Sitanan Chathongyos1, Panadda Ngamsom3

1Division of Social and Administrative Pharmacy, Department of Pharmaceutical Care, School of Pharmaceutical Sciences, University of Phayao, Phayao, Thailand
2Pharmacoepidemiology, Social and Administrative Pharmacy (PSAP) Research Unit, School of Pharmaceutical Sciences, University of Phayao, Phayao, Thailand
3Pharmacy Department, Chiangkham Hospital, Phayao, Thailand

Background: No comprehensive assessment of the quality of medications used in older outpatients has been conducted in Thailand. This study aimed to ascertain the prevalence of and factors contributing to older outpatients’ use of potentially inappropriate medications (PIMs).

Methods: This cross-sectional study retrospectively assessed the prescriptions of older (≥60 years) outpatients at a secondary-care hospital. For PIM identification, the 2019 American Geriatric Society (AGS) Beers criteria were applied, considering all five PIM categories: PIM category I (medications that are potentially inappropriate in most older adults), II (disease-/syndrome-exacerbating drugs), III (medications that should be used with caution), IV (clinically important drug–drug interactions), and V (medications that should be avoided or have their dosage reduced based on renal function).

Results: This study included 22,099 patients (mean age, 68.86 ± 7.64 years). Nearly three-fourths of patients were prescribed PIMs, with 68.90%, 7.68%, 44.23%, 15.66%, and 3.05%, respectively, receiving category I–V medications. The positive factors associated with PIM use included female sex (odds ratio [OR]=1.08; 95% confidence interval [CI], 1.01–1.16), age ≥75 years (OR=1.10; 95% CI, 1.01–1.21), polypharmacy (OR=10.21; 95% CI, 9.31–11.21), ≥3 diagnostic categories: (OR=2.31; 95% CI, 2.14–2.50), and ≥3 chronic morbidities (OR=1.46; 95% CI, 1.26–1.68). The negative factor associated with PIM use was a comorbidity score of ≥1 (OR=0.78; 95% CI, 0.71–0.86).

Conclusion: PIM use among older outpatients remains highly prevalent in clinical practice. The results of this study identified polypharmacy as the strongest factor affecting PIM use.

Key Words: Frail elderly, Inappropriate prescribing, Beers criteria, Quality of medication use

INTRODUCTION

The number of older adults is markedly increasing worldwide. Thailand is currently an aging society, and older people constitute approximately 19% of the total population. Because they are at a higher risk of adverse drug events (ADEs), older adults must be especially cautious when taking medications. According to the Health Product Vigilance Center (HPVC), 26.62% of ADE reports were from older adults, accounting for 17.90% of drug-related mortalities. Many medications are considered potentially inappropriate for use by older adults and are frequently referred to as potentially inappropriate medications (PIMs). Several sets of PIM detection criteria are currently available for use as assessment or screening tools to reduce the use of PIMs in older patients. The American Geriatric Society (AGS) Beers criteria is a well-known and frequently cited tool among existing criteria. The AGS Beers criteria contain drug-specific and explicit criteria that address various aspects of inappropriate prescriptions.

Copyright © 2023 by The Korean Geriatrics Society
This is an open access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.
including PIM categories I (medications that may be inappropriate in most older adults), II (medications that may worsen the disease or syndrome), III (medications that should be used with caution), IV (clinically significant drug–drug interactions), and V (medications that should be avoided or whose dosage should be adjusted based on renal function). For each criterion, the risk rationale, recommendation, and strength of recommendation are clearly stated. For example, first-generation antihistamines are strongly advised to be avoided because of their strong anticholinergic effects. The AGS Beers criteria are applicable to all levels of healthcare services, both inpatient and outpatient, and are unaffected by the patient’s level of frailty.

Secondary-care hospitals may have limited healthcare resources, such as geriatricians and clinical pharmacists, limited alternative medications, and less geriatric clinics, resulting in insufficient medication reviews. There are no reports on the quality of medication use in older outpatients receiving both short- and long-term care from secondary-care hospitals in Thailand. The current study sought to ascertain the prevalence of PIM use as determined by all aspects of the 2019 AGS Beers criteria as well as the factors associated with PIM use.

MATERIALS AND METHODS

Study Design and Setting

This study used a descriptive cross-sectional design. Data on older outpatients were obtained from the electronic medical record (EMR) database of a public hospital. The study hospital was a 231-bed secondary-care hospital located in the metropolitan district of Phayao Province, Thailand, that serves patients from the hospital district and five surrounding districts. Data from the EMR database were retrieved by the hospital staff working at the hospital data center.

We selected this hospital as the study setting because it offers a comprehensive EMR database. All data, including demographics, diagnoses, laboratory results, and prescriptions, were recorded in the EMR database. All medications prescribed in the outpatient and inpatient departments were recorded separately in the EMR database.

The study protocol was reviewed and approved by the Human Ethics Committee of the University of Phayao (Code No. UP-HEC 1.1/013/65, Date: June 8, 2022) and the Institutional Review Board of the study hospital (Code No. 006/2565, Date: July 8, 2022) before data collection.

Study participants

This study included all patients aged ≥ 60 years (referred to as “older” Thais) who visited the outpatient department (OPD) between January 1, 2020, and December 31, 2021 (a 2-year period). Patients lacking data on their diagnoses or prescriptions or those who were only administered the coronavirus disease 2019 (COVID-19) vaccine were excluded from the study.

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

Procedure

The EMR database contains all patient and medical data, including demographics (i.e., sex, age, age groups of 60–74 and ≥ 75 years), health insurance (universal coverage [UC] and non-UC), and clinical data (i.e., diagnostic categories, chronic morbidity, and the co-morbidity score calculated for each patient using the Charlson Co-morbidity Index). The International Classification of Diseases, 10th revision (ICD-10) coding schemes proposed by Glasheen et al. and Tonelli et al. were used to identify all chronic morbidities; OPD prescriptions (i.e., the number of prescriptions received by the patient between the index date, defined as the first date of an OPD visit with a prescription, and December 31, 2021); and polypharmacy, defined as a prescription containing ≥ 5 medications. Patients were assigned to the polypharmacy group if they had at least one prescription with polypharmacy.

Assessment of PIM Use

We primarily applied the 2019 AGS Beers criteria for the identification of all five PIM categories. All medications or medication classes were extracted from Tables 2–7 of the 2019 AGS Beers criteria and checked for availability in the study hospital. Among these, 102 PIM-related medications were identified. Hospital drug codes relevant to each medication were used to extract medications from electronic OPD prescriptions.

The PIM assessment considered the conditions related to PIM. Insulin regimens containing only short- or rapid-acting insulin (e.g., regular insulin) and no concurrent use of basal or long-acting insulin (e.g., insulin mix 70/30 or neutral protamine Hagedorn [NPH] insulin) were classified as category I PIMs. Only medications prescribed to patients with any of the 10 targeted diseases or syndromes, such as opioid use in patients with a history of falls or fractures, were identified as PIM category II. Low-dose aspirin use was considered PIM category III based on the age group (60–69 vs. ≥ 70 years). Only the co-prescription of objects and interacting drugs, such as opioids and gabapentin, was identified as PIM category IV. Only medication prescribed to patients with renal dysfunction was identified as PIM category V, such as colchicine use in a patient with an estimated glomerular filtration rate (eGFR) of < 30 mL/min/1.73 m² on the date of the medication prescription.
Additionally, a group of medications with high anticholinergic effects (Table 7 of the Beers criteria), listed as PIM categories I and II (delirium, dementia/cognitive impairment, and lower urinary tract symptoms [LUTS] or benign prostatic hyperplasia [BPH]) and IV (concurrent use of two anticholinergics), were assessed.

### Statistical Analysis

We expressed continuous variables with normal distributions as mean ± standard deviation and used independent-sample t-tests to compare PIM use with no PIM use. We expressed continuous variables with non-normal distributions as median and interquartile range (Q1–Q3), and used Mann–Whitney U tests to compare PIM use with no PIM use. We expressed categorical variables as frequencies and percentages and used chi-square or Fisher exact tests for comparisons between PIM use and no PIM, as applicable.

This study considered the patient as the unit of analysis. We calculated the prevalence of overall PIM use, PIM category use, and individual PIM use as a percentage by dividing the number of patients prescribed PIM by the total number of patients. To reflect the consistency of PIM use, we calculated the number of times a PIM was prescribed, expressed as a median and interquartile range (Q1–Q3) for each PIM.

To determine the factors associated with PIM use, we performed binary logistic regression analysis to calculate crude odds ratio (OR), adjusted odds ratio (aOR), and 95% confidence interval (CI). Factors with p < 0.2 in the univariate analysis were included in the adjustment analysis. The variance inflation factor (VIF) for each factor was calculated to diagnose multicollinearity (high correlation of two independent variables). Factors with a VIF > 5 were excluded from the model. 20 We then identified the associated

### Table 2. PIM use distribution by PIM category (n=22,099)

<table>
<thead>
<tr>
<th>PIM category</th>
<th>Prevalence (%)</th>
<th>n (%)</th>
<th>Number of times PIM prescribed</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Medications that may be inappropriate in most older adults</td>
<td>68.90 (n = 15,226)</td>
<td>8,574 (38.80)</td>
<td>2 (1–3)</td>
</tr>
<tr>
<td>Orphenadrine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naproxen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dimenhydrinate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II. Medications that may worsen the disease or syndrome</td>
<td>7.68 (n = 1,697)</td>
<td>831 (3.76)</td>
<td>1 (1–2)</td>
</tr>
<tr>
<td>Tramadol (falls or fracture)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orphenadrine (LUTS, BPH)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorazepam (falls or fracture)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline (falls or fracture)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine (falls or fracture)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III. Medications that should be used with caution</td>
<td>44.23 (n = 9,775)</td>
<td>4,141 (18.74)</td>
<td>1 (1–2)</td>
</tr>
<tr>
<td>Tramadol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dextromethorphan</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furosemide</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low dose aspirin (age ≥ 70)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV. Drug-drug interactions that are clinically significant</td>
<td>15.66 (n = 3,460)</td>
<td>783 (3.54)</td>
<td>1 (1–2)</td>
</tr>
<tr>
<td>Amitriptyline + orphenadrine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dimenhydrinate + orphenadrine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol + gabapentin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxazosin + furosemide</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydroxyzine + orphenadrine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V. Medications that should be avoided or whose dosage should be adjusted based on renal function</td>
<td>3.05 (n = 675)</td>
<td>347 (1.57)</td>
<td>2 (1–5)</td>
</tr>
<tr>
<td>Colchicine (CrCl &lt; 30 mL/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol (CrCl &lt; 30 mL/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabapentin (CrCl &lt; 60 mL/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spironolactone (CrCl &lt; 30 mL/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin (CrCl &lt; 30 mL/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>74.70 (n = 16,507)</td>
<td>32 (0.14)</td>
<td>1 (1–1)</td>
</tr>
</tbody>
</table>

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

PIM, potentially inappropriate medication; LUTS, lower urinary tract symptoms; BPH, benign prostatic hyperplasia; CrCl, creatinine clearance.

*In each PIM category, the top five most prescribed PIMs are presented in descending order of frequency.*
factors using a backward elimination method, in which the factor with the least significance was discarded at each step until all remaining factors in the model had p < 0.05.

We used STATA 14.0 (StataCorp LLC, College Station, TX, USA) to perform all the statistical analyses. All the hypothesis tests were two-tailed. Statistical significance was set at p < 0.05.

RESULTS

Patient Characteristics

Fig. 1 illustrates the patient recruitment process. Initially, 29,095 outpatients aged 60 years and older were enrolled. Due to ineligibility, 6,996 patients were excluded (132, 5,382, and 1,482 patients lacked data on diagnosis and prescription and were prescribed only the COVID-19 vaccine, respectively). Thus, this study included 22,099 older outpatients.

Table 1 presents the characteristics of the study participants. Most of the patients (52.92%) were female, and the average age was 68.86 ± 7.64 years. The primary source of health insurance was UC (70.81%). Most patients (71.53%) had ≥ 3 diagnostic categories, with a median of 4 (IQR 2–6). As illustrated in Fig. 2, cardiovascular disorders were the most common (45.3%), followed by musculoskeletal diseases (37.0%) and endocrine and metabolic diseases (36.6%). Approximately one-fifth of patients had ≥ 3 chronic morbidities, with a median of 1 (IQR 0–2). The most common condition was hypertension (38.11%), followed by mild-to-moderate chronic renal disease (21.58%) and diabetes without complications (14.73%). PIM users had a significantly higher prevalence of polypharmacy, chronic morbidities, and co-morbidity scores than non-users. More than half (53.86%) of the patients received at least one polypharmacy prescription.

Prevalence of PIM Use

Table 2 summarizes the general prevalence of PIM use in each PIM category. Nearly three-fourths of patients (74.70%) were prescribed at least one PIM, with 29.80%, 25.19%, 15.75%, 3.56%, and 0.39% prescribed 1, 2, 3, 4 and 5 categories, respectively. The distribution of PIM in each category is detailed in Supplemental Tables S1–S5.

For category I PIMs (medications that may be inappropriate for most older adults), except for nifedipine immediate release, amobarbital, ethinyl estradiol, and dipyridamole, all PIMs were prescribed to patients. Of these patients, 68.90% were administered at least one PIM. The top five most prescribed PIMs were orphenadrine (38.80%), omeprazole (29.16%), naproxen (11.82%), dimenhydrinate (11.43%), and lorazepam (10.26%). More than half the patients (53.39%) were prescribed at least one anticholinergic medication (Supplement Table S1).

For category II PIMs (medications that may worsen the disease or syndrome), except for urinary incontinence (all forms) in women, PIMs were prescribed for all ten targeted diseases or syndromes. A total of 7.68% of the patients were administered at least one PIM. The most frequently prescribed PIMs were observed in patients with a history of falls or fractures, with tramadol being the most prescribed (3.76%), followed by lorazepam (1.16%), amitriptyline (0.93%), and morphine (0.57%). In cases of other diseases or syndromes, patients with dementia, cognitive impairment, delirium, LUTS, or BPH received anticholinergics. Patients with heart failure and chronic kidney disease stage 4 or higher were prescribed all types of non-steroidal anti-inflammatory drugs (NSAIDs), including non-specific cyclooxygenase (COX), COX-2-selective and COX-2-specific inhibitors, whereas patients with a history of gastric or duodenal ulcers were prescribed non-specific COX and COX-2-selective inhibitors (Supplemental Table S2).

Category III PIMs (medications that should be used with caution) were prescribed to 44.23% of patients. Tramadol was the most commonly prescribed (18.74%), followed by low-dose aspirin (14.73%) and dextromethorphan (8.06%). Nearly half (46.16%) the patients receiving low-dose aspirin were aged > 70 years (Supplemental Table S3).

Among category IV PIMs (clinically significant drug–drug interactions), a pair of objects and an interacting drug was prescribed to 15.66% of patients. The concurrent use of two anticholinergics was most common (9.33%), most commonly amitriptyline and orphenadrine (3.54%), followed by dimenhydrinate and orphenadrine (2.24%). The four most prescribed PIM were orphenadrine-based regimens. Among opioid users, the concurrent use of tramadol and gabapentin was the most common (1.78%), followed by tramadol and lorazepam (1.01%). Although combinations of the three central nervous system (CNS)–active drugs were slightly more common, each regimen was consistently prescribed.
Table 1. Characteristics of the study participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 22,099)</th>
<th>PIM use (n = 16,507)</th>
<th>No PIM use (n = 5,592)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient prescriptions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of prescriptions</td>
<td>158,985</td>
<td>141,063</td>
<td>17,922</td>
<td></td>
</tr>
<tr>
<td>Number of prescriptions/patients</td>
<td>5 (2–9)</td>
<td>6 (2–10)</td>
<td>2 (1–5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>11,902 (53.86)</td>
<td>11,148 (67.53)</td>
<td>754 (13.48)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>10,405 (47.08)</td>
<td>7,622 (46.17)</td>
<td>2,783 (49.77)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Female</td>
<td>11,694 (52.92)</td>
<td>8,885 (53.83)</td>
<td>2,809 (50.23)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Age (y)</strong></td>
<td>68.86 ± 7.64</td>
<td>69.11 ± 7.78</td>
<td>68.13 ± 7.18</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>60–74</td>
<td>17,459 (79.00)</td>
<td>12,812 (77.62)</td>
<td>4,647 (83.10)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 75</td>
<td>4,640 (21.00)</td>
<td>3,695 (22.38)</td>
<td>945 (16.90)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Health insurance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Universal coverage</td>
<td>15,648 (70.81)</td>
<td>11,725 (71.03)</td>
<td>3,923 (70.15)</td>
<td>0.213</td>
</tr>
<tr>
<td>Non-universal coverage</td>
<td>6,451 (29.19)</td>
<td>4,782 (28.97)</td>
<td>1,669 (29.85)</td>
<td></td>
</tr>
<tr>
<td>Number of diagnostic categories</td>
<td>4 (2–6)</td>
<td>5 (3–7)</td>
<td>2 (1–4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>1–2</td>
<td>6,291 (28.47)</td>
<td>3,347 (20.28)</td>
<td>2,944 (52.65)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 3</td>
<td>15,808 (71.53)</td>
<td>13,160 (79.72)</td>
<td>2,648 (47.35)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Number of chronic morbidities</td>
<td>1 (0–2)</td>
<td>1 (0–3)</td>
<td>0 (0–1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>0–2</td>
<td>17,233 (77.98)</td>
<td>11,991 (72.64)</td>
<td>5,242 (93.74)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 3</td>
<td>4,866 (22.02)</td>
<td>4,516 (27.36)</td>
<td>350 (6.26)</td>
<td></td>
</tr>
<tr>
<td><strong>Types of chronic morbidities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>8,423 (38.11)</td>
<td>7,243 (43.88)</td>
<td>1,180 (21.10)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CKD, mild to moderate</td>
<td>4,770 (21.58)</td>
<td>4,282 (25.94)</td>
<td>488 (8.73)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>DM without complications</td>
<td>3,279 (14.84)</td>
<td>2,620 (15.87)</td>
<td>659 (11.78)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>3,104 (14.05)</td>
<td>3,014 (18.26)</td>
<td>90 (1.61)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>DM with complications</td>
<td>1,493 (6.76)</td>
<td>1,323 (8.01)</td>
<td>170 (3.04)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Chronic heart failure</td>
<td>974 (4.41)</td>
<td>954 (5.78)</td>
<td>20 (0.36)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>946 (4.28)</td>
<td>828 (5.02)</td>
<td>118 (2.11)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>881 (3.99)</td>
<td>806 (4.88)</td>
<td>75 (1.34)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>803 (3.63)</td>
<td>738 (4.47)</td>
<td>65 (1.16)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cancer, non-metastatic</td>
<td>751 (3.40)</td>
<td>621 (3.76)</td>
<td>130 (2.32)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Severe constipation</td>
<td>717 (3.24)</td>
<td>653 (3.96)</td>
<td>64 (1.14)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CKD, severe</td>
<td>677 (3.06)</td>
<td>644 (3.90)</td>
<td>33 (0.59)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Depression</td>
<td>435 (1.97)</td>
<td>432 (2.62)</td>
<td>3 (0.05)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Liver disease, mild</td>
<td>434 (1.96)</td>
<td>377 (2.28)</td>
<td>57 (1.02)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>424 (1.92)</td>
<td>419 (2.54)</td>
<td>5 (0.09)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AIDS</td>
<td>343 (1.56)</td>
<td>289 (1.75)</td>
<td>54 (0.97)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Asthma</td>
<td>339 (1.53)</td>
<td>301 (1.82)</td>
<td>38 (0.68)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>335 (1.52)</td>
<td>314 (1.90)</td>
<td>21 (0.38)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>315 (1.43)</td>
<td>277 (1.68)</td>
<td>38 (0.68)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>271 (1.23)</td>
<td>228 (1.38)</td>
<td>43 (0.77)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Alcohol misuse</td>
<td>210 (0.95)</td>
<td>197 (1.19)</td>
<td>13 (0.23)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hemiplegia or paraplegia</td>
<td>183 (0.83)</td>
<td>168 (1.02)</td>
<td>15 (0.27)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Peptic ulcer disease</td>
<td>178 (0.81)</td>
<td>173 (1.05)</td>
<td>5 (0.09)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>133 (0.60)</td>
<td>122 (0.74)</td>
<td>11 (0.20)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cancer, metastatic</td>
<td>127 (0.57)</td>
<td>113 (0.68)</td>
<td>14 (0.25)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>114 (0.52)</td>
<td>94 (0.57)</td>
<td>20 (0.36)</td>
<td>0.056</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>110 (0.50)</td>
<td>108 (0.65)</td>
<td>2 (0.04)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Comorbidity score</td>
<td>0 (0–1)</td>
<td>0 (0–2)</td>
<td>0 (0–0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 1</td>
<td>12,603 (57.03)</td>
<td>8,382 (50.78)</td>
<td>4,221 (75.48)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Values are presented as median (interquartile range) or number (%) or mean±standard deviation.
PIM, potentially inappropriate medication; CKD, chronic kidney disease; DM, diabetes mellitus; AIDS, acquired immune deficiency syndrome.
The p-value compares PIM use against no PIM use.
Warfarin and other drugs have a minor interaction. Nevertheless, the concomitant use of warfarin and low-dose aspirin was administered to 64 individuals, with a median of 5 prescriptions (IQR 2–9) (Supplementary Table S4).

Only 3.05% of patients were prescribed category V PIMs (medications that should be avoided or whose dosage should be adjusted based on renal function). Colchicine (1.57%), tramadol (0.82%), and spironolactone (0.20%) were the most commonly administered drugs to patients with significantly compromised renal function (eGFR < 30 mL/min/1.73 m²) (Supplementary Table S5).

Factors Associated with PIM Use
Table 3 presents the results of univariate and multivariate analyses of the factors associated with PIM use. Women exhibited an OR of 1.08 (95% CI, 1.01–1.16) compared to that in men. Patients aged ≥ 75 years exhibited an OR of 1.10 (95% CI, 1.01–1.21) compared to those aged 60–74 years. Polypharmacy exhibited an OR of 10.21 (95% CI, 9.31–11.21) compared to non-polypharmacy. Patients with ≥ 3 diagnostic categories exhibited an OR of 2.31 (95% CI, 2.14–2.50) compared to those with 1–2 diagnostic categories. Patients with ≥ 3 chronic morbidities exhibited an OR of 1.46 (95% CI, 1.26–1.68) compared to those with 0–2 chronic morbidities. Patients with a comorbidity score of ≥ 1 exhibited an OR of 0.78 (95% CI, 0.71–0.86) compared to those with a score of 0.

DISCUSSION
This study evaluated the quality of medication use in older outpatients receiving care at a single secondary-care hospital. According to the 2019 AGS Beers criteria, PIM use is particularly prevalent among older outpatients, accounting for up to three-fourths being prescribed PIM. All five PIM categories were identified. Polypharmacy was the most significant predictor of PIM use.

Prevalence of Overall PIM Use
The overall prevalence of PIM use among our outpatients in this secondary-care hospital was up to 74.70%, which was greater than that in hospitalized patients in tertiary-care hospitals—61.9% in a study by Sharma et al.21 and 64.80% in a study by He et al.22 Secondary-care hospitals may have fewer healthcare resources such as alternative drugs, geriatricians, clinical pharmacists, and geriatric clinics, compared to tertiary-care hospitals, resulting in insufficient quality of geriatric care. Outpatients are more likely to use PIMs than hospitalized patients because they have more morbidities that require long-term treatment in the OPD. In our study, more than half the patients had ≥ 3 diagnostic categories and up to five prescriptions during the study period.

Prevalence of the Use of Each PIM Category
Category I PIMs (medications that may be inappropriate for most older adults) showed the highest prevalence of PIM use (68.90%), consistent with both foreign and Thai study results.16,21-26 In those studies, the most prescribed PIM classes were first-generation antihistamines, benzodiazepines (BZDs), proton-pump inhibitors (PPIs), antidepressants, and oral NSAIDs. In this study, dimenhydrinate, chlorpheniramine, and hydroxyzine were frequently used as first-generation antihistamines in older Thai patients, consistent with the results of previous Thai studies.16,26-27 Lorazepam was the most prescribed BZD (10.26%), consistent with previous Thai research.16,26 Although short-acting
BZDs appear to be safer than long-acting BZDs (older adults have slower metabolism of long-acting agents), the Beers criteria strongly advise avoiding all BZDs because they can increase the risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in older adults.11

As previously reported, omeprazole was frequently prescribed as a PPI in hospitals.21,22,24 The Beers criteria strongly advise against using PPIs for > 8 weeks unless in high-risk patients (e.g., chronic use of oral glucocorticoids or NSAIDs) or for approved indications (e.g., erosive esophagitis) because their use can increase the risk of Clostridium difficile infection, bone loss, and fractures.11 PPIs may be prescribed inappropriately, with unapproved indications, co-prescriptions with glucocorticosteroids, and excessive dosages.22,29 Furthermore, older age is a predictor of inappropriately initiated PPI use, with an OR of 1.03 (95% CI, 1.03–1.03).30 In our study, amitriptyline was the most commonly prescribed antidepressant, consistent with the findings of previous Thai studies.11,24,27 The Beers criteria strongly advise against antidepressant use due to the increased risk of highly anticholinergic effects, sedation, and orthostatic hypotension.11 Most studies on PIM safety reported associations between both non-COX and COX-2-selective NSAID use and increased risks of gastrointestinal bleeding, high blood pressure, and kidney injury.16,22,26,27,34 Thus, the Beers criteria strongly advise against the long-term (≥ 3 months) use of NSAIDs unless other alternatives are ineffective, and the use of a gastroprotective agent to reduce the risk.11 Interestingly, our results revealed that orphenadrine, a skeletal muscle relaxant, was the most commonly prescribed PIM. Most muscle relaxants are poorly tolerated by older adults due to their strong anticholinergic effects, sedation, and increased risk of fracture.11

Category II PIMs (medications that may worsen the disease or syndrome) were found in all 10 diseases or syndromes except for urinary incontinence (all types) in women. Patients with a history of falls or fractures had the highest prevalence of use (4.77%), with tramadol being the most commonly prescribed medication (3.76%), consistent with the report by Walker et al.25 The 2019 AGS Beers criteria recommend avoiding opioid use in older adults with a history of falls or fractures as these medications can cause ataxia, impaired psychomotor function, syncope, and additional falls.11 The patients in the present study were prescribed lorazepam, risperidone, haloperidol, and anticholinergics (orphenadrine and amitriptyline) for the treatment of delirium, whereas Sharma et al.21 reported the use of ranitidine and hydrocortisone. Lorazepam, risperidone, and anticholinergics (orphenadrine, trihexyphenidyl, and dimenhydrinate) were prescribed to patients with dementia or cognitive impairment, consistent with previous reported findings.24,26,31 The 2019 Beers criteria recommend avoiding the prescription of anticholinergics, antipsychotics, and BZDs in older patients with delirium or dementia as these medications can worsen the disease.11 Pioglitazone and all types of NSAIDs were prescribed to our patients with heart failure, consistent with the results of a study by Duangsong et al.,34 who reported a 19.67% prevalence of PIMs in patients with heart failure based on the 2019 AGS Beers criteria.

Antipsychotics (haloperidol and risperidone), diuretics (furosemide, spironolactone, and hydrochlorothiazide), selective serotonin reuptake inhibitors (SSRIs) (sertraline and fluoxetine), tricyclic antidepressants (TCAs) (amitriptyline), and tramadol were frequently prescribed among category III PIMs (medications that should be used with caution). These medication classes should be used with caution because they may aggravate or cause inappropriate antidiuretic hormone secretion (SIADH) or hyponatremia.11 He et al.22 reported that tramadol was the most commonly used of these medications. Diuretics and SSRIs were the other two PIM classes exhibiting frequent use, consistent with previous research findings.22,24,35 Because heart failure is commonly diagnosed in older patients, diuretics are a commonly prescribed PIM.36 Because low-dose aspirin provides no net benefit to older adults with cardiovascular risk factors when used for primary prevention, the Beers criteria strongly advise caution in using low-dose aspirin in

---

**Table 3. Factors associated with PIM use (n=22,099)**

<table>
<thead>
<tr>
<th>Factors</th>
<th>Crude OR (95% CI)</th>
<th>p-value</th>
<th>Adjusted OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>1.15 (1.09–1.23)</td>
<td>&lt; 0.001</td>
<td>1.08 (1.01–1.16)</td>
<td>0.028</td>
</tr>
<tr>
<td>Age, ≥ 75 y</td>
<td>1.42 (1.31–1.53)</td>
<td>&lt; 0.001</td>
<td>1.10 (1.01–1.21)</td>
<td>0.038</td>
</tr>
<tr>
<td>Universal coverage</td>
<td>1.04 (0.98–1.11)</td>
<td>0.213</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>13.35 (12.28–14.51)</td>
<td>&lt; 0.001</td>
<td>10.21 (9.31–11.21)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Diagnostic categories, ≥ 3</td>
<td>4.37 (4.10–4.66)</td>
<td>&lt; 0.001</td>
<td>2.31 (2.14–2.50)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Chronic morbidities, ≥ 3</td>
<td>5.64 (5.03–6.32)</td>
<td>&lt; 0.001</td>
<td>1.46 (1.26–1.68)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Comorbidity score, ≥ 1</td>
<td>2.98 (2.79–3.19)</td>
<td>&lt; 0.001</td>
<td>0.78 (0.71–0.86)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

With variance inflation factors ranging from 1.25 to 3.23, no multicollinearity was discovered.

PIM, potentially inappropriate medication; OR, odds ratio; CI, confidence interval.

*Factors with p-values less than 0.2 were incorporated into a multivariate analysis.*
adults aged > 70 years to avoid the risk of major bleeding.\textsuperscript{11} Although we could not directly assess the appropriateness of low-dose aspirin use, up to 46.16\% of aspirin users were > 70 years of age.

We observed almost all drug–drug interactions listed in PIM category IV (clinically significant), with anticholinergics being the most concurrent prescriptions. Because of the increased risk of cognitive decline, the Beers criteria strongly recommend limiting the number of anticholinergic drugs used concurrently.\textsuperscript{11} The Beers criteria also strongly advise against combining NSAIDs and glucocorticoids because they can increase the risk of peptic ulcer disease or gastrointestinal bleeding.\textsuperscript{11} We observed the interaction between NSAIDs and glucocorticoids (e.g., naproxen + prednisolone), consistent with a study by Sharma et al.\textsuperscript{21} that reported the interaction of hydrocortisone and ketorolac. Except for the use of warfarin and low-dose aspirin, we observed no concomitant use of warfarin and NSAIDs. A Thai study reported the prescription of this combination therapy to 9.2\% of patients with non-valvular atrial fibrillation.\textsuperscript{36} However, a recent study found that adding low-dose aspirin to patients receiving warfarin without a clear indication for aspirin (e.g., mechanical heart valve replacement, recent percutaneous coronary intervention, or acute coronary syndrome) may increase the risk of bleeding without additional therapeutic benefits.\textsuperscript{37} Thus, close monitoring for bleeding is required when these medications are used together.\textsuperscript{11}

We observed the use of many category V PIMs (medications that should be avoided or whose dosage should be adjusted based on renal function), including gabapentin, enoxaparin, ranitidine, tramadol, dabigatran, and spironolactone, consistent with previous reports.\textsuperscript{22,23,30} Colchicine was also mentioned in our research. Because it has been linked to gastrointestinal, neuromuscular, and bone marrow toxicity, the Beers criteria strongly recommend lowering the dose.\textsuperscript{11}

Factors Associated with PIM Use
Female sex is frequently identified as a patient-related factor.\textsuperscript{22,25} In this study, individuals aged ≥ 75 years were more likely to be prescribed PIMs, consistent with the results of earlier studies, as various morbidities, including sleep problems, delirium, dementia, chronic pain, and heart failure, are typically diagnosed in this age group.\textsuperscript{25,26} Polypharmacy was the most important component identified in previous studies on PIM.\textsuperscript{22,24,25,33} The likelihood of PIM use can increase with polypharmacy. Individuals with ≥ 3 diagnostic categories or chronic morbidities in the present study were more likely to be prescribed PIMs, consistent with previous research findings.\textsuperscript{25,26} Individuals with comorbidity scores of ≥ 1 were less likely to be administered PIMs and, according to Tian et al.,\textsuperscript{23} physicians should use caution while providing PIMs to patients with higher illness burdens.

Strengths
Our study has several advantages. First, we reported the prevalence of PIM use detected using the 2019 AGS Beers criteria, which considers all five PIM categories. Second, we used real-world data from a large population of older adults to measure PIM use. Third, we evaluated numerous prescriptions per patient (rather than only one), which increased the likelihood of identifying PIM use. Finally, we reported the use of PIMs in terms of frequency and continuity to provide a better understanding.

Limitations
Our study had some limitations. First, because only one hospital was analyzed, it could not cover all PIM-related medications; therefore, this study did not evaluate medications that might be available in other hospitals. Second, we were unable to evaluate the connection between individual chronic morbidity and PIM use because PIMs can be used for various indications. Instead, we determined the specific groups associated with PIM use. Third, because we evaluated the prescriptions received by each patient from the index date to the end of 2021, some patients had a short study period for PIM assessment. Moreover, the patients may have received PIM from sources other than hospitals. Thus, PIM use may have been more prevalent in both cases than indicated in this study. Fourth, because we analyzed numerous PIM categories, we were unable to exclude PIM-related drugs from the patients’ prescriptions. When polypharmacy was identified, PIM-related drugs were included in the drug count. Our results showed that polypharmacy was the most important factor influencing PIM use, with the highest OR. Finally, our findings should not be applied to other contexts involving various medications and prescription practices.

Conclusion
In conclusion, both the overall PIM use and the use of each PIM category remained high in older Thai outpatients. Compliance with the Beers criteria is necessary to reduce all aspects of inappropriate prescriptions. These measures should be aimed at individuals at high risk of using PIMs, such as those > 75 years of age, with several morbidities, and on multiple medications.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST
The researchers claim no conflicts of interest.
FUNDING
This research project was supported by the Thailand Science Research and Innovation Fund and the University of Phayao (Grant No. FF66-RIM046).

AUTHOR CONTRIBUTIONS
Conceptualization, KJ; Data curation, KW, SC, PN; Formal analysis, KJ, KW, SC, J; Investigation, KJ, KW, SC, J; Methodology, KJ, KW, SC, J; Visualization, KJ, PN; Project administration, KJ; Supervision, KJ; Writing-original draft, KJ; Writing-review & editing, KJ.

SUPPLEMENTARY MATERIALS
Supplementary materials can be found via https://doi.org/10.4235/agmr.23.0036.

REFERENCES
24. Chinthalapudi SS, Cheeti S, Bajpai A, Deepika S, Thunga G,


Mortality-Related Risk Factors in Geriatric Patients with Hip Fracture

Rıdvan Gönül, Pınar Tosun Tasar, Kutsi Tuncer, Omer Karasahin, Dogan Nasır Binici, Can Sevinc, Mustafa Turgut, Sevnaz Sahin

1 Internal Medicine Clinic, Ağrı Doğubayazıt Dr. Yaşar Eryılmaz State Hospital, Agri, Turkey
2 Division of Geriatrics, Department of Internal Medicine, Atatürk University Hospital, Erzurum, Turkey
3 Orthopedic Clinic, Private Medical Park Bahcelievler Hospital, Bahcelievler, İstanbul, Turkey
4 Infectious Diseases Clinic, Erzurum Regional Training and Research Hospital, Erzurum, Turkey
5 Internal Medicine Clinic, Erzurum Regional Training and Research Hospital, Erzurum, Turkey
6 Division of Nephrology, Department of Internal Medicine, Atatürk University Hospital, Erzurum, Turkey
7 Internal Medicine Clinic, Aksaray Regional Training and Research Hospital, Aksaray, Turkey
8 Division of Geriatrics, Department of Internal Medicine, Ege University Hospital, Izmir, Turkey

Background: Mortality rates after hip fractures increase by up to 30% with age. This study investigated the contribution of various parameters to prognosis and mortality.

Methods: Our study prospectively examined patients with hip fracture aged 65 years and over who applied to the Atatürk University Medical Faculty Hospital Orthopedics Service in 2020–2021.

Results: The 120 patients included in the study had a mean age of 79.71 ± 7.27 years, and 51.7% were female. Twenty patients (16.7%) died within the first 30 days after a hip fracture. They had a significantly lower median Lawton–Brody instrumental activities of daily living (IADL) scale score (p=0.045) and a higher rate of malnutrition according to the Mini Nutritional Assessment (MNA) score (p=0.016). Additionally, these patients with 30-day mortality had a significantly lower rate of surgical treatment (p=0.027) and a longer time from injury to surgery (p=0.014). The time to surgery was a significant independent risk factor for 30-day mortality, with each 1-hour delay increasing the odds of mortality by 1.066 (odds ratio [OR]=1.066; 95% confidence interval [CI], 1.001–1.013; p=0.013). In addition, the presence of malnutrition was another independent risk factor that increased the odds of mortality by 4.166 times (OR=4.166; 95% CI, 1.285–13.427; p=0.017).

Conclusion: We recommend placing more importance on supportive treatment in patients presenting with hip fractures, especially in those with malnutrition; performing surgical intervention as early as possible; and more closely following up with patients with the aforementioned risk factors.

Key Words: Geriatrics, Hip fractures, Mortality, Prognosis

INTRODUCTION

Improved healthcare and living standards have increased the average life expectancy. As the human lifespan lengthens, older adults are increasing in both number and proportion of the total population. According to the Turkish Statistical Institute’s (TurkStat) “Statistics of Older Adults 2021” bulletin, the population aged 65 years and over in Turkey rose by 24% over 5 years, from 6,651,503 in 2016 to 8,245,124 in 2021, and the proportion of older adults within the total population rose from 8.3% in 2016 to 9.7% in 2021. Aging leads to many physiological changes in the human body. Among these, reduced muscle mass and strength, loss of bone mass, and nervous system effects result in a decline in neuromuscular function, which leads to impairments in proprioception, balance, and coordination and increases the risk of falls.

Comorbidities and polypharmacy increase with age and nega-
tively affect the musculoskeletal and nervous systems. In addition, older adults are more likely than younger adults to experience fractures after low-energy trauma due to osteoporosis, which is more common in postmenopausal women. These fractures are mostly observed in the upper and lower extremities; however, hip fractures also occur and are concerning. Fractures adversely impact daily life and result in death in many cases.

Among studies on the incidence of hip fractures and prevalence of osteoporosis in Turkey, the FRACtURK study in 2011 reported that the incidence of hip fractures increased with age. The annual number of new hip fractures is estimated to reach 60,000 by 2035. A study in Korea between 2002 and 2011 reported an annual incidence of hip fractures of 4.3%, while a retrospective study in Spain showed that the incidence of hip fractures increased markedly in persons aged 85 and older.

Older adults have a prolonged recovery period after a hip fracture and difficulty returning to their activities of daily living. During recovery, patients are usually bedridden and dependent on family members or nursing home workers. Despite medical advances, the mortality rate of hip fractures remains high in geriatric populations, with reported 1- and 3-year mortality rates of 30% and up to 40%, respectively. Considering the growing geriatric population and high incidence of hip fractures and mortality, this issue will become increasingly important. This study investigated the risk factors associated with the prognosis of hip fractures in geriatric patients, who are a known risk group for mortality.

**MATERIALS AND METHODS**

The inclusion criteria for this prospective, observational study were as follows: individuals > 65 years of age who were admitted to the orthopedic ward due to a hip fracture between April 1, 2020 and August 30, 2021, who volunteered to participate in the study, and who signed the informed consent form.

The exclusion criteria were individuals ages < 65 and older who had refused to participate in the study and who did not sign the informed consent form.

This study evaluated demographic and clinical characteristics such as age, sex, marital status, education level, chronic diseases, the presence of osteoporosis before the fracture, and the use of osteoporosis medication. Osteoporosis and fractures were specified in the questionnaire, and all participants indicated whether they were currently undergoing treatment or had been diagnosed with the disease.

The Acute Physiology and Chronic Health Evaluation II (APACHE-II), Charlson Comorbidity Index (CCI), American Society of Anesthesiologists (ASA) classification, Lawton–Brody instrumental activities of daily living (IADL) scale, Barthel Index, Edmonton Frail Scale (EFS), and Mini Nutritional Assessment (MNA) scores were calculated at the time of admission. The MNA consists of six global assessment items covering the level of independence, medications used, mobility, mental status, skin changes, and the presence of acute stressors during the previous 3 months. The MNA yields a score between 0 and 14. Scores of 12–14 indicate normal nutritional status (being well-nourished), 8–11 indicate malnutrition risk, and 0–7 indicate malnourishment.

The Barthel Index, reported in 1967, consists of 10 question groups. The validity and safety of the Turkish version were reported in 2000 by Kucukdeveci et al. The 10 question groups include nutrition, moving from wheelchair to bed and vice versa, personal care, using the toilet, walking on a smooth surface, using a wheelchair, going up and down stairs, dressing, undressing, urine and stool continence, and washing. The total score is 100, in which 0–20 points indicate full dependence, 21–61 points indicate severe dependence, 62–90 points indicate moderate dependence, 91–99 points indicate slight dependence, and 100 points indicate complete independence. The Lawton–Brody IADL was developed by Lawton and Brody in 1969. It consists of eight questions, including using the telephone, managing money, cooking, cleaning the house, washing laundry, and using a transportation vehicle. The maximum possible score is 24 points, with scores of 0–8, 9–16, and 17–24 points defined as dependent, semi-dependent, and independent, respectively. The EFS is a simple and easily administered scale consisting of 11 questions that provide information about cognition, general health status, dependence, social support, medication, nutrition, depression, incontinence, and physical performance. Each question is scored between 0 and 2. Total scores of 0–5, 6–7, 8–9, 10–11, and 12–17 indicate no frailty, vulnerability, mild frailty, moderate frailty, and severe frailty, respectively.

To assess geriatric syndromes, the number of falls in the previous year, the presence of dementia, and whether delirium occurred after a hip fracture were determined. White blood cell, neutrophil, and lymphocyte counts; mean platelet volume (MPV); hematocrit; hemoglobin; blood urea nitrogen (BUN); and creatinine, sodium, potassium, calcium, phosphorus, alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, and C-reactive protein (CRP) levels at the time of admission to the emergency department were recorded. The length of stay in the emergency department; whether the patient underwent surgery; and if so, how many hours later; the anesthesia method; any postoperative complications; and the length of stay in the orthopedic ward were also noted.
The 30-day survival data of the patients were retrieved from the Death Reporting System of the Republic of Turkey Ministry of Health, General Directorate of Public Health, using patient citizenship numbers.

**Statistics**

Statistical analyses were performed using the IBM SPSS Statistics for Windows, version 21.0 program (IBM, Armonk, NY, USA). Descriptive statistics are presented as medians and ranges, or numbers and percentages. Data were compared between surviving and non-surviving patients.

A receiver operating characteristic curve analysis was performed to evaluate the relationship between the variables and mortality. The area under the curve was calculated, and the cutoff points were determined using the Youden index (J = sensitivity + specificity – 1). The chi-square test was used to compare categorical data between the surviving and non-surviving groups, while continuous data with non-normal distributions were compared using the nonparametric Kruskal–Wallis and Mann–Whitney U tests. A Kaplan–Meier analysis was performed to identify the risk factors associated with survival time. Significant risk factors in the Kaplan–Meier analysis were included in a Cox regression model to identify independent risk factors. Results were calculated with 95% confidence intervals (CIs), and p < 0.05 was considered statistically significant.

This study was performed after obtaining approval from the Clinical Research Ethics Committee of Erzurum Regional Training and Research Hospital (No. 2020/07-87, dated April 6, 2020). Also, this study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.227

**RESULTS**

The 120 patients included in the study had a mean age of 79.71 ± 7.27 years, and 51.7% were female. Twenty patients (16.7%) died within the first 30 days after the hip fracture. Table 1 shows a comparison of demographic characteristics and comorbidities according to 30-day mortality.

The presence and treatment of osteoporosis and the number of falls in the previous year were compared according to 30-day mortality (Table 2). Having had two or more falls causing injury within the last year was significantly more common among patients who died within 30 days of the hip fracture (p = 0.011).

Table 3 shows the comparison of the assessment scores and laboratory findings at admission according to the 30-day mortality. Patients who died within 30 days of a hip fracture had a significantly lower median Lawton–Brody IADL scale score (p = 0.045) and a higher rate of malnutrition according to the MNA score (p = 0.016).

Comparisons between patients with and without 30-day mortality in terms of length of hospital stay, surgical treatment, and complications are shown in Table 4. Patients with 30-day mortality had a significantly lower rate of surgical treatment (p = 0.027) and a longer time from injury to surgery (p = 0.014).

The last line of logistic regression analysis, including 30-day mortality risk factors in older patients with hip fractures, is shown in Table 5. Patients who died within 30 days of a hip fracture had a significantly lower median Lawton–Brody IADL scale score (p = 0.045) and a higher rate of malnutrition according to the MNA score (p = 0.016).
Table 2. Comparison of the frequency of osteoporosis, treatment for osteoporosis, and falls in the last year according to 30-day mortality

<table>
<thead>
<tr>
<th></th>
<th>No (n = 100)</th>
<th>Yes (n = 20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoporosis (OP)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently under treatment</td>
<td>8 (8.0)</td>
<td>5 (25.0)</td>
<td>0.263</td>
</tr>
<tr>
<td>Treated previously</td>
<td>15 (15.0)</td>
<td>2 (10.0)</td>
<td></td>
</tr>
<tr>
<td>Never treated</td>
<td>77 (77.0)</td>
<td>13 (65.0)</td>
<td></td>
</tr>
<tr>
<td>Fracture associated with osteoporosis</td>
<td>19 (19.0)</td>
<td>3 (15.0)</td>
<td>0.477</td>
</tr>
<tr>
<td>Two or more falls causing injury in the last year</td>
<td>39 (39.0)</td>
<td>14 (70.0)</td>
<td>0.011*</td>
</tr>
</tbody>
</table>

Values are presented as number of frequency (%).
*p<0.05.

Table 3. Comparison of assessment scores and laboratory findings at hospital admission according to 30-day mortality

<table>
<thead>
<tr>
<th></th>
<th>No (n = 100)</th>
<th>Yes (n = 20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCI</td>
<td>4.5 (2–9)</td>
<td>5 (3–12)</td>
<td>0.288</td>
</tr>
<tr>
<td>APACHE-II</td>
<td>10 (5–24)</td>
<td>11 (5–24)</td>
<td>0.284</td>
</tr>
<tr>
<td>ASA class</td>
<td>3 (2–3)</td>
<td>3 (2–3)</td>
<td>0.412</td>
</tr>
<tr>
<td>Edmonton Frail Scale</td>
<td>7 (1–15)</td>
<td>7.5 (3–14)</td>
<td>0.118</td>
</tr>
<tr>
<td>Fraility according to Edmonton Frail Scale (%)</td>
<td>17 (17.0)</td>
<td>5 (25.0)</td>
<td>0.288</td>
</tr>
<tr>
<td>MNA</td>
<td>12 (4–14)</td>
<td>10.5 (2–14)</td>
<td>0.181</td>
</tr>
<tr>
<td>Malnutrition according to MNA (N(%))</td>
<td>13 (13.0)</td>
<td>7 (35.0)</td>
<td>0.016*</td>
</tr>
<tr>
<td>Lawton–Brody IADL scale</td>
<td>6 (0–18)</td>
<td>2 (0–13)</td>
<td>0.045*</td>
</tr>
<tr>
<td>Barthel Index</td>
<td>80 (0–100)</td>
<td>70 (0–90)</td>
<td>0.226</td>
</tr>
<tr>
<td>Laboratory result</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>22 (8.80–63.5)</td>
<td>26 (3–123)</td>
<td>0.110</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.80 (0.30–5.50)</td>
<td>1.07 (0.50–8.68)</td>
<td>0.079</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>138.5 (127–155)</td>
<td>138 (132–148)</td>
<td>0.823</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>3.95 (2.70–33)</td>
<td>3.95 (2.40–39)</td>
<td>0.868</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>24 (12–269)</td>
<td>27 (13–262)</td>
<td>0.265</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>13 (2–74)</td>
<td>12 (3–171)</td>
<td>0.722</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>8.60 (6.70–10.4)</td>
<td>8.20 (4.40–10.5)</td>
<td>0.157</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>2.90 (1.20–5.60)</td>
<td>2.95 (1.60–4.50)</td>
<td>0.961</td>
</tr>
<tr>
<td>White blood cells (mm$^3$)</td>
<td>10,205 (4,130–36,300)</td>
<td>10,750 (6,400–20,960)</td>
<td>0.497</td>
</tr>
<tr>
<td>Neutrophils (mm$^3$)</td>
<td>7,490 (2,570–16,000)</td>
<td>7,570 (3,200–18,440)</td>
<td>0.997</td>
</tr>
<tr>
<td>Lymphocytes (mm$^3$)</td>
<td>1,150 (320–5,650)</td>
<td>1,085 (470–3,230)</td>
<td>0.336</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11.6 (6.10–18.4)</td>
<td>11.2 (7.50–13.8)</td>
<td>0.336</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>35.5 (18.5–57.8)</td>
<td>34.4 (24.9–42.9)</td>
<td>0.367</td>
</tr>
<tr>
<td>MPV (FL)</td>
<td>10.1 (8.30–12.3)</td>
<td>10 (8.80–11.8)</td>
<td>0.895</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>10.4 (9.7–267)</td>
<td>20.8 (10.6–268)</td>
<td>0.073</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.40 (2.50–3.80)</td>
<td>3.25 (2.40–3.70)</td>
<td>0.165</td>
</tr>
</tbody>
</table>

Values are presented as median (range).
APACHE-II, Acute Physiology and Chronic Health Evaluation II; CCI, Charlson Comorbidity Index; ASA, American Society of Anesthesiologists; IADL, instrumental activities of daily living; MNA, Mini Nutritional Assessment; BUN, blood urea nitrogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; MPV, mean platelet volume; CRP, C-reactive protein.
*p<0.05.

In Table 5, among the factors directly associated with mortality risk, we created a logistic regression model that included surgery, time until surgery, presence of postoperative complications, presence of perioperative delirium, Lawton–Brody IADL scores, presence of malnutrition according to the MNA, and presence of two or more falls causing injury in the previous year. Time to surgery was a significant independent risk factor for 30-day mortality, with each 1-hour delay increasing the odds of mortality by 1.066 (odds...
DISCUSSION

In our study of geriatric patients, 16.7% died within 30 days of experiencing a hip fracture. Moreover, the odds of mortality increased by 1.066-fold with each hour of delay in surgery and by 4.166-fold in patients with malnutrition.

Turhan et al. reported a 1-year mortality rate of 21.73% in their study of 138 geriatric patients in Turkey who underwent surgery for hip fractures, while Guzon-Illescas et al. reported a 1-year mortality rate of 33% in their study of 3,992 patients with hip fractures. Kim et al. reported 1- and 5-year mortality rates after hip fractures of 20.9% and 67.2%, respectively. In our study, 20 patients died (16.7%) within the first 30 days, which was attributed to mortality associated with hip fractures and possible complications.

The positive relationship between mortality rate and age reported in recent studies is noteworthy. In their meta-analysis of 54 studies, including 22,817 cases from 2008 to 2018, Cui et al. reported 1-year mortality rates of 2.65% in patients aged 50–54 years and 28.91% in those aged 95–99 years. A retrospective study of 1,004 patients by Cher et al. showed that older age was an independent risk factor for 30-day mortality. Contrary to the literature, in the present study, mortality did not increase with age. This difference could be attributed to the small sample size.

Although the incidence of hip fractures is higher in women, the mortality rate is higher in men. In a retrospective study including 32,175 patients in Norway, Riska et al. compared mortality rates between male and female patients with similar comorbidities. They reported estimated 1-year mortality risks of 44% for women and 53% for men among patients with a CCI of ≥ 2. A retrospective study by Prodocic et al., which included 597 cases, showed a 25% higher cumulative quarterly mortality rate in men. Similarly, mortality was higher among the men in our study, although the difference was not statistically significant.

Malnutrition in older adults can be associated with various factors, such as a shift to catabolic metabolism and low oral intake secondary to comorbidities, and may contribute to higher mortality after hip fractures. In this meta-analysis of 19 studies, including 34,363 cases, Li et al. reported higher mortality among patients classified as malnourished or at risk of malnutrition according to the MNA. Another meta-analysis of 44 studies and 26,281 patients by Malafarina et al. showed higher mortality rates in malnourished patients. Previous studies on nutritional evaluation reported a correlation between serum albumin levels and postoperative survival. Three of these studies observed a correlation between serum albumin levels and total lymphocyte count, nutrition, and postoperative survival. In addition, a recent review reported a relationship between weight loss and serum albumin levels. However, serum albumin levels and total lymphocyte counts can be affected by existing inflammatory processes and underlying diseases. Similar to our study, a retrospective study of 236 older patients, which included 226 patients evaluated using the MNA, reported 1-year mortality rates of 27% overall and 46% in patients with malnutrition. Finally, in their study, including 88 patients, Guimieiro et al. reported a relationship between MNA score and 6-month mortality. Similar to these studies, we observed that malnutrition was an independent factor associated with an increased risk of mortality after a hip fracture.

Surgery for patients with hip fractures may be delayed depending on their medical condition or organizational challenges at health institutions. A meta-analysis of 28 studies that investigated the effect of surgical delay on mortality after hip fracture reported a
higher mortality rate among patients operated on after 48 hours or more.\textsuperscript{59} Similarly, Leer-Salvesen et al.\textsuperscript{41} reported higher mortality among patients who underwent surgery after 48 hours or more. In a prospective study by Lizard-Utrilla et al.\textsuperscript{42} with 1,234 patients, waiting did not affect mortality in medically unstable patients, whereas surgical delay in stable patients increased 1-year mortality. Our results showed that surgical delay was an independent risk factor for 30-day mortality, with each 1-hour delay increasing the odds of 30-day mortality by 1.066-fold.

Delirium is an organic brain pathology that frequently occurs in older patients owing to surgery, trauma, and stress.\textsuperscript{43} As it may be an indicator of mortality and stress, several studies have reported on this topic. A meta-analysis of 21 studies and 6,288 cases by Bai et al.\textsuperscript{44} showed that perioperative delirium is a risk factor for increased short- and long-term mortality. A retrospective study by Mitchel et al.\textsuperscript{45} that included 27,888 patients showed that the incidence of perioperative delirium increased the risk of 1-year mortality. Another study involving 463 patients reported higher 1-year mortality.\textsuperscript{46} Our results support the literature, as patients with perioperative delirium were significantly more likely to die within 30 days of a hip fracture.

Comorbidities increase with age and adversely affect healing. Additionally, mortality increases with the number of comorbidities. A retrospective study of 1,004 patients by Cher et al.\textsuperscript{27} evaluated comorbidity status according to the CCI and reported a positive association between mortality and the number of comorbidities. Another retrospective study of 3,992 patients by Guzon-Illscas et al.\textsuperscript{23} showed that the presence of stage 4–5 chronic kidney disease, diabetes mellitus, chronic obstructive pulmonary disease, dementia, congestive heart failure, vision and hearing problems, and urinary incontinence increased the risk of mortality. In another retrospective study that included 19,682 patients with hip fractures, the presence of congestive heart failure, diabetes mellitus, and malignancy increased 30-day mortality.\textsuperscript{25} As expected, we observed a higher mortality rate among patients with three or more comorbidities, which is consistent with the literature.

In a study including 802 cases of hip fractures that occurred between 2008 and 2018, the presence of postoperative complications increased the risk of 1-year mortality.\textsuperscript{46} Similarly, Gurger\textsuperscript{40} and Barbosa et al.\textsuperscript{40} showed that postoperative complications were associated with higher 1-year mortality. Although we did not individually evaluate the postoperative complications in our study, we observed that frail patients had higher mortality rates in the presence of complications.

Consistent with our findings, Drevet et al.\textsuperscript{11} also demonstrated the importance of activities of daily living in preventing the negative consequences of such trauma in their prospective study on the effects of IADL performance on mortality in 113 patients.

Few studies have investigated the effects of hip fractures on mortality in older patients. The strength of our study was its prospective design. The limitations of this study were that it was conducted in a single center and included a small number of patients. Another limiting factor was that patients with advanced dementia were not included. Moreover, patient mobilization status was not assessed during the postoperative period. Finally, no distinction was made based on the type of hip fracture.

In conclusion, to reduce high mortality rates, patients with hip fractures should undergo a detailed geriatric evaluation before surgery, and their medical problems should be stabilized as early as possible. Thus, planning surgery immediately for patients with indications for surgery and closely following patients with malnutrition is important to reduce mortality after hip fracture.

**ACKNOWLEDGMENTS**

**CONFLICT OF INTEREST**

The researchers claim no conflicts of interest.

**FUNDING**

None.

**AUTHOR CONTRIBUTIONS**

Conceptualization, RG, PTT, OK, KT, DNB, SS; Data curation, RG, PTT, CS, MT; Investigation and Methodology, OK; Writing—original draft, RG, PTT, OK, KT, DNB, SS; Writing-review & editing, SS.

**REFERENCES**

2012;23:949-55.
34. Lavernia CJ, Sierra RJ, Baerga L. Nutritional parameters and

www.e-agmr.org
The Mediating Role of Social Participation in Motoric Cognitive Risk and its Relation to Depression and Loneliness in Older Adults

Ji Hyeun Park¹, Sangmi Park³, Jae Hyung Jung⁵, Su Yeong Bae¹, Sohyeon Yun¹, Anastassiya Khan¹, Ikpyo Hong¹, Ji-Hyuk Park³

¹Department of Occupational Therapy, Graduate School, Yonsei University, Wonju, Korea
²Department of Rehabilitation, Gyeonggi Provincial Medical Center, Anseong, Korea
³Department of Occupational Therapy, College of Software and Digital Healthcare Convergence, Yonsei University, Wonju, Korea

Corresponding Author:
Ji-Hyuk Park, PhD, OT
Department of Occupational Therapy, Yonsei University College of Software and Digital Healthcare Convergence, 1 Yonseidae-gil, Wonju 26493, Korea
E-mail: otscientist@yonsei.ac.kr
ORCID: https://orcid.org/0000-0002-1041-2266

Received: January 19, 2023
Revised: May 30, 2023
Accepted: June 12, 2023

Background: Motoric cognitive risk syndrome (MCR) reduces the quality of life, independence, and social interaction in older adults. Social participation is a potentially modifiable factor that benefits cognitive and mental health. This study explored the mediating roles of social participation between MCR and depression and between MCR and loneliness. Methods: We performed a secondary analysis of data from the 2015–2016 National Social Life, Health, and Aging Project. Slow gait speed and cognitive decline were used to assess MCR. Mediation analysis was applied to two models, both of which used MCR as an exposure and social participation as a mediator. The outcomes were depression and loneliness for each model, respectively. Results: Among 1,697 older adults, 196 (11.6%) had MCR. The mediating role of social participation was statistically significant in both models. The indirect effect \( \beta = 0.267, p = 0.001 \) of MCR on depression through social participation comprised 11.97% of the total effect \( \beta = 2.231, p < 0.001 \). The indirect effect \( \beta = 0.987, p = 0.001 \) of MCR on loneliness through social participation was 19.48% of the total effect \( \beta = 0.503, p < 0.001 \). Conclusion: Interventions to increase social participation may reduce depression and loneliness of older adults with MCR.

Key Words: Cognition, Frail elderly, Mental health, Walking speed

INTRODUCTION

Motoric cognitive risk syndrome (MCR) is characterized by cognitive impairment, slow gait speed, and age > 65 years.¹ MCR can increase the risk of adverse outcomes such as falls and dementia² and may result in diminished quality of life, dependent daily living, and reduced social interaction.³ The prevalence of MCR is approximately 10% but varies by region and population.⁴,⁵ Older adults with MCR experience not only negative physical consequences but also mental health issues. A large cross-sectional study reported that anxiety-depressive disorder and depression were associated with MCR.⁶

Additionally, MCR has been linked to loneliness.⁷ MCR and mental health problems are related; therefore, it is vital to identify their contributing factors.

Depression is a common symptom in older adults with MCR.⁸ Untreated depression can progress to dementia.⁹ Moreover, social participation is related to depression in older adults. Poverty or a lack of social relations or integration can lead to depression.¹⁰ In contrast, older adults who participate in social activities frequently report fewer depressive feelings.¹¹ An increase in depression among older adults is closely related to a decrease in social participation due to aging.¹² These findings support the notion that social participation is essential for preventing depression. However, it remains unclear whether the relationship between social participation and depression is the same among older adults with MCR.

Social participation can be defined as individuals engaging in interactions within their community or society through social activities.¹³ Previous studies reported negative associations between age and social network size³ and between cognitive impairment and...
social participation. Similarly, social participation may be lacking in older adults with MCR. Moreover, a lack of social engagement negatively affects individuals with depression.

Loneliness is a common interpersonal experience in the subjective appraisal of the extent of social relationships. Loneliness negatively impacts physical and mental health, well-being, and mortality. In their analysis of 140,000 older adults from 30 countries, Chawla et al. reported a pooled prevalence of loneliness among older adults of 25.9%. Previous studies showed that older adults who frequently participate in social activities are less likely to feel lonely and that an increase in loneliness among older adults is closely related to a decrease in social participation due to aging.

MCR symptoms such as cognitive impairment, physical weakness, and decreased mental health create significant challenges for patients, families, healthcare professionals, and the government. Therefore, exploring the factors that may contribute to depression and loneliness in individuals with MCR is crucial. Understanding the complex associations between MCR, depression, and loneliness by examining the influence of social participation could inform the development of practical interventions to help slow or prevent the transition to dementia. To our knowledge, no previous studies have explored the relationship between MCR and depression or loneliness mediated by social participation. Therefore, this study investigated the mediating effect of social participation on the relationships among MCR, depression, and loneliness.

**MATERIALS AND METHODS**

**1. Study Data and Participants**

We retrieved data on 4,377 older adults from the 2015–2016 National Social Life, Health, and Aging Project (NSHAP) (round 3). The NSHAP collects health information on community-dwelling older American adults, including their physical health, cognitive function, social interaction, and emotions. This national survey provides information for developing policies and understanding the aging population. The inclusion criteria for this study were: age 65 years or older and no dementia. The protocol of this secondary data analysis study was approved by the Yonsei University Mirae Campus Institutional Review Board (No. 1041849-202211-SB-199-01) and written informed consent was exempted. Also, this study compiled the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.

**2. Study Variables**

The independent variable (X) was MCR, which was assessed based on the Montreal Cognitive Assessment (MoCA) test score and gait speed (m/s). Table 1 presents the gait speed cutoff for defining slow gait in MCR. The participants were assigned a code of 1 if they had a MoCA score < 26 points and exhibited slow gait speed (m/s), and a code of 0 if their MoCA score was > 26 and they did not display slow gait speed. The NSHAP questionnaires include the Survey-Adapted Montreal Cognitive Assessment (MoCA-SA) for assessing cognitive function. The MoCA-SA score was transformed into the MoCA score, as described previously. The cutoff score for slow gait speed was set below the average speed score by 1 standard deviation by age and sex.

One dependent variable (Y1) was depression, which was measured using the Center for Epidemiological Studies Depression Scale (CESD-11). Each of the 11 items is scored on a 4-point scale (0, rarely or none of the time; 1, sometimes; 2, occasionally; and 3, most of the time). The total score ranges from 0 to 33 points. The sum of the scores was used as the dependent variable. Higher CESD-11 scores indicated more severe depressive symptoms.

The other dependent variable (Y2) was loneliness, which was assessed using the University of California Los Angeles Loneliness Scale, version 3 (UCLA). The loneliness variable consisted of three indicators (companion, isolated, and left out). The UCLA scores comprise a 20-item scale (0, never; 1, hardly ever; 2, sometimes; and 3, often). The total score ranges from 0 to 9 points. We used the sum of the scores as the loneliness variable.

The mediating variable (M) was social participation. The social participation variable consisted of three domains (attend, social, and volunteer) and was measured using the following three questions: "In the past 12 months, how often did you attend meetings of any organized group?" "In the past 12 months, how often did you get together socially with friends or relatives?" "In the past 12 months, how often have you volunteered to work for religious, charitable, political, health-related, or other organizations?" These were scored on a 7-point Likert scale (0 “never” to 6 “several times a week”). We used the total score of the three questions (ranging from 0 to 18 points) as the mediating variable, with a higher score indicating positive social participation.

**Table 1. Gait speed cutoff for slow gait**

<table>
<thead>
<tr>
<th>Age group (y)</th>
<th>Cutoff for slow gait (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
</tr>
<tr>
<td>65–69</td>
<td>0.6</td>
</tr>
<tr>
<td>70–74</td>
<td>0.5</td>
</tr>
<tr>
<td>75–79</td>
<td>0.4</td>
</tr>
<tr>
<td>80–84</td>
<td>0.4</td>
</tr>
<tr>
<td>≥85</td>
<td>0.4</td>
</tr>
</tbody>
</table>
3. Statistical Analyses

We performed descriptive analyses to explore the demographic characteristics. We used the independent t-test for continuous variables and the chi-squared test for categorical variables to examine the difference between two groups with and without MCR. Mediation analysis was used to investigate the role of social participation in mediating the relationship between MCR and depression. Baron and Kenny proposed a mediation analysis that applies a specific analytic procedure to adequately measure and test our hypotheses. This procedure consists of a three-step regression analysis (X for Y, X for M, and M for Y). However, there is a disadvantage in that the indirect effect is estimated to be low. In this study, we checked whether individual pathways were statistically significant in determining the indirect effects. Additionally, this method can only use Sobel’s test to examine the significance of the indirect effects. The bootstrapping method has been proposed to replace Sobel’s test because it relies on the assumption of a normal distribution. We also estimated the parameters using the maximum likelihood method with robust standard errors. Therefore, we applied path analysis to estimate the indirect and direct effects of MCR, social participation, and depression. The significance of the indirect and direct coefficients was examined using bootstrapping methods. The identification of the outliers in terms of low-speed gait for sensitivity analysis revealed no outliers in the dataset. We used SAS version 9.4 (SAS Institute, Cary, NC, USA) for data preprocessing and descriptive statistics and Mplus version 8 (Los Angeles, CA, USA) for mediation analysis.

RESULTS

The sample size for this study was 1,697 older adults after excluding those with missing values (n = 423), those aged < 64 years (n = 2,116), and those with dementia according to the cutoff MoCA score of 17 points (n = 141) (Fig. 1).

Table 2 shows the demographic characteristics of the 1,697 participants. The MCR group comprised 196 (11.6%) participants, including 93 (47.4%) men and 103 (52.6%) women. The non-MCR group comprised 1,501 (88.4%) participants, including 695 (46.3%) men and 806 (53.7%) women. Women predominated in both groups. Additionally, 1,046 (61.6%) participants engaged in physical activity each week, 102 (52.0%) of whom were in the MCR group. The average age did not differ significantly between the MCR (74.27 ± 6.39 years) and non-MCR (74.27 ± 7.23 years) groups. However, we observed significant differences between the MCR and non-MCR groups in CESD-11 score (6.75 ± 5.63 vs. 4.52 ± 4.35), ULCA score (3.27 ± 2.39 vs. 2.77 ± 2.14), and gait speed (0.39 ± 0.12 vs. 0.74 ± 0.22 m/s).

Table 3 and Fig. 2 present the results of the mediation analyses. MCR was significantly associated with depression (β = 1.964; 95% confidence interval [CI], 1.151–2.777; p < 0.001) and social participation (β = -1.514; 95% CI, -2.159–-0.869; p < 0.001). Additionally, social participation and depression were significantly associated (β = 0.177; 95% CI, -0.226–-0.128; p < 0.001). The indirect and total effects of MCR on the occurrence of depression were 0.267 (95% CI, 0.130–0.404) and 2.231 (95% CI, 1.280–3.181), respectively (Fig. 2A). Therefore, the total effect of our first model of the mediation analysis between non-standardized coefficients consisted of 11.93% indirect effect and 88.03% direct effect. Both were significant (indirect effect, p = 0.001; direct effect, p < 0.001).

Our analysis showed that the MCR also was significantly associated with loneliness (β = 0.405; 95% CI, 0.048–0.762; p = 0.026) and social participation (β = -1.514; 95% CI, -2.159–-0.869; 2015–2016 National Social Life, Health and Aging Project (n=1,377)
Participants aged >65 years (n=2,261; 51.66%)
Participants with Montreal Cognitive Assessment score >18 points (n=2,120; 48.44%)
Excluded: Participants aged <64 years (n=2,116; 48.34%)
Excluded: Participants with Montreal Cognitive Scale score <17 points (n=141; 3.22%)
Excluded: Participants with missing data (n=423; 9.66%)
- missing only data on gait speed (n=143)
- missing only data on dementia diagnosis (n=141)
- missing only data on HTN, CVA, CAD, CESD-11, and sum of social participation (n=139)
Final sample (n=1,697; 38.77%)

Fig. 1. Participant flow diagram. CAD, coronary artery disease; CESD-11, Center for Epidemiologic Studies Depression Scale-11; CVA, cerebrovascular accident; HTN, hypertension.

www.e-agmr.org
Table 2. Demographic characteristics of the study participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total samples</th>
<th>Participants with MCR</th>
<th>Participants without MCR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>1,697 (100)</td>
<td>196 (11.6)</td>
<td>1,501 (88.4)</td>
<td>0.761</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>788 (46.4)</td>
<td>93 (47.4)</td>
<td>695 (46.3)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>909 (53.6)</td>
<td>103 (52.6)</td>
<td>806 (53.7)</td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>74.27 ± 6.49</td>
<td>74.27 ± 7.23</td>
<td>74.27 ± 6.39</td>
<td>0.995</td>
</tr>
<tr>
<td>Educational attainment</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Less than high school</td>
<td>551 (32.5)</td>
<td>90 (45.9)</td>
<td>461 (30.7)</td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>597 (35.2)</td>
<td>75 (38.3)</td>
<td>522 (34.8)</td>
<td></td>
</tr>
<tr>
<td>Above college</td>
<td>549 (32.3)</td>
<td>31 (15.8)</td>
<td>518 (34.5)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>White</td>
<td>1,437 (84.7)</td>
<td>131 (66.8)</td>
<td>1,306 (87.0)</td>
<td></td>
</tr>
<tr>
<td>Black/African American</td>
<td>167 (9.8)</td>
<td>48 (24.5)</td>
<td>119 (7.9)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>93 (5.5)</td>
<td>17 (8.7)</td>
<td>76 (5.1)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td>0.286</td>
</tr>
<tr>
<td>Have a partner</td>
<td>1,174 (69.2)</td>
<td>129 (65.8)</td>
<td>1,045 (69.6)</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>523 (30.8)</td>
<td>67 (34.2)</td>
<td>456 (30.4)</td>
<td></td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
<td></td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>Never</td>
<td>330 (19.5)</td>
<td>56 (28.6)</td>
<td>274 (18.3)</td>
<td></td>
</tr>
<tr>
<td>Per month</td>
<td>321 (18.9)</td>
<td>38 (19.4)</td>
<td>283 (18.8)</td>
<td></td>
</tr>
<tr>
<td>Per week</td>
<td>1046 (61.6)</td>
<td>102 (52.0)</td>
<td>944 (62.9)</td>
<td></td>
</tr>
<tr>
<td>Chronic disease, yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>854 (50.3)</td>
<td>115 (58.7)</td>
<td>739 (49.2)</td>
<td>0.015*</td>
</tr>
<tr>
<td>Diabetes</td>
<td>230 (13.6)</td>
<td>39 (19.9)</td>
<td>191 (12.7)</td>
<td>0.007**</td>
</tr>
<tr>
<td>Stroke</td>
<td>87 (5.1)</td>
<td>10 (5.1)</td>
<td>77 (5.1)</td>
<td>1.000</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>140 (8.3)</td>
<td>27 (13.8)</td>
<td>113 (7.5)</td>
<td>0.005**</td>
</tr>
<tr>
<td>CESD-11</td>
<td>4.77 ± 4.57</td>
<td>6.75 ± 5.63</td>
<td>4.52 ± 4.35</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>UCLA</td>
<td>2.82 ± 2.17</td>
<td>3.27 ± 2.39</td>
<td>2.77 ± 2.14</td>
<td>0.002**</td>
</tr>
</tbody>
</table>

Values are presented as number (%) or mean±standard deviation.
MCR, Motoric cognitive risk syndrome; CESD-11, Center for Epidemiologic Studies Depression Scale-11; UCLA, University of California Los Angeles Loneliness Scale.
*p<0.05, **p<0.01, ***p<0.001.

Table 3. Results of the bias-corrected bootstrap analyses of the pathways (n=1,697)

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Unstandardized estimate</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct effect MCR (X) → Depression (Y1)</td>
<td>1.964</td>
<td>&lt; 0.001***</td>
</tr>
<tr>
<td>Direct effect MCR (X) → Social participation (M)</td>
<td>-1.514</td>
<td>&lt; 0.001***</td>
</tr>
<tr>
<td>Direct effect social participation (M) → Depression (Y1)</td>
<td>-0.177</td>
<td>&lt; 0.001***</td>
</tr>
<tr>
<td>Indirect effect MCR (X) → Depression (Y1)</td>
<td>0.267</td>
<td>0.001***</td>
</tr>
<tr>
<td>Total effect MCR (X) → Depression (Y1)</td>
<td>2.231</td>
<td>&lt; 0.001***</td>
</tr>
<tr>
<td>Direct effect MCR (X) → Loneliness (Y2)</td>
<td>0.405</td>
<td>0.026***</td>
</tr>
<tr>
<td>Direct effect MCR (X) → Social participation (M)</td>
<td>-1.514</td>
<td>&lt; 0.001***</td>
</tr>
<tr>
<td>Direct effect social participation (M) → Loneliness (Y2)</td>
<td>-0.065</td>
<td>&lt; 0.001***</td>
</tr>
<tr>
<td>Indirect effect MCR (X) → Loneliness (Y2)</td>
<td>0.098</td>
<td>0.001***</td>
</tr>
<tr>
<td>Total effect MCR (X) → Loneliness (Y2)</td>
<td>0.503</td>
<td>&lt; 0.001***</td>
</tr>
</tbody>
</table>

MCR, Motoric cognitive risk syndrome.
*p<0.05, **p<0.01, ***p<0.001.

Fig. 2. Mediation analysis models. (A) Mediating role of social participation between MCR and depression. (B) Mediating role of social participation between MCR and loneliness. Unstandardized coefficients were presented.
p < 0.001). Social participation and loneliness were also significantly associated ($\beta = -0.065; 95\% CI, -0.089--0.041; p < 0.001$). The indirect effect of MCR on loneliness was 0.098 (95% CI, 0.041–0.155), and the total effect was 0.503 (95% CI, 0.089–0.917) (Fig. 2B). Therefore, the total effect of the second model of the mediation analysis between MCR and loneliness by social participation was also significant (indirect effect, $p = 0.001$; direct effect, $p < 0.001$), which included both indirect (19.48%) and direct (80.52%) effects.

**DISCUSSION**

Our findings showed that social participation is mediated the relationship between MCR and two types of mental health indicators (depression and loneliness). MCR directly and indirectly influenced older adults with depression or loneliness by decreasing their social participation. This study aimed to clarify the adverse health outcomes of older adults with MCR whose social networks are reduced due to cognitive decline and reduced gait speed which is significantly impacts their mental health. The association between MCR and social participation was supported by previous studies reporting that MCR is related to emotional (tangible, affectionate feelings) and social support. Studies have also shown that social participation facilitates better health among older adults. Our study provides evidence supporting these findings. Moreover, we identified the mediating function of social participation on the relationship between MCR and depression and loneliness.

This study has two major findings. The first was the direct effect of MCR on two types of mental health (i.e., depression and loneliness). These results suggest that declines in gait speed and cognitive function are associated with depression and loneliness. The associations identified in this study align with those of previous studies, supporting the association between MCR and mental health. A Canadian cross-sectional study reported an association between MCR, anxiety, and depression. A Chinese 4-year prospective study also reported that depression was related to MCR and required special consideration to reduce dementia following the development of MCR. Regarding the association between MCR and loneliness, a Chinese longitudinal study focusing on female older adults demonstrated an association between loneliness and the development of MCR. Therefore, the association between MCR and depression/loneliness found in this study can direct clinicians to pay attention to the symptoms of MCR, which may be perceived as a natural aging process.

The second finding is the mediating effect of social participation on the relationship between MCR and mental health (i.e., depression and loneliness). These mediating effects can be explained by the associations of the two sub-factors of MCR (i.e., slow gait speed and cognitive decline) with social participation and the association between social participation and mental health. A study in Singapore including older adults demonstrated that slow gait speed is associated with potential social isolation owing to reduced physical activity and infrequent contact with others. Similarly, an aging study conducted on older adults in China suggested that maintaining normal gait speed was associated with higher engagement in social activities and participation, which promoted physical health and walking speed. A meta-analysis examining cognitive decline revealed a consistent relationship between social activities and participation.

Social participation is associated with mental health outcomes. A Taiwanese longitudinal study over 18 years that explored the trajectory of social activity participation and depression symptoms in older adults showed that continuous participation or the initiation of social activity in old age was significantly related to the reduction of symptoms of depression. Previous research has indicated that greater social participation is correlated with reduced loneliness. Therefore, our findings regarding the indirect effects of social participation on MCR and mental health align with existing mechanisms and highlight the importance of social participation as a crucial factor related to the mental well-being of older adults with MCR.

Our study has several limitations. We measured social participation using three items: (1) participation in organized group activities, (2) social meetings with family and relatives, and (3) volunteering. This operationalized definition aligns with the concept of social participation in the Occupational Therapy Practice Framework 4, in which social participation is defined as activities that encompass social interaction with family, friends, and community members and promote social interdependence. However, we did not assess engagement in leisure activities, a commonly used measure of social participation, as the NSHAP data do not include items related to leisure activities. Second, our study used a cross-sectional design that could not establish causality. Thus, longitudinal studies to examine the causal effect of MCR on each factor (i.e., depression and loneliness) are needed, in addition to developing approaches for the early detection and intervention of MCR.

In conclusion, our study investigated the mediating effect of social participation on the relationship between MCR and depression and MCR with loneliness. The findings revealed the indirect association of social participation as a mediator. Our results showed that increased social participation among older adults with MCR may reduce depression and loneliness. Based on these results, further research is warranted to examine the effectiveness of
REFERENCES


**Integrated Effects of Thai Essential Oil and Balance Exercise on Parameters associated with Falls in Older Adults at Risk of Falling: A Randomized Controlled Study**

Pattanasin Areeudomwong¹, Thidarat Duangyod², Chatchada Sutalangka¹, Vitsarut Buttagat¹

¹Department of Physical Therapy, School of Integrative Medicine, Mae Fah Luang University, Chiang Rai, Thailand
²Department of Applied Thai Traditional Medicine, School of Integrative Medicine, Mae Fah Luang University, Chiang Rai, Thailand

**Background:** Reducing the risk of falling by improving balance and leg strength may be a preventive strategy. This study evaluated the integrated effects of Thai essential oil and balance exercises on parameters associated with falls in community-dwelling older adults at risk of falling.

**Methods:** Fifty-six participants were randomly allocated to either the intervention group (IG), which performed balance exercises while smelling Thai essential oil scents of Zanthoxylum limonella (Dennst.) Alston, or the control group (CG), which performed balance exercises while receiving a control patch. Balance exercises were practiced for 12, 30-minute sessions over 4 weeks. Static and dynamic balance with eyes open and eyes closed (EC), leg muscle strength, agility, and fear of falling were assessed at baseline, after the 4-week intervention, and at 1 month after the last intervention session.

**Results:** Both groups showed significant improvements in static and dynamic balance, ankle plantarflexor strength, and agility after the 4-week intervention (p<0.05), which persisted at the 1-month follow-up (p<0.05). Compared to the CG, the IG demonstrated significantly better static balance in terms of elliptical sway area (p=0.04) and center of pressure (CoP) velocity (p=0.001) during EC, as well as ankle plantarflexor strength (p=0.01). The IG also maintained a significantly greater improvement in CoP velocity during EC (p=0.01).

**Conclusion:** Integrated Thai essential oil and balance exercises improved static balance and ankle plantarflexor strength compared to the balance exercise with a control patch in older adults at risk of falling.

**Key Words:** Older adults, Martial arts, Odorants, Physical fitness, Postural balance, Accidental falls

INTRODUCTION

Although advances in medicine and public health have increased life expectancy, the sanitary and social costs associated with dependency and mortality have risen considerably.¹ Falls are a major public health issue in community-dwelling older adults, resulting in a lower quality of life and dependency.²³ In particular, impaired balance and sensory perception, leg muscle weakness, and decreased agility have been proposed as major risk factors for falls and increased fear of falling.³⁻⁴ Previous research identified moderate correlations between poor balance, low physical activity, and decreased agility in older adults.⁵ Therefore, potential and simple-to-implement interventions focusing on improving balance and physical fitness in older adults at risk of falling may be advantageous.⁶

Postural control is a complex motor task that involves maintaining, achieving, or restoring balance during any posture or activity.⁷ Maintaining postural control requires three major systems: the visual, vestibular, and somatosensory systems. However, the functions of these systems deteriorate with age.⁸ Balance exercises have...
been used to improve balance ability and reduce the rate of falling in older adults. Martial art-based balance exercises, such as Thai boxing exercise (TBE), could make exercise more appealing to older adults. Areudomwong et al. supported the use of TBE in older adults at risk of falling to improve static and dynamic balance, leg muscle strength, body flexibility, and agility.

Neurophysiological studies have revealed that various brain structures, in addition to the three major systems, appear to play important roles in balance and postural control. For instance, postural orientation and balance may be involved in automated and reflexive spinal programs influenced by the cerebral cortex, olfactory bulb, cerebellum, brainstem, and several distinct and separate supraspinal centers.

Scent strongly stimulates a wide range of areas of the cerebral cortex, including the orbitofrontal cortex, the insula cortex, and the cerebellum. Moreover, scent stimulation can improve balance control and reduce falls in older adults. Essential oils of *Zanthoxylum limonella* (Dennst.) Alston, an evergreen tree belonging to the Rutaceae family, have been used in traditional Thai medicine. Limonene, a monoterpane with an orange aroma, is one of the main compounds in *Z. limonella*. A recent study reported that use of *Z. limonella* (Dennst.) Alston as an essential massage oil reduced calf muscle pain. One study on the effects of d-limonene on transient cerebral ischemia and physical function in stroke-prone spontaneously hypertensive rats reported that d-limonene may provide protective effects against ischemic damage and increase grip strength in rats; however, neither *Z. limonella* (Dennst.) Alston nor limonene have been studied in older adults.

Kwon et al. proposed that scent stimulation may induce positive feelings, decrease fatigue, and improve exercise performance. Thus, the present study investigated the integrated effects of a Thai essential oil (TEO; *Z. limonella* (Dennst.) Alston) patch and TBE on balance, leg muscle strength, agility, and fear of falling in community-dwelling older adults at risk of falling.

MATERIALS AND METHODS

Study Design and Setting

This randomized controlled trial was conducted in the Physiotherapy Laboratory of Mae Fah Luang University, Chiang Rai, Thailand, between December 2021 and September 2022. The Human Research Ethics Committee of the Mae Fah Luang University approved the study protocol (COA 275/2021), which was registered in the Thai Clinical Trials Registry (TCTR20211114002).

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

Participants

Fifty-six eligible male and female non-disabled, community-dwelling older adults living in Chiang Rai, Thailand, were recruited to participate in this study through local advertisements. The older adults were asked to complete a questionnaire that included demographic information such as marital status and education level. They were also screened by a medical doctor who was blinded to the recruitment and intervention methods. The inclusion criteria were age 60 years and older and the ability to walk independently without the use of ambulation aids, a Berg Balance Scale, used to assess the risk of falling, score of < 49; clear comprehension, and adequate vision and hearing. Older adults with a Mini-Mental State Examination score of < 24, major unstable cardiopulmonary conditions, neurological conditions, neuropathy, anosmia, vestibular conditions, allergic reaction to the smell, or regular use of *Z. limonella* (Dennst.) Alston essential oil or almond base oil, cancer, and serious orthopedic conditions such as stenosis, joint infection, arthritis of the lower limbs, and lower limb discomfort of more than 4 on the numerical rating scale, as determined by oral history taking and physical examination, were excluded.

The objectives and processes of this study were explained to all participants, who provided informed written consent before their study participation.

Sample Size and Randomization

The G*Power software (version 3.1.9.2) sample size calculation showed that 56 participants were needed to detect an effect size of 0.20 with a power of 90%, a significance level of p < 0.05, two intervention groups, three measurement times, and correlations among repetitive measures.

Convenience sampling was used to select the study population, which was randomly divided into an intervention group (IG) or a control group (CG) using block randomization with block sizes of two, four, and six. The randomization results were concealed in sealed and opaque envelopes. Randomization was performed by a research assistant blinded to the assessment and intervention procedures.

Measurements

A trained assessor with 5 years of experience in clinical evaluation, who was blinded to the randomization method, assessed the outcomes. The participants were evaluated at baseline, at the end of the 4-week intervention, and 1 month after the last intervention session. The adverse effects of the interventions were recorded during the 4-week intervention period.

The primary outcome measures were static and dynamic balance abilities, which were tested using a force platform (PDM-S,
The fear of falling was assessed using the Thai version of the Falls Efficacy Scale-International (Thai FES-I). It consists of 16 items rated on a four-point Likert scale that assesses the level of concern about falling during daily activities. The total score ranges from 16 to 64, with a higher score indicating greater fear of falling.\(^{31}\)

**Intervention Procedures**

The participants were randomly assigned to either the IG (receiving TEO of *Z. limonella* (Dennst.) Alston patch while performing 4-week TBE) or CG (4-week TBE with a control patch). One week before the experiment, the participants in both groups were acquainted with the TBE, which was designed as a group exercise with a maximum of ten participants. Participants in both groups received TBE training from three certified instructors with 5 years of TBE teaching experience. The protocol described by Areeudomwong et al.\(^7\) was followed for the TBE intervention, which included warm-up, TBE, and cool-down sessions.

The participants performed specific patterns and stepped in a square-like direction following a Thai boxing song. During TBE, a TEO patch was attached to each IG participant with three drops (0.3 mL) of *Z. limonella* (Dennst.) Alston essential oil (100% essential oil made by the Medical Plant Innovation Center of Mae Fah Luang University, Thailand) on their clothing in the manubrium area. A control patch containing three drops (0.3 mL) of sweet almond base oil (Chanjao Longevity Co., Ltd., Bangkok, Thailand) was attached to the clothing of the CG participants in the manubrium area. During the TBE practice, all participants in both groups were asked to inhale the scent from their patches.

**Statistical Analysis**

IBM SPSS version 20.0 (IBM Corp, Armonk, NY, USA) was used for statistical analysis based on the intention-to-treat method. The mean, standard deviation, and 95% confidence interval (95% CI) for each outcome measure are shown. The Kolmogorov–Smirnov test confirmed a normal distribution of the data. A 3 × 2 mixed-model analysis of variance (ANOVA), with time (baseline, 4-week intervention, and 1-month follow-up) as a within-subject variable and group (IG and CG) as a between-subject variable, was used to analyze the effects of interventions on the outcome measures and to identify significant group-by-time interactions. Significant interaction effects were compared using post hoc Bonferroni pairwise comparisons. Statistical significance was set at p < 0.05. The between-group effect size was calculated using Cohen’s d coefficient with effect sizes (ES) of 0.15, 0.40, and 0.75 considered small, moderate, and large, respectively.\(^{32}\)

**RESULTS**

Fig. 1 depicts the flow of the participants in this study. Of the 80 participants, 56 were considered eligible and 24 were excluded. Table 1 shows that the baseline characteristics of the participants were similar across groups. The participants complied at a high
rate, and there were no dropouts during the study period. The participants in this study reported no adverse effects of the interventions.

**Static Balance Performance**

The $3 \times 2$ mixed-model ANOVA revealed a significant time × group interaction effect for elliptical sway area and CoP velocity during the TST with EC ($F_{2,108} = 3.32$, $p = 0.04$ and $F_{2,108} = 3.81$, $p = 0.03$, respectively). The participants in IG had a greater decrease in both elliptical sway area and CoP velocity after the 4-week intervention compared to those in the CG (between-group mean difference [BGMD] elliptical sway area = 57.39 mm$^2$, 95% CI 57.39–27.56, $p = 0.04$; CoP velocity = 3.62 mm/s, 95% CI 2.14–112.64, $p = 0.001$) (Fig. 2). The elliptical sway area and CoP velocity had a moderate ES of 0.56 and a large ES of 0.91, respectively.

At the 1-month follow-up, the IG had a greater reduction in CoP velocity compared to the CG, with a moderate ES of 0.69 (BGMD = 3.30 mm/s, 95% CI 0.73–5.87, $p = 0.01$) (Fig. 2). Comparison of the baseline data at each time point in each group revealed reductions in the elliptical sway area and CoP velocity during the TST with EC at 4-week intervention ($p < 0.001$) in both the IG and CG, and the effects in both groups on CoP velocity were maintained at the 1-month follow-up ($p < 0.01$). While the CG showed a retention effect on the elliptical sway area ($p = 0.001$), the IG did not (Table 2).

Although we observed no statistically significant interactions for the elliptical sway area ($F_{2,108} = 0.49$, $p = 0.61$) and CoP velocity ($F_{2,108} = 2.50$, $p = 0.09$) during the TST with EO, we observed a significant main effect of time, with both groups showing im-

---

**Table 1. Baseline characteristics of the participants**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intervention group (n = 28)</th>
<th>Control group (n = 28)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>76.13 ± 3.25</td>
<td>75.67 ± 4.22</td>
<td>0.83</td>
</tr>
<tr>
<td>Sex, female</td>
<td>20 (71.43)</td>
<td>22 (78.57)</td>
<td>0.88</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>157.43 ± 4.19</td>
<td>156.68 ± 3.11</td>
<td>0.90</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>60.94 ± 2.67</td>
<td>60.45 ± 2.92</td>
<td>0.96</td>
</tr>
<tr>
<td>MMSE score</td>
<td>28.62 ± 1.33</td>
<td>28.35 ± 1.64</td>
<td>0.97</td>
</tr>
<tr>
<td>Marital status, single/married (%)</td>
<td>3.57/96.43</td>
<td>3.32/92.86</td>
<td>0.98</td>
</tr>
<tr>
<td>Education, primary school (%)</td>
<td>89.29</td>
<td>92.86</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation or number (%). MMSE, Mini-Mental State Examination.
proved elliptical sway area and CoP velocity at all follow-up periods (p < 0.05) (Table 2).

Dynamic Balance Performance
The mixed-model ANOVA did not reveal a statistically significant interaction effect for the elliptical sway area and CoP velocity during the FRT (F2,108 = 2.42, p = 0.09 and F2,108 = 0.29, p = 0.75, respectively) (Fig. 2). We observed a main effect of time, with both groups showing a decreased elliptical sway area (FM2,54 = 31.57, p < 0.001) and CoP velocity (F2,54 = 16.07, p < 0.001) after the 4-week intervention compared with those at baseline (p < 0.001). At the 1-month follow-up, the IG demonstrated a reduction in CoP velocity (p = 0.002), whereas the CG demonstrated a reduction in the elliptical sway area (p = 0.001) (Table 2).

Lower Limb Strength
A 3 × 2 mixed-model ANOVA showed a significant interaction for ankle plantarflexor strength (F2,108 = 2.70, p = 0.04) but not for hip flexors (F2,108 = 0.87, p = 0.42), hip extensors (F2,108 = 0.13, p = 0.88), knee flexors (F2,108 = 0.07, p = 0.93), knee extensors (F2,108 = 0.08, p = 0.93), and ankle dorsiflexors (F2,108 = 1.44, p = 0.24). The IG had a greater increase in ankle plantarflexor strength than that of the CG after the 4-week intervention (BGMD = 1.67 kg, 95% CI 0.40–2.96, p = 0.01), with a moderate ES of 0.70 (Fig. 3). Comparison of lower limb strength within each group showed improved ankle plantarflexor strength alone at the 4-week intervention in both groups (p < 0.05) (Table 2).

Agility
The mixed-model ANOVA showed no statistically significant interaction in the 8-foot up and go test (F2,108 = 0.93, p = 0.07) (Fig. 2). There was a main effect of time (F2,54 = 6.48, p = 0.003), with IG significantly increasing agility at the 1-month follow-up when compared to that at baseline (p < 0.001) (Table 2).

Fear of Falling
Mixed-model ANOVA revealed no significant interaction effect for the Thai FES-I (F2,108 = 1.15, p = 0.32) (Fig. 2), nor was there a main effect of time (Table 2).

DISCUSSION
To our knowledge, this is the first randomized controlled study to investigate the integrated effects of TEO (Z. limonella (Dennst.) Alston) and TBE as a balance exercise in older adults at risk of falling. Our findings showed that both groups demonstrated significantly increased static and dynamic balance abilities, ankle plantarflexor strength, and agility after the 4-week intervention. At the 1-month follow-up, the detraining effects of greater balance abilities were observed in both groups. The IG outperformed the CG
Table 2. Comparison of groups at baseline versus follow-ups for static and dynamic balance performance, agility, fear of falling, and lower limb strength analyzed using the 3×2 mixed-model analysis of variance

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control group (n = 28)</th>
<th>Intervention groups (n = 28)</th>
<th>Baseline</th>
<th>At 4 wk</th>
<th>At 1 mo follow-up</th>
<th>Baseline vs. at 1 mo follow-up</th>
<th>Baseline</th>
<th>At 4 wk</th>
<th>At 1 mo follow-up</th>
<th>Baseline vs. at 1 mo follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elliptical sway area during EO in TST (mm²)</td>
<td>225.9 ± 36.40</td>
<td>195.9 ± 34.24</td>
<td>21.3 ± 43.70</td>
<td>30.0 ± 40.3</td>
<td>13.6 ± 47.1</td>
<td>220.5 ± 33.95</td>
<td>182.3 ± 33.07</td>
<td>204.4 ± 32.21</td>
<td>38.1 ± 5.01</td>
<td>160.8 ± 6.05</td>
</tr>
<tr>
<td>CoP velocity during EO in TST (mm/s)</td>
<td>22.67 ± 4.81</td>
<td>18.00 ± 4.35</td>
<td>20.98 ± 4.47</td>
<td>4.67 ± 0.57</td>
<td>1.70 ± 0.51</td>
<td>21.3 ± 5.30</td>
<td>17.7 ± 5.06</td>
<td>18.7 ± 5.15</td>
<td>3.64 ± 0.62</td>
<td>2.61 ± 0.65</td>
</tr>
<tr>
<td>Elliptical sway area during EC in TST (mm²)</td>
<td>618.8 ± 140.17</td>
<td>513.56 ± 127.84</td>
<td>565.84 ± 140.99</td>
<td>105.30 ± 13.79</td>
<td>53.02 ± 17.16</td>
<td>625.88 ± 93.67</td>
<td>450.28 ± 79.13</td>
<td>576.37 ± 156.81</td>
<td>175.60 ± 20.10</td>
<td>49.51 ± 30.41</td>
</tr>
<tr>
<td>CoP velocity during EC in TST (mm/s)</td>
<td>34.31 ± 2.87</td>
<td>31.23 ± 3.79</td>
<td>32.68 ± 3.44</td>
<td>3.09 ± 0.67</td>
<td>1.63 ± 0.46</td>
<td>33.13 ± 4.36</td>
<td>27.25 ± 4.16</td>
<td>29.36 ± 5.84</td>
<td>5.88 ± 0.76</td>
<td>3.77 ± 0.90</td>
</tr>
<tr>
<td>Elliptical sway area in FRT (mm²)</td>
<td>1,589.26 ± 248.88</td>
<td>1,281.11 ± 148.72</td>
<td>1,425.33 ± 197.91</td>
<td>308.16 ± 52.37</td>
<td>163.93 ± 28.32</td>
<td>1,525.89 ± 115.25</td>
<td>1,210.03 ± 135.77</td>
<td>1,429.56 ± 210.74</td>
<td>315.86 ± 32.56</td>
<td>96.34 ± 40.81</td>
</tr>
<tr>
<td>CoP velocity in FRT (mm/s)</td>
<td>42.00 ± 10.00</td>
<td>34.45 ± 8.72</td>
<td>38.85 ± 8.24</td>
<td>7.55 ± 1.42</td>
<td>3.16 ± 1.35</td>
<td>40.65 ± 10.38</td>
<td>34.12 ± 8.56</td>
<td>37.49 ± 11.22</td>
<td>6.33 ± 1.25</td>
<td>3.16 ± 0.84</td>
</tr>
<tr>
<td>8-foot up and go test (s)</td>
<td>8.02 ± 2.03</td>
<td>7.68 ± 1.63</td>
<td>7.54 ± 1.44</td>
<td>0.35 ± 0.17</td>
<td>0.48 ± 0.19</td>
<td>8.26 ± 1.59</td>
<td>8.03 ± 1.37</td>
<td>7.88 ± 1.46</td>
<td>0.23 ± 0.13</td>
<td>0.39 ± 0.09</td>
</tr>
<tr>
<td>Thai version of FES-I score</td>
<td>32.79 ± 10.33</td>
<td>29.29 ± 9.23</td>
<td>31.39 ± 12.15</td>
<td>3.50 ± 1.38</td>
<td>1.39 ± 1.57</td>
<td>31.86 ± 11.27</td>
<td>28.11 ± 9.42</td>
<td>33.61 ± 8.33</td>
<td>3.75 ± 2.34</td>
<td>1.75 ± 1.96</td>
</tr>
<tr>
<td>Lower limb strength (kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip flexors</td>
<td>6.50 ± 1.55</td>
<td>6.68 ± 1.96</td>
<td>6.46 ± 2.05</td>
<td>0.18 ± 0.22</td>
<td>-0.04 ± 0.22</td>
<td>6.68 ± 2.16</td>
<td>6.93 ± 2.48</td>
<td>7.00 ± 2.37</td>
<td>0.25 ± 0.20</td>
<td>0.32 ± 0.21</td>
</tr>
<tr>
<td>Hip extensors</td>
<td>5.61 ± 2.54</td>
<td>5.57 ± 2.32</td>
<td>5.43 ± 1.99</td>
<td>-0.04 ± 0.35</td>
<td>-0.18 ± 0.32</td>
<td>5.64 ± 1.91</td>
<td>5.71 ± 1.58</td>
<td>5.68 ± 1.36</td>
<td>0.07 ± 0.35</td>
<td>0.04 ± 0.32</td>
</tr>
<tr>
<td>Knee flexors</td>
<td>6.11 ± 2.50</td>
<td>6.43 ± 3.04</td>
<td>6.21 ± 2.83</td>
<td>0.32 ± 0.32</td>
<td>-0.01 ± 0.23</td>
<td>6.39 ± 1.69</td>
<td>6.71 ± 2.14</td>
<td>6.61 ± 1.87</td>
<td>0.32 ± 0.21</td>
<td>0.21 ± 0.18</td>
</tr>
<tr>
<td>Knee extensors</td>
<td>5.00 ± 1.22</td>
<td>5.46 ± 0.92</td>
<td>5.21 ± 1.10</td>
<td>0.46 ± 0.18</td>
<td>0.21 ± 0.23</td>
<td>5.25 ± 1.60</td>
<td>5.61 ± 1.66</td>
<td>5.43 ± 1.69</td>
<td>0.36 ± 0.24</td>
<td>0.18 ± 0.23</td>
</tr>
<tr>
<td>Ankle plantarflexors</td>
<td>5.18 ± 1.76</td>
<td>5.68 ± 2.23</td>
<td>6.11 ± 2.66</td>
<td>0.50 ± 0.18</td>
<td>0.93 ± 0.23</td>
<td>5.86 ± 1.63</td>
<td>7.36 ± 2.54</td>
<td>7.00 ± 2.42</td>
<td>1.50 ± 0.49</td>
<td>1.14 ± 0.48</td>
</tr>
<tr>
<td>Ankle dorsiflexors</td>
<td>5.79 ± 1.50</td>
<td>6.93 ± 3.40</td>
<td>6.86 ± 3.48</td>
<td>1.14 ± 0.61</td>
<td>1.07 ± 0.58</td>
<td>5.82 ± 1.59</td>
<td>6.18 ± 1.87</td>
<td>6.11 ± 1.75</td>
<td>0.36 ± 0.16</td>
<td>0.29 ± 0.18</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation (95% confidence interval).
EO, eyes open; EC, eyes closed; TST, tandem stance test; FRT, functional reach test; FES-I, Falls Efficacy Scale International.

**a**Integument Zanthoxylum limonella Alston essential oil and Thai boxing exercise.

*p<0.05, **p<0.01, ***p<0.001.
in terms of elliptical sway area, CoP velocity during EC, and ankle plantarflexor strength. Furthermore, compared to the CG, the IG demonstrated better static balance control during EC due to a lower CoP velocity at the 1-month follow-up.

We observed that both the IG and CG had greater improvements in the elliptical sway area and CoP velocity variables of static balance in EO and EC conditions, and dynamic balance, after 4 weeks and 1-month follow-up compared to the baseline values; however, the detraining effects at 1 month were not observed in the IG for the elliptical sway area of the TST and dynamic balance. Although the studies differed in methodology and interventions, making comparisons difficult, previous studies that used martial arts-based exercises support our findings.33,34 Areeudomwong et al.7 showed that TBE training improved static and dynamic balance, leg strength, body flexibility, and agility in older adults compared to a fall prevention booklet intervention. Noopud et al.34 reported that traditional Thai dance prevented age-related mobility and balance declines, and risk of falls in older adults. Furthermore, Buransri and Phanpheng33 demonstrated improved dynamic balance among community-dwelling older adults after 12 weeks of practicing traditional Srichiangmai dance.

The plausible mechanisms underlying the effects of TBE on balance parameters include the following: (1) TBE involves placing light loads on the knees and ankles, requiring a body transition from double-leg standing to alternating feet or single-leg standing, emphasizing weight shifts and changing the base of support, which may challenge the postural control system7,34 and (2) TBE stepping was designed to be performed in a square shape, which may increase balance performance in multiple directions. This speculation was supported by the results reported by Dejvajara et al.35 that multidirectional step exercises could improve the dynamic balance of community-dwelling older adults.

At 4 weeks of intervention and the follow-up, neither group showed an improvement in the strength of the hip and knee flexors and extensors. This contradicts the findings of Areeudomwong et al.7 who found greater improvement in hip and knee strength after 4-week TBE practice. Although our study used the TBE protocol of Areeudomwong et al.7 in both groups, the differences in the results may be due to differences in participant age between the studies. The average age of our participants was 75–76 years, whereas that of the participants in the study by Areeudomwong et al.7 was 66–67 years. A previous study proposed that muscle and physical functions may differ in community-dwelling older adults aged 75 years compared to those in younger older adults.36

The results of this study revealed that, compared to the CG, the IG using a TEO patch while performing a 4-week TBE provided a
greater improvement in static balance during the EC condition. Additionally, we observed a greater increase in ankle plantarflexor strength in the IG than that in the CG. The mechanism by which Z. limonella (Dennst.) Alston essential oil improves balance is speculative. The improved static balance parameters and ankle plantarflexor strength in the IG during EC could be attributed to widespread cerebral cortex stimulation.13-15 Numerous brain structures, in addition to the visual, vestibular, and somatosensory systems, may play a role in balance and postural control.11 Although no studies have investigated the effects of Z. limonella Alston (Rutaceae) essential oil on balance-related outcomes in older adults, previous research has shown that other types of essential oils can help with balance in older adults. Additionally, limonene may have anti-stress effects and improve cognitive function.37 Freeman et al.17 showed that lavender and black pepper essential oils reduced postural sway in frail older adults while standing. Sakamoto et al.18 reported that lavender oil reduced the incidence of falls among older adults. Standing balance is a complex task that requires automated and reflexive spinal programs influenced by vestibular, visual, and proprioceptive senses; cognitive integration; attention and executive function; cerebellar function; and somatosensory feedback.3,8,11-13 Scent is one of the strongest stimuli through a wide area of the cerebral cortex, particularly the insular cortex.33-35 The insula integrates and processes various sensory inputs, including olfactory, visual, vestibular, attention, and emotion processing.38-40 Z. limonella (Dennst.) Alston essential oil may activate the insular cortex and cerebellum, providing additional benefits for static balance in older adults at risk of falling. Because our TEO may stimulate different brain areas, particularly the motor cortex, it may provide a greater increase in ankle plantarflexor strength compared to that in the controls. As a result, the greater ankle plantarflexor strength in older adults may be related to a greater ability to recover balance if it is distorted unexpectedly, such as in a forward fall, which is a high-intensity perturbation.34

The strengths of this study include the assessor-blinded randomized controlled design, which reduced the possibility of measurement bias. Furthermore, the results were not affected by participant attrition. This study had several limitations. First, most participants in this study were female; thus, future studies should include more male participants. Second, this study only examined the effectiveness of combining Z. limonella (Dennst.) Alston essential oil with TBE on balance-related parameters; other outcomes, such as cognitive function, attention, and cardiovascular fitness should be investigated further. Third, we observed no evidence of an association between Z. limonella (Dennst.) Alston essential oil and balance, physical performance, and brain function in older adults at risk of falling. The effects of Z. limonella (Dennst.) Alston essential oil, longer intervention periods, and longer follow-up should be performed. Finally, as the study was conducted among community-dwelling older adults, the results cannot be extrapolated to those living in nursing homes or hospitals. In conclusion, integrating Z. limonella (Dennst.) Alston essential oil while performing 4-week TBE results in greater improvements in static balance ability during EC and ankle plantarflexor strength than TBE with a sweet almond base oil in community-dwelling older adults at risk of falling.

ACKNOWLEDGMENTS

This study would like to thank the primary hospitals in the districts of Nang Lae and Mae Khao Tom, Chiang Rai, Thailand, for recruiting participants, as well as all participants for their cooperation throughout the study period.

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

This study has received funding support from the National Science, Research and Innovation Fund (NSRF) of Thailand (Fund ID: 6510001507).

AUTHOR CONTRIBUTIONS

Conceptualization, PA, VB; Funding acquisition, PA; Formal analysis, PA, VB; Investigation, PA, TD, CS, VB; Methodology, PA, CS, VB; Resource, TD; Validation, PA, VB; Writing-original draft, PA, VB; Writing-review & editing, PA, TD, CS, VB.

REFERENCES

4. Ambrose AF, Paul G, Hausdorff JM. Risk factors for falls among...


Matrix Metalloproteinases/Tissue Inhibitors of Metalloproteinases Ratio: A Biomarker of Bone Resorption in Geriatric Osteoporosis?

Bahar Bektan Kanat, Gulru Ulugerger Avci, Osman Faruk Bayramlar, Damla Unal, Ozge Sonmez, Ibrahim Murat Bolayirli, Alper Doventas, Deniz Suna Erdincler, Hakan Yavuzer

Division of Geriatric Medicine, Department of Internal Medicine, Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey
Bakirkoy District Health Directorate, Turkish Ministry of Health, Istanbul, Turkey
Department of Internal Medicine, Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey
Department of Biochemistry, Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey

Background: Matrix metalloproteinases (MMPs) play an important role in bone resorption and are regulated by tissue inhibitors of metalloproteinases (TIMPs). We investigated the use of MMP2/TIMP2 and MMP9/TIMP1 ratios as biomarkers of bone resorption in geriatric osteoporosis and evaluated the relationship between osteoporosis and geriatric syndromes.

Methods: This analytical cross-sectional study involved 87 patients (41 with osteoporosis) treated at the geriatric outpatient clinic of a university hospital. The demographic characteristics, comprehensive geriatric assessment scores, laboratory findings, and bone mineral density of the patients were recorded. Serum MMP9, TIMP1, MMP2, and TIMP2 levels were analyzed by enzyme-linked immunosorbent assay (ELISA).

Results: We enrolled 41 and 46 patients with and without osteoporosis, respectively. The groups showed no significant differences in MMP2/TIMP2 and MMP9/TIMP1 ratios (p=0.569 and p=0.125, respectively). While the basic activities of daily life (BADL) scores in the osteoporosis group were higher than those in the group without osteoporosis, the instrumental activities of daily life (IADL) scores were significantly lower (p=0.001 and p=0.007, respectively). No significant differences were observed in Mini-Nutritional Assessment, Mini-Mental State Examination, and Geriatric Depression Scale scores (p=0.598, p=0.898, and p=0.287, respectively).

Conclusion: This is the first study to examine the relationship between osteoporosis and several geriatric syndromes, as well as the relationship between osteoporosis and serum MMP, TIMP values, and MMP/TIMP ratios in geriatric patients. Our results showed that osteoporosis causes dependency in both BADLs and IADLs, and that the MMP2/TIMP2 and MMP9/TIMP1 ratios provided no additional benefit in demonstrating bone resorption in geriatric osteoporosis.

Key Words: Osteoporosis, Geriatrics, Matrix metalloproteinases, Tissue inhibitors of metalloproteinases

INTRODUCTION

Osteoporosis and osteoporosis-related fractures are among the leading public health problems worldwide and are common in the geriatric population. Osteoporosis is a progressive metabolic bone disease characterized by low bone mass, microarchitectural deterioration, and decreased bone strength.1 It causes significant morbidity and mortality, particularly in geriatric patients. In addition to imaging methods for the diagnosis of osteoporosis, many biochemical markers have been investigated; however, no consensus has been reached regarding specific markers.

Matrix metalloproteinases (MMPs) were first identified in 1962 by Gross and Lapiere.2 MMPs are enzymes responsible for the degradation of extracellular matrix proteins during growth, normal

Copyright © 2023 by The Korean Geriatrics Society
This is an open access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.
tissue formation, organogenesis, and angiogenesis and play an important role in the regulation of intercellular communication and immunity.\(^3\) MMP2 and MMP9 are two leading MMPs that influence bone development and homeostasis.\(^4\) MMP activity is regulated by specific tissue inhibitors of metalloproteinases (TIMPs) that bind to MMPs and inhibit their functions.\(^5\) The balance between MMPs and TIMPs is important for maintaining bone quality. Although it is accepted that the shift of the balance between MMPs and TIMPs in the direction of MMP activity causes the destruction of the matrix and pathophysiological events such as atherosclerosis, cardiovascular diseases, inflammatory diseases, cancers, and osteoporosis occur, there remains confusion about this issue.\(^6\)

Osteoporosis, which is considered a geriatric syndrome, has been placed in a separate class by others. Geriatric syndromes such as malnutrition, cognitive impairment, dependence on basic and instrumental activities of daily living (BADL and IADL), and depression may have a common pathogenesis, as they are considered clinical conditions with common risk factors. If a relationship between osteoporosis and other geriatric syndromes can be found, common pathophysiological pathways can be revealed, and existing uncertainties can be clarified.\(^7\)

We searched for the terms “osteoporosis” and “geriatric syndromes” together in the PubMed search engine to identify studies that investigated the relationship of osteoporosis with only one of the geriatric syndromes or that accepted osteoporosis as a geriatric syndrome. However, no study has been conducted so far that comprehensively and collectively evaluated the relationship between osteoporosis and several geriatric syndromes. In addition, we found few studies on the use of the MMP/TIMP ratio in osteoporosis, and the results were inconsistent. We comprehensively evaluated the relationship between osteoporosis and geriatric syndromes and investigated the use of MMP2/TIMP2 and MMP9/TIMP1 ratios as biomarkers of bone resorption in geriatric osteoporosis.

**MATERIALS AND METHODS**

**Study Design**

This was an observational, descriptive, and cross-sectional epidemiological study.

**Study Population and Design**

Our study sample consisted of 41 osteoporotic and 46 non-osteoporotic (23 with osteopenia) individuals aged 65 years and older who were admitted to the geriatric outpatient clinic of a university hospital. The sample was chosen using a non-probability consecutive sampling method. Although we divided the patients into groups with and without osteoporosis, we also divided the same patient population into three groups—osteoporosis, osteopenia, and control—and performed a subgroup analysis. Patients with osteopenia were included in the non-osteoporosis group as they did not meet the diagnostic criteria for osteoporosis. Informed consent was obtained from all participants. The study protocol was approved by the Local Ethical Review Committee of Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine (No. 2019-22507). Also, this study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.\(^8\)

**Exclusion and Inclusion Criteria**

The study included patients aged 65 and above who underwent comprehensive geriatric assessment, underwent dual-energy X-ray absorptiometry (DEXA) in the last 1 month, and did not meet the exclusion criteria.

Patients < 65 years of age with advanced organ failure and pathologies that may cause secondary osteoporosis, patients for whom the DEXA device could not be used, and patients who did not want to participate in the study despite meeting the appropriate criteria were excluded.

**Comprehensive Geriatric Assessment Scales**

All patients underwent a comprehensive geriatric assessment. The Katz BADL and Lawton–Brody IADL scales were used to assess the independence of the study participants. The Katz BADL scale scores range between 0 and 27, with higher scores indicating increasing patient dependence.\(^9\) On the Lawton–Brody IADL scale, patients are scored between 0 and 17, with decreasing scores indicating increased patient dependence.\(^10\) The Mini-Mental State Examination (MMSE) was used to screen cognitive function, with scores below 24 points considered indicative of cognitive dysfunction.\(^11\) The Geriatric Depression Scale (GDS) short form was used to identify depression possibility, with scores ≥ 5 points indicating possible depression.\(^12\)

**Bone mineral density measurement and osteoporosis definition**

DEXA was used to diagnose osteoporosis. Expert radiotechnologists measured bone mineral density (BMD) using the Hologic QDR 4500 Elite (Hologic Inc., Bedford, MA, USA) instrument. The precision expressed as the coefficient of variation (CV, %) was 1.6 at the total hip and 1.9 at the lumbar spine. These values were calculated after BMD measurements were performed twice for
each of the 30 patients. The total femur or femoral neck T-scores were used to evaluate femoral measurements, and total (L1–L4) or at least two vertebral scores were used for vertebral measurements. Patients with a T-score below -2.5 standard deviation (SD) on DEXA were included in the osteoporosis group, those between -1 and -2.5 in the osteopenia group, and those above -1 SD in the control group. BMD values of the total femur, femoral neck, and lumbar spine (L1–L4) were noted.

**Blood sampling and biochemical analysis**

We recorded calcium, phosphorus, albumin, parathyroid hormone, and 25-hydroxyvitamin D (25(OH)D3) levels. To measure MMP2, TIMP2, MMP9, and TIMP1 levels, blood was drawn from all participants between 08:00 and 09:00 after at least 8 hours of fasting. Blood was first transferred into an 8 mL tube without any additives or gel and centrifuged at 2,000–3,000 RPM for 15 minutes. The samples were stored at -80°C until analysis. MMP2, TIMP2, MMP9, and TIMP1 levels were determined by solid-phase sandwich enzyme-linked immunosorbent assay (ELISA) using commercial kits (Bioassay Technology Laboratory, Beijing, China). For these parameters, the intra- and inter-CVs were < 8% and < 10%, respectively. The detection limits were as follows: MMP2, 5.6–3000 ng/mL; TIMP2, 2.4–1800 pg/mL; MMP9, 15.1–9000 ng/mL; and TIMP1, 0.23–200 ng/mL. The kit inserts were followed to examine the analytes in our study. Geriatric and biochemical physicians performed the preanalytical process.

**Statistical Analysis**

A power analysis using G*Power version 3.1.9.6 (http://www.gpower.hhu.de) showed an effect size of 0.63 (< 0.7 is an acceptable limit). The number of samples required to reach 80% power with “alpha error of 0.05” values was 41/45. We enrolled 41/46 (total 87) patients. Chi-square or Fisher exact tests were used for categorical variables. Student t-test or Mann–Whitney U test was used for continuous variables. Continuous variables are presented as mean ± SD (if normally distributed) or median values with interquartile range (IQR) (if not normally distributed). This study analyzed the associations between osteoporosis and age, sex, body mass index, MMP9/TIMP1, and MMP2/TIMP2 using the univariate logistic regression (LR), and associations are reported as odds ratio (OR) with 95% confidence interval. Spearman correlation analysis was performed for the MMP/TIMP ratio and BMD values. Statistical significance was set at p < 0.05. IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA) was used to analyze the clinical data.

**RESULTS**

Our study included 41 patients with osteoporosis (26 women) and 46 without osteoporosis (28 women). The mean age of the osteoporosis and control groups did not differ significantly (77.68 ± 6.39 vs. 76.10 ± 6.19 years; p = 0.228). The BADLs scores were significantly higher and the IADLs scores were significantly lower in the osteoporosis group (p = 0.001 and p = 0.007, respectively). We observed no significant differences between the two groups in terms of MNA, GDS, and MMSE scores (p = 0.598, p = 0.898, and 0.287, respectively). On laboratory examination, calcium, phosphorus, parathyroid hormone, albumin, or 25(OH)D3 levels did not differ significantly between the two groups (p = 0.251, p = 0.528, p = 0.682, p = 0.082, and p = 0.356, respectively) (Table 1).

The median MMP2/TIMP2 ratio of the group without osteoporosis was higher, but the difference was not significant (p = 0.569). Likewise, while the median MMP9/TIMP1 ratio of the osteoporosis group was higher than that of the non-osteoporosis group; the difference was not significant (p = 0.152). Similarly, we observed no significant differences between the two groups in MMP2, TIMP2, MMP9, or TIMP1 levels (p = 0.538, p = 0.912, p = 0.718, and p = 0.377, respectively). A detailed analysis is presented in Table 2.

Analysis of the association of osteoporosis with age, sex, body mass index, and MMP9/TIMP1 and MMP2/TIMP2 ratios using univariate LR showed no statistically significant association. The results of the LR analysis, including ORs, are presented in Table 3.

We analyzed the correlation of MMP/TIMP ratios with femur, femoral neck, and lumbar spine BMD using Spearman correlation analysis, the results of which are shown in Table 4. We observed no statistically significant correlation between the MMP9/TIMP1 and MMP2/TIMP2 ratios and BMD values of the femur, femoral neck, and lumbar spine.

As men and women have different levels of sex hormones and associations with bone metabolism, we performed separate analyses for both sexes. We observed no significant differences in MMP9, TIMP1, MMP2, TIMP2, MMP9/TIMP1, and MMP2/TIMP2 levels between the osteoporosis, osteopenia, and control groups in either sex, with p-values of 0.588, 0.733, 0.733, 0.436, 0.965, and 0.512 in women and 0.824, 0.267, 0.739, 0.076, 0.375, and 0.059 in men, respectively.

We also divided the same patient population into three groups—osteoporosis (n = 41), osteopenia (n = 23), and control (n = 23)—and performed a subgroup analysis. We observed no significant differences among the three groups in terms of age
### Table 1. Demographic and clinical characteristics and laboratory findings of patients with and without osteoporosis

<table>
<thead>
<tr>
<th></th>
<th>Osteoporosis (n = 41)</th>
<th>Non-osteoporosis (n = 46)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>26</td>
<td>28</td>
<td>0.807</td>
</tr>
<tr>
<td>Male</td>
<td>15</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td><strong>Age (y)</strong></td>
<td>77.68 ± 6.39</td>
<td>76.10 ± 6.19</td>
<td>0.228</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>27.94 ± 6.60</td>
<td>28.89 ± 4.93</td>
<td>0.122</td>
</tr>
<tr>
<td><strong>BADLs</strong></td>
<td>4.91 ± 1.22</td>
<td>3.87 ± 1.55</td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>IADLs</strong></td>
<td>4.21 ± 2.09</td>
<td>5.40 ± 1.87</td>
<td>0.007*</td>
</tr>
<tr>
<td><strong>Mini-Mental State Examination</strong></td>
<td>24.7 ± 5.2</td>
<td>24.6 ± 2.9</td>
<td>0.898</td>
</tr>
<tr>
<td><strong>Mini-Nutritional Assessment</strong></td>
<td>23.8 ± 2.2</td>
<td>24.2 ± 2.80</td>
<td>0.598</td>
</tr>
<tr>
<td><strong>Geriatric Depression Scale</strong></td>
<td>3.42 ± 2.46</td>
<td>4.21 ± 2.09</td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>Calcium (mg/dL)</strong></td>
<td>9.03 ± 0.55</td>
<td>8.87 ± 0.69</td>
<td>0.122</td>
</tr>
<tr>
<td><strong>Phosphorus (mg/dL)</strong></td>
<td>3.41 ± 0.48</td>
<td>3.47 ± 0.47</td>
<td>0.528</td>
</tr>
<tr>
<td><strong>Albumin (g/dL)</strong></td>
<td>3.71 ± 0.46</td>
<td>3.89 ± 0.48</td>
<td>0.082</td>
</tr>
<tr>
<td><strong>Parathormone (pg/mL)</strong></td>
<td>49.4 ± 23.3</td>
<td>51.5 ± 22.7</td>
<td>0.682</td>
</tr>
<tr>
<td><strong>25(OH)D3 (ng/dL)</strong></td>
<td>22.0 ± 12.5</td>
<td>19.8 ± 9.9</td>
<td>0.356</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation.

BMI, body mass index; BADL, basic activities of daily living; IADL, instrumental activities of daily living; 25(OH)D3, 25-hydroxyvitamin D; BMD, bone mineral density.

*p<0.05.

### Table 2. Serum MMP, TIMP levels, and MMP/TIMP ratios of patients with and without osteoporosis

<table>
<thead>
<tr>
<th></th>
<th>Osteoporosis (n = 41)</th>
<th>Non-osteoporosis (n = 46)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MMP2 (ng/mL)</strong></td>
<td>246.7 (211.6–580.3)</td>
<td>231 (192.5–777.4)</td>
<td>0.538</td>
</tr>
<tr>
<td><strong>TIMP2 (ng/mL)</strong></td>
<td>26.9 (20.9–58.7)</td>
<td>26.9 (21.3–63.9)</td>
<td>0.912</td>
</tr>
<tr>
<td><strong>MMP2/TIMP2</strong></td>
<td>9.72 (8.05–11.93)</td>
<td>10.61 (7.39–13.19)</td>
<td>0.569</td>
</tr>
<tr>
<td><strong>MMP9 (ng/L)</strong></td>
<td>482.1 (254.8–2263)</td>
<td>430.2 (254.8–2235.5)</td>
<td>0.718</td>
</tr>
<tr>
<td><strong>TIMP1 (pg/mL)</strong></td>
<td>94.3 (75.6–195.2)</td>
<td>113.9 (86.8–375.2)</td>
<td>0.377</td>
</tr>
<tr>
<td><strong>MMP9/TIMP1</strong></td>
<td>4.51 (2.85–8.25)</td>
<td>3.49 (2.15–7.07)</td>
<td>0.125</td>
</tr>
</tbody>
</table>

Values are presented as median (interquartile range).

MMP, matrix metalloproteinase; TIMP, tissue inhibitor of metalloproteinase.

### Table 3. Univariate LR analysis of the factors predicting osteoporosis in geriatric patients

<table>
<thead>
<tr>
<th></th>
<th>Univariate LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td><strong>MMP2/TIMP2</strong></td>
<td>1.033 (0.913–1.168)</td>
</tr>
<tr>
<td><strong>MMP9/TIMP1</strong></td>
<td>1.013 (0.931–1.102)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>1.092 (0.994–1.200)</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>1.014 (0.126–8.156)</td>
</tr>
</tbody>
</table>

LR, logistic regression; MMP, matrix metalloproteinase; TIMP, tissue inhibitor of metalloproteinase; BMI, body mass index.

### Table 4. Correlation between MMP/TIMP ratios and BMD values

<table>
<thead>
<tr>
<th></th>
<th>MMP2/TIMP2</th>
<th>MMP9/TIMP1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur BMD</td>
<td>-0.187</td>
<td>-0.136</td>
</tr>
<tr>
<td>Femoral neck BMD</td>
<td>-0.163</td>
<td>-0.222</td>
</tr>
<tr>
<td>Lumbar spine BMD</td>
<td>-0.048</td>
<td>-0.203</td>
</tr>
</tbody>
</table>

MMP, matrix metalloproteinase; TIMP, tissue inhibitor of metalloproteinase; BMD, bone mineral density.
The median MMP2/TIMP2 ratios were 9.72 (IQR, 8.05–11.93) in the osteoporosis group, 10.74 (IQR, 7.71–13.14) in the osteopenia group, and 10.34 (IQR, 6.45–13.33) in the control group, with no statistically significant difference between these three groups (p = 0.743) (Fig. 1). The median of the MMP9/TIMP1 ratio was 4.51 (IQR, 2.85–8.25) in the osteoporosis group, 3.29 (IQR, 2.29–6.91) in the osteopenia group, and 3.90 (IQR, 2.13–7.71) in the control group, with no significant difference (p = 0.277) (Fig. 2).

**DISCUSSION**

Based on the knowledge that MMPs cause bone resorption and that TIMPs inhibit it, we hypothesized that MMP/TIMP ratios would increase in geriatric patients with osteoporosis. In addition to investigating the utility of MMP2/TIMP2 and MMP9/TIMP1 ratios as biomarkers of bone resorption in geriatric osteoporosis, we revealed the relationship between osteoporosis and geriatric syndromes and its effect on the dependence status of patients in both BADL and IADL.

Independence in older adults is important for their quality of life. In musculoskeletal diseases, the functionality of older adult patients decreases, and the patients become dependent on ADL. The results of a study conducted on 3,097 community-dwelling participants with musculoskeletal diseases, including osteoporosis, support this issue. The Irish Longitudinal Study on Aging (TILDA) investigated factors associated with impairment of BADL and IADL in community-dwelling older adults, in which both BADL and IADL were significantly affected in individuals with chronic conditions such as osteoporosis. Similarly, in our study, patients with osteoporosis were more dependent in both BADLs and IADLs (p = 0.001 and p = 0.007, respectively).

Depression is a geriatric syndrome with high prevalence. Studies have demonstrated the complex relationship between osteoporosis and depression. Although osteoporosis can cause depression, depression can also cause osteoporosis. Chronic pain, deterioration of physical ability, loss of self-esteem, and decreased quality of life caused by osteoporosis increase the prevalence of depression. In our study, although the GDS scores were higher in the osteoporosis group, the difference was not statistically significant (p = 0.287). This may be because the GDS evaluates the possibility of depression and does not make a clear diagnosis; rather, depression is diagnosed based on clinical evaluation.

Since this study did not include patients diagnosed with secondary osteoporosis, and malnutrition was a secondary cause of osteoporosis, as expected, we observed no significant difference in MNA scores between the osteoporosis and control groups (p = 0.598).

The activation of MMPs and their release from healthy tissues are limited; however, since various hormones, growth factors, and proinflammatory cytokines increase MMP activation, a significant increase in MMP levels is observed in pathologies that cause uncontrolled tissue destruction. MMPs and TIMPs have been investigated in many diseases, ranging from atherosclerosis to nephrolithiasis, cancer to periodontal disease, and diabetes to rheumatological diseases, most of which are associated with inflammation. A study investigating the roles of MMP1, MMP2, MMP9, and their tissue inhibitors in head and neck cancer reported that an imbalance between MMPs and their inhibitors played an important role in the progression of head and neck cancer and patient prognosis. Serum MMP2 and Timp2 levels are elevated in antineu-
trophilic cytoplasmic antibody (ANCA)-associated vasculitis and chronic kidney disease. A review mentioned that MMP9 is secreted from neutrophils, macrophages, lymphocytes, and fibroblasts and contributes to cardiac remodeling by participating in both the early and late phases of post-myocardial infarction. The same review emphasized that MMP9 also affects other inflammatory diseases. We found no significant differences in MMP2, TIMP2, MMP9, and TIMP1 levels between the osteoporosis and control groups (p = 0.538, p = 0.912, p = 0.718, and p = 0.377, respectively). The lack of significance of the biomarkers examined in geriatric osteoporosis may be because it is not yet clear whether osteoporosis is an inflammatory condition. In addition, the exclusion of inflammatory conditions that may have caused secondary osteoporosis may have had an effect.

MMP2 and MMP9 play important roles in bone turnover. In our study, serum MMP2 and MMP9 levels were higher in the osteoporosis group than in the control group; however, the difference was not statistically significant (p = 0.538 and p = 0.718, respectively). This may be owing to the small sample size. Therefore, studies with larger numbers of patients are required.

While MMP consumption is generally believed to cause a loss of bone mass and because TIMP overexpression causes an increase in bone mass, some studies have shown that MMPs and TIMPs have independent effects on bone. The serum levels of MMPs and the balance between MMPs and TIMPs in osteoporosis have been the subjects of interest for researchers. Zhao et al. reported significantly higher MMP9 mRNA expression in osteoporotic bone tissues than in the control group. Similarly, Zhang et al. investigated the relationship between circulating MMP9 levels and osteoporosis in chronic obstructive pulmonary disease and found higher serum levels of MMP9 and MMP9/TIMP1 ratios in the presence of osteoporosis. In a rat study, MMP2 and MMP9 expression levels were negatively correlated with BMD. In our study, we found no significant differences in serum MMP2, TIMP2, MMP9, and TIMP1 levels, and MMP2/TIMP2 and MMP9/TIMP1 ratios between the osteoporosis, osteopenia, and control groups. The lack of difference in MMP/TIMP ratios between the osteoporosis and control groups may be because TIMPs are not the only regulators of MMPs; other proteins, such as transforming growth factor-β, bone morphogenetic protein, and Wnt/β-catenin, also interact with MMPs.

The results of our study showed no significant differences in blood MMP and TIMP levels and ratios between male and female patients with osteoporosis, osteopenia, and control patients. Collazes et al. investigated the presence of sex differences in various MMP and TIMP levels in patients with sepsis, stroke, and trauma and found that only MMP3 plasma levels were significantly higher in men than in women in each diagnostic group. Similar to our osteoporosis study, the authors found no differences in MMP2, MMP9, TIMP1, or TIMP2 levels between sexes. Experimental studies in human and rat cells have suggested that sex hormones play a small but definite role in the secretion of MMPs and TIMPs. However, the complexity of mediators and the strong effects of stimulatory and inhibitory pathways caused by concomitant diseases or infections may minimize the sex effects.

Our study had some limitations. The first is the absence of young patients with osteoporosis and young controls. Second, including bone resorption markers such as C-telopeptide would have been ideal, while examining the relationship between serum levels and the ratios of MMPs and TIMPs and bone resorption in geriatric osteoporosis. However, owing to the conditions in our country, we could not compare with other markers because we were not provided with more funds.

The strength of our study is that it is the first to comprehensively examine the relationship between osteoporosis and several geriatric syndromes, as well as the relationship between osteoporosis and serum MMP, TIMP values, and MMP/TIMP ratios in geriatric patients.

In conclusion, as found in our study, geriatric individuals with osteoporosis became more dependent on both BADLs and IADLs. Therefore, early intervention for the disease is important. In addition, our results showed that the MMP2/TIMP2 and MMP9/TIMP1 ratios did not provide additional benefits in demonstrating bone resorption in geriatric osteoporosis. However, this topic should be examined in future studies with larger numbers of patients. New biomarker studies are required to elucidate the diagnosis of osteoporosis in geriatric patients.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST
The researchers claim no conflicts of interest.

FUNDING
The study was supported by The Research Fund of Istanbul University-Cerrahpasa (Project No. 33498).

AUTHOR CONTRIBUTIONS
Conceptualization, BBK; Data curation, OFB, OS; Investigation, BBK, GUA, DU; Methodology, BBK, OFB, DU, AD; Software, AD; Supervision, IMB, HY; Validation, IMB, HY; Visualization, OFB; Writing—original draft, BBK, GUA, OFB, DU, OS; Writing—review & editing, GUA, OFB, DSE, HY.
REFERENCES

A Multiple Case Study of Older Adults’ Internal Resiliency and Quality of Life during the COVID-19 Health Emergency

Jonaid M. Sadang\(^1,2\), Daisy R. Palompon\(^2\), Deane Joy E. Agoncillo\(^3\), Namera T. Datumanong\(^1\), Jamal Tango P. Alawiya\(^1\)

\(^1\) College of Health Sciences, Mindanao State University, Marawi, Philippines
\(^2\) College of Nursing, Cebu Normal University, Cebu, Philippines
\(^3\) College of Nursing, De La Salle Medical & Health Sciences Institute, City of Dasmarinas, Philippines

**Background:** Few studies have been conducted on unique conditions such as coronavirus disease 2019 (COVID-19) as an emerging health emergency, despite the strong link between resilience and quality of life in older persons. This study validated the expanded need-threat internal resiliency theory, which claims that an older person who establishes a strong sense of internal resiliency adapts to the situation by maintaining a better disposition. **Methods:** The underlying methodology in this study was a qualitative design using multiple case studies with non-probability purposive sampling to choose the target participants aged 60 years and above. **Results:** This cross-case analysis showed two major themes that explained and described the similarities and differences between the internal resiliency and quality of life of older adult participants with their respective sub-themes. Furthermore, this study concluded that older adults who have developed a strong sense of internal resilience, as manifested in the participants’ coping strategies during the COVID-19 pandemic, have sustained quality of life and better life satisfaction. **Conclusion:** The study proposes a shift in the perspective of aging by emphasizing the importance of resilience as a dynamic process helping in the coping process and adapting to new emerging pandemics, leading to improved quality of life amid adversity.

**Key Words:** COVID-19, Older adults, Quality of life, Qualitative research, Philippines

**INTRODUCTION**

The coronavirus disease 2019 (COVID-19) pandemic, initially discovered in 2019 in Wuhan, China, caused a global public health emergency, impacting hundreds of countries and severely affecting the general population health, particularly older people, worldwide. \(^{3,4}\) The likelihood of critical disease resulting from infection with the virus is particularly concerning for those > 60 years of age. Hence, experts and older adult advocates have emphasized the importance of protecting, caring for, and supporting this vulnerable population. \(^5\) Different places throughout the country have been placed under a lockdown or community quarantine in response to the mounting threat of the pandemic, including travel restrictions, the closure of various public and private establishments and offices, and the stringent implementation of home isolation and social distancing preventive measures. \(^6,7\)

Since the COVID-19 outbreak, various researchers have investigated the impact of this pandemic on the psychological health of older people, which substantially influenced their life satisfaction and quality of life as individuals. \(^8,9\) As preventative measures, social distancing and isolation have negatively impacted the overall well-being and health of the older population. \(^7\) Most literature on the COVID-19 pandemic has identified the negative psychological impacts of such measures on older people because of their considerable implications on people’s daily life activities, affecting their holistic functioning and well-being. \(^10,11\)

During the COVID-19 global health emergency, people aged ≥ 60 years are at a higher risk of depression, poor health-related...
quality of life, and low life satisfaction.\(^1,5\) Restricted social networks and high levels of social isolation act as mediators, amplifying negative moods and reducing life satisfaction.\(^5\) Quality of life refers to one’s perception of the influence of illness or medical conditions, such as the COVID-19 crisis, on several domains of functioning, including physical, psychological, social, and spiritual aspects.\(^1,4,5\) Therefore, quality of life is a vital predictor of overall health and resilience.\(^3\) However, infectious disease outbreaks, such as emerging health emergencies, have negatively impacted these domains of functioning, particularly in older people, generating emotional distress and developing depressive symptoms, highly reducing the quality of life of this demographic group.\(^1,5\) Previous studies during the severe acute respiratory syndrome (SARS) outbreak highlighted the extensive decline in survivors’ quality of life, and its negative psychological implications, mainly because of the quarantine measures during the SARS outbreak.\(^9\)

Resilience has multiple facets that vary by age. For older people, common health problems may disproportionately affect resilience, whereas health crises such as COVID-19 exacerbate existing mental and physical conditions.\(^2\) Similarly, some people suffer from the mental effects of such situations, while others, such as the older population, are resilient and move on with their lives, as already documented.\(^4,9\) Internal resiliency refers to an older person’s ability to cope with adversity or a stressful experience (e.g., the COVID-19 crisis) and return to normalcy by surviving difficulties and positively adapting to circumstances.\(^4,11,12\) Adaptability improves life satisfaction and quality of life in older adults during emerging health emergencies.\(^8,11\)

Resilience refers to the capacity to improve after failure, making a mistake, or experiencing a poor outcome. A resilient individual would not allow difficulties or problems to impede their objectives or overall achievements. To successfully navigate challenging situations, Dr. Howard\(^13,14\) worked with hundreds of high achievers before developing the resilience pyramid, which includes Levels 1 to 5, which refer to energy, connection, thinking, awareness, and flow. Resilience is a multifaceted term and can be considered an attribute shared by all people to varying degrees, as well as a dynamic process with bidirectional relationships to developmental and environmental factors and a response or outcome to stress and adversity.\(^15\)

The original theory on need-threat internal resiliency asserts that older people’s health needs can become health threats during the COVID-19 crisis and that older people must develop internal resiliency to maintain their integrity, well-being, and quality of life.\(^4,12\) However, the theory developed in response to this pandemic may not apply to other emerging health emergencies, necessitating the development of a more comprehensive theory to explain the coexistence of needs and threats in older adults as driving forces in the development of internal resiliency. The unique characteristics of this newly expanded theory provide more specific and detailed processes and outcomes that older people experience during such situations, which is central to the lives of such age groups allowing them to efficiently and effectively cope and adapt.\(^11\)

One assumption of connection is that “an older person who established a strong sense of internal resiliency adapts to the situation by maintaining a better disposition.”\(^11\) The link between resilience and quality of life in older people is long known, and resilience is strongly and favorably associated with subjective assessments of the quality of life in this age group.\(^16\) However, few studies have investigated this link in challenging situations, such as COVID-19.\(^13\) Most studies showed that negative situations experienced by individuals during global health emergencies reduced life satisfaction; circumstances, such as positive life experiences, social support, good social relations, and psychological strength increased life satisfaction.\(^2,8,16\) Through a multi-case design, the present study explored the similarities and differences between older adults’ internal resilience and quality of life while facing a health emergency to validate the theory’s propositions. When recommendations are deeply rooted in empirical data, multiple case studies offer a more compelling approach. Thus, varying situations enable a deeper exploration of research issues and the development of theories. Theoretical replication in many case studies tests the theory by contrasting the results with fresh cases. Theoretical replication can be demonstrated by additional waves of cases with opposing propositions if a series of examples show pattern matching between the data and propositions.\(^17\)

**Study Objective**

This study aimed to validate the proposition of the expanded need-threat internal resiliency theory on emerging health emergencies, which states that older persons who establish a strong sense of internal resiliency adapt to the situation to maintain a better disposition. Hence, this study explored the similarities and differences between older adults’ internal resiliency and quality of life while facing the COVID-19 health emergency. This study included open-ended questions during interviews to achieve this; these questions enquired the participants about (1) how they perceived the COVID-19 pandemic as a person, (2) the challenges they encountered during the COVID-19 pandemic and how they coped with such situations, (3) how their coping and or adapting strategies differed from those of other older adults during this COVID-19 pandemic, (4) their living conditions during this COVID-19 pandemic, (5) their life satisfaction during this COVID-19 pandemic,
MATERIALS AND METHODS

Design
We performed a qualitative multiple-case study to provide more detailed descriptions and explanations of the phenomena. The case study method is useful for comprehending a topic in-depth in the context of a real-world event, phenomenon, or concern. In multiple case studies, several cases are carefully selected to allow for comparisons across multiple cases and/or replications. Many disciplines, particularly the social sciences, frequently use this well-known research technique. While there are numerous definitions of a case study, they all call for a detailed analysis of an event or phenomenon in its original context. For this reason, a “naturalistic” design is often used instead of an “experimental” design, which attempts to exert control over and manipulate the variable(s) of interest.

Participants and Locale
This study involved older persons aged ≥ 60 years who had been staying in Marawi City since the official declaration of the COVID-19 pandemic in 2019 until now. The inclusion criteria were: (1) at least 60 years of age at the start of the pandemic, (2) having evolved coping strategies in response to this emerging health emergency and displaying characteristics of adaptation to this health crisis through the identification of at least one or more specific types of coping activities used in facing the COVID-19 pandemic, and (3) willingness to participate in the study irrespective of their other socio-demographic profiles. Participants in the target sample were excluded if they had cognitive, memory, or physical disabilities that affected their experiences in this situation.

Sampling Technique
Non-probability purposive snowball sampling was used to select sample participants from six older adults based on data saturation. In qualitative research, purposeful sampling is widely used to identify and select cases with relevant information on the topic under study; this includes determining and selecting individuals or groups with specialist knowledge or experience in a phenomenon of interest. It also entails considering participants’ availability and willingness to participate, including their ability to convey their experiences and thoughts in a direct, expressive, and thoughtful manner. Snowball sampling is a technique in which study participants or others with access to potential participants recommend individuals having experience or characteristics comparable to the researcher’s interests (Naderifar et al. 2019). Up to 3–4 cases for comparison can be efficiently handled in a multiple-case study using purposeful sampling comparison.

Instrument and Data Collection
We conducted semi-structured interviews. The method included a guide questionnaire that allowed the order to be modified depending on the conversation, allowing the researcher to emphasize certain questions while including new ones. For instance, questions about the participant’s physical, social, psychological, and spiritual well-being (e.g., how d1praying and reading the holy book help you cope with the COVID-19 pandemic and maintain your good outlook?) as older adults during health emergencies were added to explicitly explore their quality of life from a holistic perspective. The schedule was set based on the convenience and approval of the volunteer participants. The interviews were completed within 30–60 minutes, based on the participant’s area of comfort and convenience. The guided questionnaire contained eight general questions translated into the participant’s layman’s dialect to delve further into their experiences with the phenomenon under consideration; probing questions were added based on their flexible responses to these guide questions. Before being used in the study, three qualitative research experts in the respective field of discipline thoroughly reviewed this set of questions. The most typical qualitative data source in healthcare research is semi-structured, in-depth interviews, generally utilized in qualitative investigations. This approach frequently involves discussions between the researcher and participant and uses a flexible interview methodology, including additional follow-up questions, probes, and remarks. This method enables researchers to collect unstructured data, delve into sensitive and often private subjects, and examine participants’ ideas, feelings, and viewpoints on a particular subject.

Ethical Considerations
The Research Ethics Board of Cebu Normal University approved this study before participant enrollment (No. REC-01-31-22). Additionally, the researchers requested permission from the Office of Senior Citizens of Marawi City, a unit of the Department of Social Welfare and Development. Basic ethical principles in conducting qualitative studies, such as beneficence, respect for human dignity, and justice, were observed throughout the study. Moreover, informed consent was obtained from the participants to ensure that they had received appropriate information about the study, comprehended the material, and had the right to refuse at any moment during the interview without reason.

Although they were free to avoid answering any questions that would make them uncomfortable and withdraw from the study at
any moment, the participants were not subjected to any physical or psychological threat. They were also assured that a guidance counselor would be available before and after the interview if they experienced psychological or emotional stress. The researcher ensured that the study participants’ ethical rights were upheld and that no moral lapses occurred throughout the investigation. Pseudonyms or codes were used to safeguard the respondents’ privacy. The researcher also spoke with the participants about their preference to participate in the study at home, at another location alone, or with assistance. Furthermore, COVID-19 health safety procedures were strictly adhered to protect the researcher and the participants.

Also, this study complied the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research.\(^{(35)}\)

**Data Analysis**

This study conducted a cross-case analysis. This analysis allows researchers to compare similarities and differences in the events, actions, and processes that comprise the units of analysis in this case study. Themes, similarities, and distinctions between cases are used to connect the evidence gained to the proposition using cross-case analysis.\(^{(36)}\) This research strategy simplifies the comparison of the parallels and discrepancies among the events, behaviors, and procedures that form the cornerstone of the case study analysis. With a cross-case analysis, the investigator’s expertise expands beyond a single case. It sparks the researcher’s creativity, brings up new problems, offers fresh viewpoints, produces alternative explanations, develops models, and conjures ideals and utopias.\(^{(27,28)}\) Additionally, this analysis makes it possible for researchers to identify the variables that could have affected the case’s outcomes; seek an explanation for why one case is unique or similar to others; make sense of puzzling or unusual findings; or better express concepts, hypotheses, or theories that found or developed from the initial case. Cross-case analysis helps researchers understand the potential links between disparate examples, gather data from the first case, develop and refine ideas, and establish or test theories. By applying cross-case analysis, researchers can compare examples from one or more settings, communities, or groups.\(^{(28)}\) We applied the Miles–Huberman approach, which entails three continuous flows of operations. These include (1) data reduction, the process of choosing, concentrating, simplifying, abstracting, and altering the outcomes of investigations; (2) data display, in which organization and compression of the information allows the drawing of conclusions and the taking of action utilizing a “tool-box”; and (3) conclusion drawing and verification, where qualitative analysts begin to determine what things mean from the outset of data collection by noticing regularities, patterns, explanations, potential configurations, causal processes, and propositions.\(^{(29)}\)

**Rigor and Trustworthiness**

Credibility, transferability, dependability, and confirmability, the four criteria created by Lincoln and Guba (1985) in ensuring rigor and trustworthiness, were strictly observed and used in the execution of this qualitative investigation.\(^{(30)}\) To prove its validity, the researchers reviewed each participant’s transcript to identify patterns among all participants to interpret an event so that those who have had it may relate to it easily. While describing the demographic and geographical parameters of the study to check for transferability, the researchers provided a thorough description of the groups under consideration. Peers were engaged in the analysis process for dependability and a thorough explanation of the research methodology was provided. Finally, confirmability was evaluated using a self-critical mindset that considered how the researcher’s preconceptions affected the findings.

**RESULTS**

This section discusses the results of this qualitative multiple case study that aimed to validate one of the propositions of expanded need-threat internal resiliency, that an “older person who established a strong sense of internal resiliency adapts to situation in maintaining a better disposition,” using cross-case analysis. This study included six senior citizens following set parameters, and data saturation was observed in the data analysis process during transcription. This was undertaken through unit analysis, which involved connecting the transcribed data to the proposition under consideration and interpreting the findings to support this proposition. Following the unit analysis, we developed subthemes and categorized them further into themes connected to the proposition. The results revealed two major themes and their respective subthemes. Theme 1 discusses the differences and similarities in older individuals’ coping strategies and responses to the COVID-19 pandemic, also known as “internal resiliency,” which the study participants used to cope effectively with the COVID-19 health emergency. These internal resiliency strategies include acceptance of COVID-19 as an illness, self-discipline and strict observance of health protocols, the practice of healthy lifestyle activities, trust in healthcare professionals, and a strong spirit and strengthening of spiritual beliefs.

Theme 2 describes the similarities and differences in older adults’ life disposition during the COVID-19 pandemic. The participants described their life disposition, particularly in terms of life satisfaction and quality of life, as stable and even improved despite the challenges and adversities they faced (and still face) as a result of the COVID-19 crisis, despite their vulnerability as a population group. Life disposition included a sustained source of living and ba-
sic needs, the absence of illness, family as a source of satisfaction, and a strengthened spiritual connection. We identified two notable life dispositions related to the expected consequences of COVID-19 crisis management, including restricted social life and psychological disturbances.

Participant 1 (P1) was a 64-year-old married woman residing with her extended family. Her primary means of support were family and government assistance, such as pensions for older citizens. Compared with before the pandemic, during the pandemic, she spent most of her time at home and frequently visited her relatives during the pandemic. She believed the COVID-19 pandemic to be similar to emerging illnesses in her early childhood, including fever, chills, and cough. Hence, following the authorities’ instructions to stay home was the primary step in preventing this illness.

Participant 2 (P2) was a 62-year-old married man who lived with his wife and children. He was currently employed by the government in a provincial agency. He claimed that the COVID-19 pandemic had affected the entire world and that the best way to end this crisis was to adhere to health protocols, including getting vaccinated, wearing masks and face shields, and avoiding close contact with others. He also had symptoms of COVID-19 during the outbreak but had never undergone testing.

Participant 3 (P3) was a 70-year-old married man who resided with his family in their ancestral home. He was a retired elementary school teacher and administrator who received a monthly government pension. He held a doctorate in education and had dedicated his entire life to teaching until reaching retirement age. He confined himself to their home throughout the pandemic and kept busy in their backyard with gardening as a way of coping. He claimed to have carefully observed practicing a balanced diet, exercising, and taking maintenance medications on time to avoid contracting this disease.

Participant 4 (P4) was a 61-year-old married woman who had been working as staff in a university for more than 30 years. Before the COVID-19 crisis, she preferred to visit her siblings and other family members; however, the pandemic prevented her from doing so. She nevertheless consistently showed up for work. She had been exposed to a person with COVID-19 but never tested positive for the illness. She acknowledged that the pandemic brought many difficulties and obstacles to her personal life, but she managed to overcome them.

Participant 5 (P5) was a 64-year-old married man who lived with his wife and children. Before retiring at 60 years of age, he was an overseas Filipino worker (OFW) in the Middle East. After retiring overseas, his business became his primary source of income. He claimed that his business suffered significantly due to the societal restrictions and lockdowns brought on by the pandemic, yet he was still able to operate normally, even during the peak of the crisis. He enjoyed interacting with friends and family, especially before the pandemic, but still managed to maintain the same attitude during the pandemic.

Participant 6 (P6) was a 67-year-old woman who was a retired elementary-level teacher. As she was already widowed, her primary source of income, especially in light of the COVID-19 pandemic, was her government-issued monthly pension. She claimed that the lockdowns and social limitations imposed on the community at the height of the crisis made this pandemic one of the most difficult periods of her life. She had to roam around malls after receiving her monthly pension but could not do so after the pandemic began; however, she enjoyed staying at home with her family, especially her grandchildren.

Table 1 shows the cross-case matrix of the participants’ profiles in terms of age, sex, marital status, religion, highest educational attainment, source of living, level of resiliency, coping strategies, and life disposition. This study involved three male and three female Muslim older adults aged between 61 and 70 years, most of whom were married. Majority had earned graduate degrees or at least college degrees. Four relied on jobs, employment, and pensions to make ends meet. Their levels of resiliency were based on Howard’s resilience pyramid, which has five levels: level 1 (energy), level 2 (awareness), level 3 (mindset), level 4 (connection), and level 5 (flow).

In level 1 (energy), a person must improve their physical vigor. Controlling energy requires examining routines and ways of life to determine what is or is not working. This pyramid level supports the other levels and serves as the basis for resilience. The pyramid’s base level, or level 2, is awareness and aids in stabilizing the foundation. The important markers of this level are growing self-awareness and understanding of the causes of stress and how to deal with them. At this level, concentration on what is vital is achieved by controlling stress triggers. Level 3 (mindset) calls for intentionally using thoughts to focus on answers and avoid ruminating on difficulties once control over energy and awareness of the manifestation of our stress is achieved. Level 2 strategies were beneficial. In this step, individuals should also make goals and have a vision for each day or their lives.

In level 4 (connection), a person can help others to become more powerful. Individuals at this level should already be able to manage their emotions and energy levels, as well as set boundaries and be aware of their limitations. Individuals should also encourage others to be their best versions while simultaneously emphasizing the value of their limits to prevent demotivation and burnout.

Finally, in level 5 (flow), individuals safeguard their value as human beings and treat themselves as high-performing. By incorpo-
<table>
<thead>
<tr>
<th>Code</th>
<th>Sex/Age (y)</th>
<th>Marital status</th>
<th>Religion</th>
<th>Highest educational attainment</th>
<th>Source of living</th>
<th>Levels of internal resiliency</th>
<th>Coping strategies</th>
<th>Life disposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>F/64</td>
<td>Married</td>
<td>Islam</td>
<td>High school graduate</td>
<td>Government aid and family support</td>
<td>Level 4 (Awareness): She was aware of the existence and risk of COVID-19 and had plans in place to avoid contracting the illness.</td>
<td>Acceptance of COVID-19, prayers and other spiritual activities, compliance with health protocols.</td>
<td>Sustained basic needs, not infected, improved and sustained spiritual connection.</td>
</tr>
<tr>
<td>P2</td>
<td>M/62</td>
<td>Married</td>
<td>Islam</td>
<td>Graduate degree</td>
<td>Work or employment</td>
<td>Level 1 (Energy): He claimed that it was imperative to follow safety precautions to avoid contracting the illness during this COVID-19 outbreak.</td>
<td>Compliance with health protocols, proper lifestyle practices, trust in healthcare workers, prayers and other spiritual activities, acceptance of COVID-19.</td>
<td>Sustained basic needs, not infected, improved and sustained spiritual connection.</td>
</tr>
<tr>
<td>P3</td>
<td>M/70</td>
<td>Married</td>
<td>Islam</td>
<td>Post-graduate degree</td>
<td>Pension</td>
<td>Level 3 (Mindset): He managed and enjoyed alternative activities to make the most of his time while confined to his home and avoid becoming overly worried or distracted by the COVID-19 pandemic.</td>
<td>Compliance with health protocols, proper lifestyle practices, trust in healthcare workers, prayers and other spiritual activities, use of diversional activities.</td>
<td>Sustained basic needs, not infected, mental discomfort, improved and sustained spiritual connection.</td>
</tr>
<tr>
<td>P4</td>
<td>F/61</td>
<td>Married</td>
<td>Islam</td>
<td>College graduate</td>
<td>Work or employment</td>
<td>Level 4 (Awareness): She claimed that the pandemic has posed many difficulties, but that she had learned to manage her stress responses and focus on what mattered most.</td>
<td>Prayers and other spiritual activities, acceptance of COVID-19, compliance with health protocols.</td>
<td>Sustained basic needs, not infected, mental discomfort, limited activities, improved and sustained spiritual connection.</td>
</tr>
<tr>
<td>P5</td>
<td>M/64</td>
<td>Married</td>
<td>Islam</td>
<td>College graduate</td>
<td>Business</td>
<td>Level 2 (Connection): He managed to withstand the effect of COVID-19 on his normal routines (e.g., business) and avoid getting distracted. He also maintained strong relationships with the people around him.</td>
<td>Acceptance of COVID-19, prayers and other spiritual activities, compliance with health protocols.</td>
<td>Sustained basic needs, not infected, improved and sustained spiritual connection.</td>
</tr>
<tr>
<td>P6</td>
<td>F/67</td>
<td>Widowed</td>
<td>Islam</td>
<td>Graduate degree</td>
<td>Pension</td>
<td>Level 2 (Connection): She spent quality time with her family, especially her grandchildren, without becoming distracted by the fact that the COVID-19 pandemic prevented her from engaging in her typical outdoor activities.</td>
<td>Prayers and other spiritual activities, compliance with health protocols, use of diversional activities.</td>
<td>Sustained basic needs, not infected, limited activities, improved and sustained spiritual connection, use of diversional activities.</td>
</tr>
</tbody>
</table>
rating these steps, obstacles can be overcome, and progress can continue. Through this process, individuals discover more about themselves, develop new abilities, and overcome the overwhelming feelings that formerly held them back.\textsuperscript{13,14}

**Thematic Results**

Two major themes were derived with their respective subthemes to explain and describe the differences and similarities in coping strategies and life dispositions of the older adult participants amid the COVID-19 crisis. These coping strategies and measures, known as "internal resiliency," were assumed to be the underlying factors that helped these individuals to effectively adapt to such health emergencies, leading to the maintenance of stability and better life disposition in late life, consistent with the proposition of the expanded need-threat internal resiliency theory, which states that "older person who established a strong sense of internal resiliency adapts to situation in maintaining a better disposition." These themes and subthemes are summarized in Table 2 and discussed further in the following sections.

**Theme 1: Coping strategies and measures used by older adults to adapt well to the COVID-19 pandemic**

This theme describes the differences and similarities in coping strategies used by older adults to adapt to the COVID-19 pandemic. These "internal resiliency" strategies were created by such people to adapt well to dangers, trauma, or significant sources of stress, collectively known as emerging health emergencies, to achieve and maintain a sense of purpose and vigor, and to emerge stronger amid such trying circumstances, resulting in sustenance or improved outlook in later life. The internal resiliency strategies used by the participants included acceptance of COVID-19 as an illness, self-discipline and strict observance of health protocols, the practice of healthy lifestyle activities, trust in healthcare professionals, and a strong spirit and strengthening of spiritual beliefs.

**Sub-theme 1 (Acceptance of COVID-19 as an illness):** The first sub-theme refers to the acceptance of the existence of COVID-19 as an illness, which is among the emotion-focused coping strategies practiced by older adults in facing emerging health emergencies. This subtheme was supported by the following participant statements:

"Sakun na kagya adun a wata akun a miklas sa medicine na ditawn die makapangi-ngisa na paniwala ako a adun talaga a covid-19 sie sa ingud tano aya. Pkaylay tano sa social media a mg news a tanto a madakul a kya apektowan ago so pud na mindod sa limo o ALLAH swt misabap sa gyangkae a paniya-kit." [Since I have a son who has studied medicine and was able to ask questions, I believe in the existence of COVID-19 in my community in my situation. We see on social media and the news that many have been affected, and others have even died of this illness]. – P2

"So mga restrictions na tanto a margun lalo so kapakindolon ko pud a tanw, ogaid na paka adap-ako ka kagya inaccept akun angkae a masoswa-swa ago dapat na pka follow tanto so mga bitikan ago policy." [The restrictions are very difficult, especially in terms of socializing with other people, but I cope with this by accepting the situation and the need to follow rules and regulations.] – P5

**Sub-theme 2 (Self-discipline and strict observance of health protocols):** The second subtheme considers the participants' self-discipline and strict adherence to health protocols during the COVID-19 crisis to successfully avoid contracting the illness and adjust to the situation. This problem-focused coping mechanism can be employed when facing difficulties. This subtheme was supported by the following participant statements:

**Table 2. Derived themes and sub-themes**

<table>
<thead>
<tr>
<th>Themes</th>
<th>Sub-themes</th>
</tr>
</thead>
</table>
| Theme 1: Coping strategies and measures used by older adults to adapt well to the COVID-19 pandemic. | Sub-theme 1: Acceptance of COVID-19 as an illness.  
Sub-theme 2: Self-discipline and strict observance of health protocols.  
Sub-theme 3: Practice of healthy lifestyle activities.  
Sub-theme 4: Trust in healthcare professionals.  
Sub-theme 5: Strong spirit and strengthening of spiritual beliefs. |
| Theme 2: Life dispositions of older adults in the COVID-19 pandemic. | Sub-theme 1: Sustained source of living and basic needs.  
Sub-theme 2: Absence of illness.  
Sub-theme 3: Family as a source of satisfaction.  
Sub-theme 4: Strengthened spiritual connection.  
Sub-theme 5: Restricted social life and finding alternative ways to connect.  
Sub-theme 6: Psychological disturbance. |

www.e-agmr.org
Sub-theme 3 (Practice of healthy lifestyle activities): The third subtheme focused on the participants’ adoption of healthy lifestyle practices to strengthen their immunity to COVID-19, allowing them to respond effectively to the community’s ongoing emergent health emergency. These lifestyle practices included eating a balanced diet, exercising, ensuring strict compliance with medication maintenance, taking vitamin supplements, and engaging in various diversionary activities for mental health. These measures are dimensions of both problem- and emotion-focused coping strategies. This subtheme was supported by the following participant statements:

“Gyangkae a covid-19 na myakapanang-gila so taw. So di pag-exercise na myakapag exercise. Apya so dingka kun na myakan ka lagido gulay ago prutas ka pantagbo sa an pakabbugur so lawas ka para kaiwasan ka gyoto a covid-19 a paniyakit.” [People must be careful about COVID-19. Those who don’t exercise are able to exercise. Even if you don’t eat vegetables and fruits, you are now eating them to strengthen your body and avoid getting infected with this illness.] – P2

“Dyakopm die mag exercise ago regular so kapaginom akun sa maintenance akun a bolong para sa highblood ago vitamins. Dy- yakopm die garden sa walay para pkatumbang apya maito.” [I exercise and regularly take my maintenance medication for high blood pressure, and I take vitamins. I also do some gardening at home so that I remain entertained somehow.] – P3

Sub-theme 4 (Trust in healthcare professionals): The fourth subtheme refers to the trust given by the participants to healthcare professionals facing the COVID-19 pandemic. These people have served as sources of information and guidance, especially for observing health protocols against such illnesses and managing symptoms related to COVID-19. This practice is part of problem-focused coping, particularly using informational support to adapt and emerge well in such emerging health emergencies. This subtheme was supported by the following participant statements:

“Sie rakun na kagya adun a mga wata akun a miklas sa medicine na pagisaan akun siran ago sie ako kiran puk-wa sa advice.” [For my part, since I have a son studying medicine, I usually ask him for advice.] – P2

“Sakun na paratiyayaan akun so mga pkanug akun ko mga doc tor ago nurses a health measure sa gya covid-19. Di ako basta basta psong ko madakul a taw ago bako ployo a daa sabhap a iplyo akun.” [As for me, I believe what I hear from doctors and nurses about health measures for covid-19. I don’t just go out to meet many people and come out for no good reason.] – P3

Sub-theme 5 (Strong spirit and strengthening of spiritual beliefs): The fifth subtheme refers to the strong spiritual relationships developed by the participants as an overarching coping strategy in facing and adapting to the COVID-19 crisis. These activities involved the practice of the five daily prayers as Muslims, reading the holy book (Qur’an), putting their trust in the creator, doing a lot of dhikr, or constantly remembering the name of God (ALLAH SWT). This type of coping is emotion-focused coping, which is unique and widely used among the older population during times of adversity. This subtheme was supported by the following participant statements:

“Naka-adjust ako dahil nilakasan ko ang boob ko at basta mala ka e paratiyaya ko ALLAH (swt) na pkakayangang apya anto naa klase a problema. Pakakadulakan ka so simbangka ago so tas bik ka, ago kapangadi sa qur'an, na In shaa ALLAH na ikpami mo o ALLAH swt so manosiya a lagidot o. So kasambayang na aya mala pakawgop rakun nago aya lalayon akun a pipikirin na so ALLAH swt.” [I was able to adjust because I took courage, and as long as you have great faith in ALLAH (SWT), you can withstand any problem. We must increase our prayers and always read the Qur’an (a holy book for Muslims); surely, he will always help and bless us. Our prayers can help us a lot.
Theme 2: Life dispositions of older adults in the COVID-19 pandemic
This theme describes the similarities and differences in the life dispositions of older adults during the COVID-19 pandemic. The participants sustained or even achieved better life satisfaction and quality of life despite the challenges and adversities they faced as persons in this health crisis, in addition to their vulnerabilities as a population group. This life disposition, as described by the participants, includes a sustained source of living and basic needs, the absence of illness, family as the source of satisfaction, and a strengthened spiritual connection. However, we identified two notable life dispositions related to the expected consequences of the management of the COVID-19 crisis, including restricted social life and psychological disturbance.

Sub-theme 1 (Sustained source of living and basic needs):
The first subtheme describes how older adults in this study have sustained their sources of living and basic needs while facing the COVID-19 crisis despite the challenges that this pandemic has posed to the financial and economic stability of the community. Most participants stated that their primary source of living and basic needs, the absence of illness, family as the source of satisfaction, and a strengthened spiritual connection. However, we identified two notable life dispositions related to the expected consequences of the management of the COVID-19 crisis, including restricted social life and psychological disturbance.

Sub-theme 2 (Absence of illness): The second subtheme describes how, despite their vulnerability as a population group, older persons in this study managed to avoid getting sick during the COVID-19 pandemic. However, they accepted the fact that certain physiological changes exist due to their age, which is a normal part of aging and is not directly related to the illness caused by COVID-19 virus. The absence of illness during health emergencies has helped older adults sustain their life satisfaction and quality of life amid adversities. This subtheme was supported by the following participant statements:

“Sa prayer ko dinadadaan ang lahat. Ang ALLAH swt lang ang nakaka control sa mga bagay bagay.” [In my prayer, everything goes through. Only ALLAH swt can control things.] – P4

“Okay nman ang pamumuhay ko kahit covid-19 pandemic kasi government employee tayo at may sweldo parin kahit papano. Mas nakatipid pa tayo kasi hindi tayo makalabas at pasyal sa mga malls.” [Good, my living conditions are the same. In Shaa ALLAH, there are no changes because I can still eat well and have no money issues since I am not a luxury person.] – P1

Sub-theme 3 (Family as a source of satisfaction): The third subtheme describes how older adults sustained their quality of life despite the COVID-19 crisis with the help of their families, who served as sources of satisfaction. This source of satisfaction made their lives easier and more resilient in dealing with such a health emergency in the community, despite the challenges and struggles of the movement restrictions and lockdowns, especially for vulnerable groups such as the older population. This subtheme was supported by the following participant statements:

“Alhamdulillah ka mapipiyatadn ago satisfied ako ka pka lay akun so familyakan ago mapiya so environment akun.” [Alhamdulillah, I am still good and satisfied as long as I can see my family and have a good environment.] – P3

Sub-theme 4 (Strengthened spiritual connection): The fourth subtheme describes how the older adults in this study have sus-
tained their living conditions despite the adversities brought about by the COVID-19 pandemic through a strengthened spiritual connection with ALLAH (swt), which led to a sustained and even enhanced quality of life in old age. Their prayers and faith in God helped, guided, and aided them in facing this health emergency. This subtheme was supported by the following participant statements:

“Mas myakabagur so paratiyaya akun ko ALLAH swt na sie ako mambo puksa wa bagur para magagakn angkaya a t’pung a imbg nylon ruktano.” [My faith in ALLAH swt grew stronger than before, and that is where I draw courage to pass this test that he gave us.] – P1

“So sambayang akon ago paratiyaya ko ALLAH swt na aya mala a myakawegop rakun para magagakun langon aya ago mawyag-oyag lagid o kapka-oyag-oyag akun kayko dapun a COVID.” [My prayers and faith in ALLAH swt helped me overcome everything and live the same way as before when there was no pandemic.] – P4

**Sub-theme 5 (Restricted social life and finding alternative ways to connect):** The fifth subtheme describes how the older adults in this study experienced changes in their normal routines of socialization due to the COVID-19 pandemic, particularly when lockdowns and movement restrictions were put in place in the community to mitigate the rapid spread of illness among the general population, including older adults. However, such restrictions have resulted in a lack of community socialization but have not totally hindered their communicating means with friends and relatives. The participants used alternative means such as social media and other digital platforms to consistently connect with other people. This subtheme was supported by the following participant statements:

“Sie ko kapakindudulona ko pud a taw na myakayo kagya babawalan kmi ran mhyo-lyyo ago kokontrol’n eran so kandadalakaw kagya so edad ame mambo malbod katakadon a gya paniyakit. Ogaidsa so kapakimbityarae ko mga tunganay ago layok akun na siwe siwe parin ago knaba pman myaputol ka adun a facebook akun ago pakatawag ako kiran parin sag yaya a cell phone akun.” [Socialization is minimal only because it is forbidden to go outside because movements are restricted and limited because of our age vulnerabilities. However, my communication with my relatives and friends is still consistent and was not totally cut off because I have Facebook and can still call them via mobile phone.] – P4

“Diyakodn makipundodolona odi na makipumbityarae s apud a taw ago di ako dn pagattend sa mga kalilimod lagido ka-kawing ka dikun kapakay lalo sie rkami a mga myaka edad.” [I no longer socialize with other people and can no longer attend gatherings like weddings because it is prohibited, especially for older adults.] – P6

**Sub-theme 6 (Psychological disturbance):** The sixth subtheme describes how the COVID-19 crisis caused psychological disturbances in older adults. Most admitted that its uncertainty as an illness resulted in some fear and worrying while facing the adversities of such a health emergency. Although it has created some disturbances in their mental health as a person, the crisis has not completely negatively affected their life dispositions because of their strong faith and belief in God (ALLAH swt) as the controller of all things in this world and hereafter. According to them, the pandemic was destined to happen and will eventually disappear in God’s perfect time. This subtheme was supported by the following participant statements:

“Sie ko kapamimikiran na mapipiyakodn ogaid na datar oba sa didalum na maaluk akobo ka obako badn masakit sag yaya covid-19. Pero so ALLAH swt na malae limo ka asar ka panarig kawn ago pakabagarun ka so paratiyaya kawn na In shaa ALLAH na dikadn maribat ka pagogopan niyan ago ikalimo kanyan.” [I am still good in terms of psychological health; however, underneath this, I have little fear of getting infected with this illness. However, ALLAH swt is merciful as long as we trust him and continually strengthen our faith in him, then he will help us, especially in times like this.] – P3

“Mapipiyakodn so kapamimikiran akun ogaid na igira kwan na pkapikir akun a ibarat oba-ako katakdi odi na so isako pamiliyakan sangkae a covid na di siran pakabaw ago dadun a kataam eran, inoto diyakun plipatan obako di makasusulot sa mask ago pamangni ako sa tabang ko ALLAH swt.” [I still have a good mind, but sometimes this thought haunts my mind what if I or one of my family members get infected with it and are unable to smell or taste anything, so I always wear a mask and ask for help from ALLAH swt.] – P4

**DISCUSSION**

This study was primarily conducted to validate one of the propositions of expanded need-threat internal resiliency theory, which states that in times of emerging health emergency (e.g., the COVID-19 crisis), “an older person who established a strong sense of internal resiliency adapts to the situation in maintaining a better disposition.” This multiple-case study identified two major themes...
addressing this proposition, describing the similarities and differences between coping strategies known as “internal resiliency” developed by older adults to adapt and cope well with such stressful and challenging situations, resulting in sustained or improved life dispositions.

These themes included Theme 1 “Coping strategies and measures of older adults used in adapting well to the COVID-19 pandemic.” This theme included five subthemes (acceptance of COVID-19 as an illness, self-discipline and strict observance of health protocols, the practice of healthy lifestyle activities, trust in healthcare professionals, and strong spirit and strengthening of spiritual beliefs); and Theme 2 “Life disposition of older adults in the COVID-19 pandemic.” This theme included six subthemes (sustained source of living and basic needs, absence of illness, family as the source of satisfaction, strengthened spiritual connection, restricted social life, and psychological disturbance).

Older people are frequently considered a high-risk population owing to high incidence and fatality rates in most emergent health emergencies, such as the COVID-19 crisis. This is one of the most recent trends. 31) People must make significant adjustments to their daily routines to cope with challenging life events such as the COVID-19 pandemic. 32) Other containment measures implemented in residential care communities and residences are exceptionally harmful to older individuals, such as limiting outdoor activities and visiting schedules. 31,32) These measures go beyond general social distancing policies. However, some factors, including a person’s coping strategies and resilience, may influence whether potentially stressful situations arising because of the pandemic lead to better or poorer health and well-being. 31)

Resilience and coping skills are cognitive and behavioral capabilities that might assist older persons in adjusting to changes in their way of life caused by adversities, such as health crises. 12,39) Studies on older adults in Asia, particularly in The Philippines and South Korea, have reported positive correlations between resilience, coping mechanisms, life satisfaction, and quality of life. Therefore, coping mechanisms and resilience play critical roles in protecting and promoting a better way of life, particularly among older adults. 33)

Quality of life is one dimension impacted by contextual circumstances experienced during this life period, such as emerging health emergencies like the COVID-19 pandemic. 37) These contextual elements can negatively affect the central components of life. Individuals’ coping mechanisms for dealing with environmental stressors mediate the connection between the two. 1,34)

The results of this study highlighted that older adult participants made use of both problem-focused (e.g., self-discipline and strict observance of health protocols, the practice of healthy lifestyle activities, and trust in healthcare professionals) and emotion-focused
Conclusion
The theory of expanded need-threat internal resilience in emerging health emergencies defines the internal resilience of older adults as their capacity to perceive and recognize the threat of an emerging health emergency, allowing them to develop specific coping skills, such as physical, psychological, social, and spiritual strategies, to successfully and efficiently recover from adversities; thrive with persistent purpose; evolve in turbulent, challenging, and uncertain situations, resulting in sustained or improved quality of life while facing a global health crisis. The results of the present study provide strong evidence supporting the claim of the proposition of the expanded need-threat internal resiliency theory that during an emerging health emergency, “an older person who established a strong sense of internal resiliency adapts to the situation in maintaining a better disposition.” This further provides a foundational structure for existing knowledge about the relationship between internal resilience as a vital factor for older adults to sustain and even improve life disposition during a health crisis. Therefore, caregivers of older adults, healthcare workers, community leaders, and those who support the older population should always consider promoting holistic coping strategies, as it empowers and supports such individuals in times of emerging health emergencies.

Limitations
To date, few studies have reported on this phenomenon, especially in this locality. Hence, this study offers baseline literature in this age range, especially considering their vulnerability to emerging health emergencies such as the COVID-19 pandemic. Moreover, this study substantially strengthens the literature body supporting the broader idea of need-threat internal resiliency in older persons. However, this study included only five adults aged ≥ 60 years in a single area. Thus, older adults in various regions may be able to describe their quality of life and develop internal resilience. Additionally, the participants’ educational backgrounds did not accurately reflect each grade or level, even though the value of a multiple case study is increased by including the experiences of participants with low levels of education. Therefore, future studies should use different research approaches and incorporate the demographics of older adults to establish how internal resilience and quality of life coexist when confronted with developing medical issues.

Recommendation
This study offers a change in the perspective of aging by highlighting the significance of resilience as a dynamic process aiding in the coping process and adapting to newly emerging pandemics, leading to successful aging, longevity, and quality of life. It also emphasizes the importance of creating policies and preventive and intervention programs that support older people’s resilience and the accompanying factors that may attenuate the negative effects of adversity on their physical and psychological health. When considering older adults from the perspective of their identified internal resilience, it is evident that dealing with spirituality is fundamental; therefore, this factor must be acknowledged to provide adequate support to older people. Thus, programs and support groups related to spirituality must be strengthened and highlighted in their communities as an essential approach to providing a holistic and people-centered response to older people amid these adversities.

The community is recommended to work on developing religious activities during these trying times with the aid of technology, such as online seminars and small-group discussions with religious leaders, as spirituality is a vital coping strategy for older people that helps them to cultivate strong internal resilience, which can be achieved through collaboration between local leaders, the general public, and line government agencies (e.g., the Department of Health and the Department of Social Welfare & Department). In addition, it is becoming increasingly clear that health professionals and care providers must be equipped with the knowledge and ability to recognize and assist patients’ spiritual needs to provide holistic care for this population group.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST
The researchers claim no conflicts of interest.

FUNDING
None.

AUTHOR CONTRIBUTIONS
Conceptualization, JMS; Data Curation, JMS; Investigation, JMS, DRP, DJEA, NTD, JTPA; Methodology, JMS, DRP; Project administration, JMS, DJEA, NTD, JTPA; Supervision, JMS, DRP; Writing-original draft, JMS; Writing-review & editing, JMS, DRP, DJEA, NTD, JTPA.

REFERENCES
13. Howard C. Resilience: the ability to bounce forward (learn the levels of resilience and how to activate yours) [Internet]. Mountain View, CA: LinkedIn.com; 2017 [cited 2023 Jun 15]. Available from: https://www.linkedin.com/pulse/resilience-ability-bounce-forward-learn-5-levels-how-cynthia.


An Uncommon Case of Weight Loss in a Nonagenarian

Gurinderjit Kaur Sidhu, Goh Kiat Sern, Htet Htet Khine
Department of Geriatric Medicine, Changi General Hospital, Singapore

Corresponding Author:
Gurinderjit Kaur Sidhu, MBBS, MRCP, MMed
Department of Geriatric Medicine, Changi General Hospital, 2 Simei Street 3, Singapore 529889
E-mail: gurinderjit.kaur.sidhu@singhealth.com.sg
ORCID: https://orcid.org/0000-0002-8202-5900

Received: February 7, 2023
Revised: March 6, 2023
Accepted: April 12, 2023

INTRODUCTION

Weight loss is a well-defined geriatric syndrome. It is a complex symptom that involves the integration of multiple factors, including physiological, psychological, and behavioral aspects (1). This condition is common among older adults, with a reported prevalence of 15% to 20% in individuals aged 65 years and older (2). Weight loss in older adults can be due to multiple causes. A systematic approach is required to pinpoint the etiology. Dysphagia is a common symptom associated with weight loss. Dysphagia can be caused by various etiologies, including esophageal motility disorders, such as achalasia (3). Achalasia is a functional esophageal disorder that causes dysphagia. It can masquerade as an aging esophagus if not carefully evaluated (4). Achalasia is defined as esophageal aperistalsis and a lack of relaxation of the lower esophageal sphincter. Among the three types of achalasia, type 2 shows intermittent periods of pressurization. Achalasia is rare, with an incidence of 0.3–1.63 per 100,000 people per year in adults (5). It is generally observed in adults aged 30–60 years (6). We describe the assessment and management of a nonagenarian patient who presented with weight loss and dysphagia secondary to type 2 achalasia.

CASE REPORT

A 93-year-old Chinese woman who required assistance in basic activities of daily living (BADLs) at home without a walking aid and was dually continent presented to the Emergency Department with recurrent vomiting, dysphagia, and an 8-kg weight loss over 6 months. She was admitted to the geriatric inpatient ward. She reported difficulty in swallowing liquids and solids, often associated with a globus sensation. She denied reflux symptoms such as heartburn and acid regurgitation. Examination showed normal vital signs and no significant findings. Her medical history included mild dementia (mixed vascular and Alzheimer’s etiology) with a Mini-Mental State Examination score of 22/30, ischemic heart disease with a left ventricular ejection fraction of 55%, postural hypotension, knee osteoarthritis and osteoporosis, and a history of falls with traumatic subdural hemorrhage. Her chronic medications included aspirin (100 mg), omeprazole (20 mg), and cholecalciferol (1000 IU) every morning. However, owing to recurrent vomiting, she had been unable to take oral medications regularly for the past 6 months.

Blood investigations revealed hypernatremia with acute kidney injury—raised urea: 17.6 mmol/L (normal limits being 2.1–8.4 mmol/L); sodium, 149 mmol/L; and creatinine, 86 μmol/L, up from a baseline creatinine of 49 μmol/L. Full blood counts showed normal hemoglobin (14.8 g/dL), leukocyte count (10 × 10^3 U/L), and platelets (159 × 10^3 U/L). Thyroid function, liver function, and other investigations were normal.

Key Words: Esophageal dysphagia, Weight loss, Frail older adults, Achalasia
troponin levels, pancreatic enzyme levels, and urinalysis results were normal. Electrocardiography and chest and abdominal radiographical findings were unremarkable. Brain computed tomography (CT) did not reveal any infarcts or new bleeding. CT of the thorax and abdomen with intravenous contrast did not reveal any masses along the esophagus or the gastroesophageal junction.

Esophagogastroduodenoscopy revealed no anatomical abnormalities. Barium swallow showed tertiary contractions with mild hold-up of contrast in the middle and distal esophagus (Fig. 1). As the patient had a good functional status and a low burden of co-morbidities, repeated discussions were held with her family regarding high-resolution esophageal manometry. The results of this investigation showed an increased median integrated relaxation pressure of 30.9 mmHg and a lack of normal peristaltic contractions of the esophagus in response to swallowing (Fig. 2). These findings are consistent with type 2 achalasia.

After establishing the diagnosis, a gastroenterologist was consulted. The suite of considered options included peroral endoscopic myotomy (POEM), pneumatic dilatation, laparoscopic Heller myotomy, botulinum injection into the gastroesophageal junction, and medical therapy via calcium channel blockers and nitrates. We also considered nasogastric tube feeding for nutritional support if prior management options were deemed unsuitable. After weighing the risks and benefits of the aforementioned treatments, surgical intervention was deemed too risky for this patient. Considering her history of significant postural hypotension and high risk of falls, treatment with calcium channel blockers and nitrates was also deemed unsuitable.

After a thorough discussion with the patient and family, botuli-
num injection was determined to be the most appropriate treatment, while emphasizing that its effect may wane after 6 month follow-up. As such, individuals may require repeated procedures, which increases the risk of esophageal fibrosis. The patient received botulinum injections and did not develop any complications during the procedure. Her dysphagia and vomiting resolved, and she could tolerate meals and liquid nutritional supplements well. The patient was discharged from the ward 1 week after the procedure. At a clinical review 3 months later, the patient remained symptom-free and was found to have gained 5 kg. She was scheduled for a subsequent outpatient gastroenterology review at 3–6 months after the procedure to observe symptom recurrence.

**DISCUSSION**

This case highlights a unique clinical presentation of dysphagia and weight loss resulting from a rare condition in a nonagenarian patient. Achalasia is generally diagnosed in middle-aged patients, i.e., between 30 and 60 years of age. Type 2 achalasia is most commonly associated with weight loss and is most responsive to botulinum treatment, as observed in our case. To add to the complexity of the diagnosis, an aging esophagus can also have laxity of the lower esophageal sphincter. Thus, without a high index of suspicion, the diagnosis of achalasia can be missed in older adults. In this case, wherein both endoscopy and contrast-enhanced CT scans did not reveal an obvious etiology, further targeted investigations helped identify achalasia as the cause. The management of this case required careful weighing of the risks and benefits of each treatment option to optimize the benefits and minimize potential harm to the patient. A literature review proposed the use of botulinum injection in adults aged >75 years with achalasia and recommended it as an efficacious yet lower-risk modality. Ideally, further research in the form of randomized controlled trials is required to prove the clinical benefits of this intervention. In conclusion, this unique case of achalasia in a nonagenarian serves as an important reminder of the uncommon causes of weight loss and dysphagia. A multidisciplinary approach involving geriatricians, gastroenterologists, geriatric nurses, therapists, and dieticians enabled the holistic management of this patient in a geriatric ward. Comprehensive investigations and carefully considered management of achalasia can markedly improve the quality of life in older adults.

**ACKNOWLEDGMENTS**

**CONFLICT OF INTEREST**
The researchers claim no conflicts of interest.

**FUNDING**
None.

**AUTHOR CONTRIBUTIONS**
Conceptualization: GKSidhu, GKSern; Data curation: HHK; Investigation: GKSidhu, GKSern, HHK; Methodology: GKSidhu, GKSern, HHK; Project administration: GKSidhu, GKSern, HHK; Supervision: GKSidhu, GKSern.

**REFERENCES**

Late life onset of psychosis causes challenges in its diagnosis owing to the array of neurobiological processes that occur in the aging brain and medical and neurological illnesses that may emerge with advanced age. The nosology and pathophysiological underpinnings of very late-onset schizophrenia-like psychosis (VLOSLP) remain unclear. Both neurodegenerative and cerebrovascular processes have been proposed, given the common neuroimaging findings of white matter hyperintensity, particularly in the periventricular regions. Owing to the lack of specific biomarkers, diagnosis is based on clinical evidence, implying the importance of a thorough anamnesis and diagnostic workup.

**CASE REPORT**

A 64-year-old retired female patient with several cerebrovascular risk factors, including a history of hypertension, dyslipidemia, diabetes, mild cognitive decline, and an ischemic stroke that had occurred more than 3 years ago with grade 4 hemiparesis on the right side and hearing loss as sequelae, was admitted to our psychiatric ward because of a psychotic episode with a two-stage progression. Initially, the patient manifested persecutory and partition delusions, in which she believed that a TV journalist could transgress...
the walls and pull her to the TV scene. After 6 months, the delusional symptoms became more striking and were accompanied by multimodal hallucinations, comprising complex visual hallucinations (scenic, lilliputian, and holocampine) and elementary auditory, cenesthetic, olfactory, and gustatory hallucinations, which profoundly impacted her daily life and well-being. No negative symptoms or formal thought disorders were observed.

Hematological and biochemical screening revealed normal thyroid function and folic acid and cyanocobalamin levels. Serological tests were negative for venereal disease research laboratory (VDRL), human immunodeficiency virus (HIV), hepatitis B and C, and transglutaminase antibodies. Neuroimaging revealed chronic microangiopathic cerebral disease with lesions in the periventricular and deep subcortical white matter regions along with deep cerebral infarct lesions in the left centrum semiovale and basal ganglia, encompassing the bilateral thalamic and striatocapsular infarctions (Fig. 1). 2.

Electroencephalography results were normal. Neuropsychological examination revealed mild-to-moderate impairments in the working memory, sustained attention, executive function, abstract thinking, and visuospatial ability. The Mini-Mental State Examination (MMSE) score was 20/30.

Treatment with risperidone and olanzapine was unsuccessful, and clinical improvement was observed after initiating clozapine

Fig. 1. Computerized tomography (CT) scan showing cerebral small vessel disease, with bilateral thalamic and striatocapsular infarctions (A) and multiple hypodense lesions in the periventricular and deep subcortical white matter regions (B and C).

Fig. 2. Brain magnetic resonance imaging (MRI) scan (4 years before the hospitalization in a psychiatric ward) revealing multiple hyperintensities in the periventricular (A and B), and subcortical frontoparietal white matter regions, alongside a gliotic lesion in the left centrum semiovale (C).
Very Late-Onset Schizophrenia-Like Psychosis

This clinical presentation of a two-stage progression psychotic episode, with partition delusions and multimodal hallucinations in the absence of formal thought disorders and negative symptoms, is typical of a VLOSLP. Several medical causes, including celiac disease, which has the second highest incidence in later life, were ruled out.

Cognitive deficits are usually present in VLOSLP, especially in the learning, abstraction, and cognitive flexibility domains. It is debatable whether our patient’s cognitive impairment could stem from prior cerebrovascular events, pathophysiological processes underlying VLOSLP, or both. Almost half of VLOSLP patients develop dementia within 5 years. However, cognitive impairment is common even in patients with VLOSLP who do not develop dementia. Therefore, it remains controversial whether the propensity to develop dementia is a true characteristic of VLOSLP or reflects an initial misdiagnosis. In this context, VLOSLP should increase the index of diagnostic suspicion of dementia with Lewy bodies (DLB), in which complex visual hallucinations are a typical early presenting feature and may co-occur with hallucinations in other sensory modalities and systematized delusions throughout its clinical course. A recent study suggested that the presence of psychomotor slowing and visual hallucinations might constitute a prodromal manifestation of DLB in cases wherein a clinical picture suggestive of VLOSLP is present, whereas the cingulate island sign in the single-photon emission computerized tomography (SPECT) scan is an indicative biomarker of DLB. However, clinical conditions characterized by partition delusions and multimodal hallucinations are uncommon. Other clinical cues that point to the diagnosis of DLB include the presence of REM behavior disorder, which is a harbinger of alpha-synucleinopathy that may be present approximately one decade before cognitive impairment; a heightened sensitivity to antipsychotic effects; parkinsonism; and a dopamine transporter scan (DaTscan) showing unraveling striatoniigral degeneration.

Some studies have suggested a specific neuropathology for VLOSLP: tauopathy restricted to the limbic regions. In addition, several cumulative age-specific neurobiological processes, such as subclinical neurodegeneration, accelerated white matter loss, and a decline in estrogen levels, lead to a mesolimbic hyperdopaminergic state, impaired neuroplasticity, immunosenescence, and neurovascular damage, which may have contributed to VLOSLP. Estrogen decline affect the expression and function of dopamine receptors and transporters and has detrimental effects on neuroprotective factors via genomic mechanisms and epigenetic modifications and on the cerebrovasculature, impairing vasodilatory mechanisms. Moreover, preclinical models of schizophrenia have suggested that estradiol ameliorates positive, negative, and cognitive symptoms. More recently, the role of immunosenescence, which encompasses the priming of microglial cells to produce an amplified inflammatory response to brain insults, has been posited in the pathophysiology of schizophrenia-like psychosis with late-life onset, in which an enhanced neuroinflammatory response mediates neurodegeneration, white matter alterations, aberrant synaptic pruning, and neurogenesis inhibition.

Based on these factors, the relevance of cerebrovascular disease in the aging brain has been widely suggested, with white matter hyperintensities occurring almost three-fold more frequently in patients with VLOSLP than that in patients with classic early-onset schizophrenia within the same age group. Neuroimaging studies have shown that lacunar infarction in the basal ganglia, along with chronic white matter small vessel ischemic disease, may be the underlying pathophysiology of psychosis via the disruption of frontal-subcortical pathways. Nevertheless, the interval between stroke and emergence of psychosis in our patient was nearly 3 years, which is an extremely long period compared with that in the previously reported cases of post-stroke psychosis, which usually resolves completely within a few months. Evidence suggests that a high burden of vascular factors is associated with late-life psychosis in patients with cognitive impairment, regardless of the presence of cerebrovascular lesions. Long-term hypertension is associated with microstructural white matter abnormalities. Several studies have demonstrated the association between hypertension, white matter lesions, and cognitive decline. Cognitive decline and VLOSLP are more strongly associated with periventricular white matter hyperintensities than with subcortical brain infarctions on magnetic resonance imaging (MRI). Additionally, several studies have suggested an association between estrogen receptor polymorphisms and vascular cognitive impairment.

This case report adds to the growing body of evidence regarding the relevance of cerebrovascular risk factors, including hypertension, basal ganglia infarctions, and microvascular brain lesions, in the pathophysiology of VLOSLP. These factors may disrupt the...
frontal-subcortical circuitry and neurobiological processes that occur in the aging brain, with a possible limbic tauopathy occurrence. Additionally, neurosensory impairment and psychosocial aspects, such as retirement and social isolation, are well-known predisposing factors of late-life psychosis.

In conclusion, the neurobiological underpinnings of VLOS LP are complex and multifaceted and may result from an interplaying array of age-specific cerebral alterations. More systematized studies are needed, including neuropathological and neuroimaging studies, such as SPECT and positron emission tomography (PET) scans, to pinpoint specific biomarkers, which would elucidate the role of these neurobiological factors and stratify them as core etiologic factors or as trigger factors. Moreover, identifying a specific biomarker would facilitate clinicians to more accurately diagnose VLOS LP differentiate it from other overlapping clinical entities, such as dementia or post-stroke psychosis, and provide a tailored treatment for the patient.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization, JR; Supervision, FMP; Writing-original draft, JR; Writing-review & editing, FMP.

REFERENCES

3. Tonkonogy JM, Geller JL. Late-onset paranoid psychosis as a distinct clinicopathologic entity: magnetic resonance imaging data in elderly patients with paranoid psychosis of late onset and schizophrenia of early onset. Neuropsychiatry Neuropsychol Behav Neurol 1999;12:230-5.
4. Sehatpour M, Javadpour A. Assessing symptoms profile and correlates of very late-onset schizophrenia-like psychosis (VLOS LP).
Dear Editor,

We read with interest the recent systematic review and meta-analysis published by Aryana et al. (1) entitled “Denosumab’s therapeutic effect for future osteosarcopenia therapy: a systematic review and meta-analysis.” The meta-analysis included four studies and concluded that denosumab (a human monoclonal antibody osteoporosis medication) improved hand grip strength (but not lumbar spine bone mineral density or gait speed) to a greater extent than bisphosphonates (another antiresorptive bone medication).

We wish to draw attention to several methodological flaws that are likely to have influenced the outcomes and interpretation of this meta-analysis.

(1) Different denosumab group comparisons were combined in the meta-analyses. For example, Fig. 3 illustrates a comparison of mean change in hand grip strength between denosumab users and bisphosphonate users from Miedany et al. (2) and a comparison between denosumab users and no therapy from the other two studies (Bonnet et al. (3) and Rupp et al. (4)). Furthermore, the Bonnet hand grip strength data in the meta-analysis are incorrect because corrected hand grip strength data published in a 2020 corrigendum (5) to the Bonnet et al. paper were not considered. In fact, mean change in hand grip strength in the denosumab group was closer to 0 kg than 3 kg, and mean hand grip strength change in the bisphosphonate group was approximately -2 kg.

(2) Data with different units of measurement were included in the meta-analyses. For example, the lumbar spine data shown in Fig. 2 represent a combination of absolute change (Bonnet et al. (3)) and percentage change (Rupp et al. (4)), and T-scores (Miedany et al. (2)). For mean change in hand grip strength, the Figure 3 forest plot represents a combination of absolute change (Bonnet et al. (3) and Miedany et al. (2)) and percentage change (Rupp et al. (4)).

(3) The authors calculated mean change from baseline in Figs. 2 and 3 for Miedany et al. (2) but appear to have simply used follow-up standard deviations instead of calculating the missing standard deviations for the change to follow-up.

(4) The absence of a “leave-one-out” sensitivity analysis makes it difficult to ascertain how individual studies contributed to the overall effect size estimate.

(5) The Hartung-Knapp-Sidik-Jonkman method (7) for random effects meta-analyses should have been applied to reflect uncertainty in the estimation of between-study heterogeneity due to the small number of studies included.

(6) The authors state that “…funnel plots of all analyses…did not reveal any significant asymmetry.” However, tests for funnel plot asymmetry are not recommended for meta-analyses including < 10 studies as the test power is too low to differentiate real asymmetry from chance.

The studies included in the meta-analysis also had notable shortcomings. None of the studies was randomised and controlled to the standard of a clinical trial. One was a non-randomised longitudinal study in which participants were classified into active (denosumab) or control (bisphosphonate) groups based on prescribed medication (3) one was a retrospective observational study with propensity score matching (4) one was a prospective observational study with participant matching (3) and one, reported in the...
format of a letter to the editor, included data from a longitudinal cohort study.\textsuperscript{9} We note our previous letter to the editor in Osteoporosis International\textsuperscript{6} that raised concerns about the methods of Rupp et al.\textsuperscript{4} including the influence of outliers and the lack of adjustment for group differences on their findings. The Bonnet et al. study\textsuperscript{5} included interesting animal data (for which a 2023 corrigendum was also recently published\textsuperscript{10}), however, the modest human data extracted from that study is lacking the basic elements of a rigorous clinical trial design. Miedany et al.\textsuperscript{3} did not report participant age, 65 of their participants were ‘contaminated’ with prior bisphosphonate exposure of unspecified duration, and Tables 2 and 3 contain mean scores for many outcome measures that are unusually similar and, in many cases, identical. Importantly, none of the included studies controlled for the confounding effect of exercise. In fact, changes in strength and/or function from baseline of any patient group who have received medical advice (as all participants presumably had) could easily reflect simultaneous advice to undertake exercise (per best practice recommendations). Thus, in the absence of a genuine control group, monitoring of exercise exposure with a validated instrument, and subsequent control for physical activity uptake in each study, it is not possible to attribute any functional changes to medications that were simultaneously prescribed.

Considering the above concerns with the methodology of the meta-analysis and notable limitations of the included studies, the conclusion of Aryana et al.\textsuperscript{1} that denosumab “…may be favoured in individuals with osteosarcopenia to improve muscular performance and reduce falls risk” based on a single dubious finding of greater hand grip strength improvements in denosumab users than bisphosphonate users is questionable. Therefore, it is premature to suggest that denosumab use per se will enhance muscle strength. The promotion of such an idea would undoubtedly be at the expense of the one therapy known to enhance muscle strength (resistance training), which would be a disservice to patients considering therapy to prevent osteoporotic fractures.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The authors claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization, BRB, DS, RMD, JK; Writing-original draft, BRB; Writing-review & editing, BRB, DS, RMD, JK.

REFERENCES

Courses and Conferences

Upcoming academic events in 2023 of the Korean Geriatrics Society.
We would like to invite members of the Korean Geriatrics Society and anyone who are interested.

[The 43th Review Training Course]
August 20, 2023
online or offline (to be announced)
For more information please contact kgskorea1968@gmail.com

[The 23th Geriatric Medicine Certification Exam]
August 27, 2023
National Medical Center auditorium
245, Eulji-ro, Jung-gu, Seoul, Republic of Korea
For more information please contact kgskorea1968@gmail.com

Membership Fee Information

Membership Fee

- Regular member (Certified by the Korean Geriatrics Society): KRW 20,000
- Other member: KRW 30,000

Payment account information
KEB Hana Bank: 630-007115-767
대한노인병학회
- Please remark the name of the sender when making bank transfer.

Information on Geriatric Medicine Certification

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

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

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

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

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

Renewal of Certification
a. Qualification: Those who earned 250 points or more within the validity period (5 years)
(The changes have been made to the article 8 of the Regulation on the Management in that one needs to earn 250 points and not 500 points for renewing the certificate.)
b. Certification renewal fee: KRW 50,000
c. Procedure: Acquisition of 250 points (check on “My Page” at the website)
→ Check mailing address
→ Send the certification renewal fee to the Korean Geriatrics Society
→ Certificate issued and sent by mail
d. Expiration policy: Valid for 5 years after renewal
Ex. September 1, 2015 - August 31, 2020

Account information
KEB Hana Bank: 630-007115-767
대한노인병학회
- Please remark the name of the sender when making bank transfer.
The Korean Geriatrics Society has become an English-language journal named Annals of Geriatric Medicine and Research (Ann Geriatr Med Res, AGMR). As a non-profit emerging global peer-reviewed journal based on Korea, we highly encourage our members to submit articles to AGMR.

**Submission Method**

1. **Journal website**  
   Log-In (http://www.e-agmr.org)

2. **Manuscript revision according to submission guidelines**  
   (file format: MS word)

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

4. **Copyright agreement via web submission system**  
   (Form available on our website or journal)

5. **Submission Completed**

Provide the Evaluation of the Society when Contributing Articles

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

**Journal Subscription Guide**

**Subscription fees**

- Subscription fee: KRW 20,000  
  (Journal mailed 4 times a year at the end of March, June, September, December)

* If you wish to receive journal by mail, please send a yearly subscription fee of KRW 20,000. Members who pay the annual fee will receive a journal letter.

**Payment account information**

KEB Hana Bank: 630-007115-767  
대한노인병학회

Please remark the name of the sender when making bank transfer, and include the comment “구독료/subscription fee” to specify that the transfer is for journal subscription. If you do not receive your mail even after transferring the payment, please confirm and correct the mailing address on "My page" after logging in.
Annals of Geriatric Medicine and Research (Ann Geriatr Med Res, AGMR) 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 a peer-reviewed English 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 clinical and biological science and issues on policymaking for older adults especially for Asian emerging countries.

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

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

Contact Us
Editor-in-Chief: Jae-Young Lim, MD, PhD
Department of Rehabilitation Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, 82 Gumi-ro 173 beon-gil, Bundang-gu, Seongnam 13620, Korea
Tel: +82-31-787-7732, Fax: +82-31-787-4056
E-mail: drlim1@snu.ac.kr

Editorial Office: Korean Geriatrics Society
401 Yuksam Hyundai Venturetel, 20 Teheran-ro 25-gil, Gangnam-gu, Seoul 06132, Korea
Tel: +82-2-2269-1039, Fax: +82-2-2269-1040
E-mail: agmr.editorial@gmail.com

ReSEARCH AND PUBliCATION ETHICS
The journal adheres to the guidelines and best practices published by professional organizations, including International Standards for Editors and Authors (https://publicationethics.org/node/11184), ICMJE Recommendations, and the Principles of Transparency and Best Practice in Scholarly Publishing (joint statement by the Committee on Publication Ethics [COPE], Directory of Open Access Journals [DOAJ], World Association of Medical Editors [WAME], and Open Access Scholarly Publishers Association [OASPA]; https://doaj.org/bestpractice). Further, all processes of handling research and publication misconduct shall follow the applicable COPE flowchart (https://publicationethics.org/resources/flowcharts).

Statement of Human and Animal Rights
Clinical research should be conducted in accordance with the World Medical Association's Declaration of Helsinki (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/). Clinical studies that do not meet the Helsinki Declaration will not be considered for publication. For human subjects, identifiable information, such as patients’ names, initials, hospital numbers, dates of birth, and other protected health care information, should not be disclosed. For animal subjects, research should be performed based on the National or Institutional Guide for the Care and Use of Laboratory Animals. The ethical treatment of all experimental animals should be maintained.

Statement of Informed Consent and Institutional Approval
Copies of written informed consent should be kept for studies on human subjects. Clinical studies with human subjects should provide a certificate, an agreement, or the approval by the Institutional Review Board (IRB) of the author’s affiliated institution. For research with animal subjects, studies should be approved by an Institutional Animal Care and Use Committee (IACUC). If necessary, the editor or reviewers may request copies of these documents to resolve questions regarding IRB/IACUC approval and study conduct.
Conflict of Interest Statement
The corresponding author of an article is asked to inform the Editor of the authors' potential conflicts of interest possibly influencing their interpretation of data. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. A potential conflict of interest should be disclosed in the manuscript even when the authors are confident that their judgments have not been influenced in preparing the manuscript. The disclosure form should be the same as the ICMJE Form for Disclosure of Potential Conflicts of Interest (http://www.icmje.org/conflicts-of-interest/).

Originality, Plagiarism, and Duplicate Publication
Redundant or duplicate publication refers to the publication of a paper that overlaps substantially with one already published. Upon receipt, submitted manuscripts are screened for possible plagiarism or duplicate publication using Crossref Similarity Check. If a paper that might be regarded as duplicate or redundant had already been published in another journal or submitted for publication, the author should notify the fact in advance at the time of submission. Under these conditions, any such work should be referred to and referenced in the new paper. The new manuscript should be submitted together with copies of the duplicate or redundant material to the editorial committee. If redundant or duplicate publication is attempted or occurs without such notification, the submitted manuscript will be rejected immediately. If the editor was not aware of the violations and of the fact that the article had already been published, the editor will announce in the journal that the submitted manuscript had already been published in a duplicate or redundant manner, without seeking the author's explanation or approval.

Secondary Publication
It is possible to republish manuscripts if the manuscripts satisfy the conditions for secondary publication of the ICMJE Recommendations (http://www.icmje.org/icmje-recommendations.pdf).

Authorship and Author's Responsibility
Authorship credit should be based on (1) substantial contributions to conception and design, acquisition of data, and analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; (3) final approval of the version to be published; and (4) agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Authors should meet these four conditions.

- A list of each author’s role should accompany the submitted paper.
- Correction of authorship: Any requests for such changes in authorship (adding author(s), removing author(s), or re-arranging the order of authors) after the initial manuscript submission and before publication should be explained in writing to the editor in a letter or e-mail from all authors. This letter must be signed by all authors of the paper. A copyright assignment must be completed by every author.
- Role of corresponding author: The corresponding author takes primary responsibility for communication with the journal during the manuscript submission, peer review, and publication process. The corresponding author typically ensures that all of the journal’s administrative requirements, such as providing the details of authorship, ethics committee approval, clinical trial registration documentation, and conflict of interest forms and statements, are properly completed, although these duties may be delegated to one or more coauthors. The corresponding author should be available throughout the submission and peer review process to respond to editorial queries in a timely manner, and after publication, should be available to respond to critiques of the work and cooperate with any requests from the journal for data or additional information or questions about the article.
- All authors of a manuscript must have agreed to its submission and are responsible for its content, including appropriate citations and acknowledgements; they must also have agreed that the corresponding author has the authority to act on their behalf on all matters pertaining to the publication of the paper.
- Description of co-first authors or co-corresponding authors is also accepted if corresponding author believes that their roles are equally contributed.
- Contributors: Any researcher who does not meet all four ICMJE criteria for authorship discussed above but contribute substantively to the study in terms of idea development, manuscript writing, conducting research, data analysis, and financial support should have their contributions listed in the Acknowledgments section of the article.

Process for Managing Research and Publication Misconduct
When the journal faces suspected cases of research and publication misconduct, such as redundant (duplicate) publication, plagiarism, fraudulent or fabricated data, changes in authorship, undisclosed conflict of interest, ethical problems with a submitted manuscript, appropriation by a reviewer of an author's idea or data, and complaints against editors, the resolution process will follow the flowchart provided by COPE (http://publicationethics.org/
resources/flowcharts). The discussion and decision on the suspected cases are carried out by the Editorial Board.

**Editorial Responsibilities**
The Editorial Board will continuously work to monitor and safeguard publication ethics: guidelines for retracting articles; maintenance of the integrity of academic records; preclusion of business needs from compromising intellectual and ethical standards; publishing corrections, clarifications, retractions, and apologies when needed; and excluding plagiarized and fraudulent data. The editors maintain the following responsibilities: responsibility and authority to reject and accept articles; avoid any conflict of interest with respect to articles they reject or accept; promote the publication of corrections or retractions when errors are found; and preserve the anonymity of reviewers.

**EDITORIAL POLICY**

**Copyright**
Copyright in all published material is owned by the Korean Geriatrics Society. Authors must agree to transfer copyright (https://www.e-agmr.org/authors/copyright_transfer_agreement.php) during the submission process. The corresponding author is responsible for submitting the copyright transfer agreement to the publisher.

**Open Access Policy**
AGMR is an open-access journal. Articles are distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by-nc/4.0/), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. Author(s) do not need to permission to use tables or figures published in AGMR in other journals, books, or media for scholarly and educational purposes. This policy is in accordance with the Budapest Open Access Initiative definition of open access.

**Registration of Clinical Trial Research**
It is recommended that any research dealing with a clinical trial be registered with a primary national clinical trial registration site such as Clinical Research Information Service (http://cris.cdc.go.kr/), or other sites accredited by the World Health Organization ICTRP (http://www.who.int/ictrp/en) and ClinicalTrials.gov (http://clinicaltrials.gov/), a service of the United States National Institutes of Health.

**Data Sharing**
AGMR encourages data sharing wherever possible, unless this is prevented by ethical, privacy, or confidentiality matters. Authors wishing to do so may deposit their data in a publicly accessible repository and include a link to the DOI within the text of the manuscript.

- **Clinical Trials:** AGMR accepts the ICMJE Recommendations for data sharing statement policy. Authors may refer to the editorial, “Data Sharing statements for Clinical Trials: A Requirement of the International Committee of Medical Journal Editors,” in the Journal of Korean Medical Science (https://dx.doi.org/10.3346/jkms.2017.32.7.1051).

**Archiving and Posting Policy**
AGMR provides electronic archiving and preservation of access to the journal content in the event the journal is no longer published, by archiving in the National Library of Korea. According to the deposit policy (self-archiving policy) of Sherpa/Romeo (http://www.sherpa.ac.uk/), authors cannot archive pre-print (i.e., pre-refereeing) but they can archive post-print (i.e., final draft post-refereeing). Authors can archive the publisher’s version/PDF.

**Correction**
If correction is needed, it will follow the ICMJE Recommendation for Corrections, Retractions, Republications and Version Control available from: http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/corrections-and-version-control.html as follows:

- Honest errors are a part of science and publishing and require publication of a correction when they are detected. Corrections are needed for errors of fact. Minimum standards are as follows: First, it shall publish a correction notice as soon as possible, detailing changes from and citing the original publication on both an electronic and numbered print page that is included in an electronic or a print Table of Contents to ensure proper indexing; Second, it shall post a new article version with details of the changes from the original version and the date(s) on which the changes were made through CrossMark; Third, it shall archive all prior versions of the article. This archive can be either directly accessible to readers; and Fourth, previous electronic versions shall prominently note that there are more recent versions of the article via CrossMark.

**SUBMISSION & PEER REVIEW PROCESS**

**Submission**
All manuscripts should be submitted online via the journal’s website (http://submit.e-agmr.org/submission/) by the corresponding author. Once you have logged into your account, the online
system will lead you through the submission process in a stepwise orderly process. Submission instructions are available at the website. All articles submitted to the journal must comply with these instructions. Failure to do so will result in the return of the manuscript and possible delay in publication.

**Peer-Review Process**

- A submitted manuscript will be evaluated by editors and reviewers. All manuscripts submitted to AGMR undergo screening by the Editorial Board, who then determines whether a manuscript undergoes external review.
- The journal uses a double-blind peer review process: the reviewers are not aware of the identity of the authors, and vice versa. They are peer reviewed by at least 3 anonymous reviewers selected by the editor. We neither guarantee the acceptance without reviewing process nor very short peer review times for unsolicited manuscripts. Commissioned manuscripts will also be reviewed before publication.
- The average time interval for an initial review process that involves both editorial and peer reviews is approximately 1 month; occasionally, there are unavoidable delays, usually because a manuscript needs multiple reviews or several revisions.
- The corresponding author will be notified as soon as possible of the editor’s decision to accept, reject, or ask for revisions. When manuscripts are returned for a revision, a cover letter from the editor provides directions that should be followed carefully. When submitting the revised manuscript, authors should include a Response Letter, which describes how the manuscript has been revised. A point-by-point response to the editor should be included with the revised manuscript. Authors who plan to resubmit but cannot meet this deadline should contact the Editorial Office. Manuscripts held for revision will be retained for a maximum of 90 days. The revised manuscript and the author’s comments will be reviewed again. If a manuscript is completely acceptable according to the criteria set forth in these instructions, it is scheduled for publication in the next available issue.

**Appeals of Decisions**

Any appeal against an editorial decision must be made within 2 weeks of the date of the decision letter. Authors who wish to appeal a decision should contact the Editor-in-Chief, explaining in detail the reasons for the appeal. All appeals will be discussed with at least one other associate editor. If consensus cannot be reached thereby, an appeal will be discussed at a full editorial meeting. The process of handling complaints and appeals follows the guidelines of COPE available from https://publicationethics.org/appeals. AGMR does not consider second appeals.

**MANUSCRIPT PREPARATION**

AGMR focuses on clinical and experimental studies, reviews, case reports, editorials and letters in geriatric medicine and gerontology. Any researcher throughout the world can submit a manuscript if the scope of the manuscript is appropriate.

**General Requirements**

- The manuscript must be written using Microsoft Word and saved as “.doc” or “.docx” file format. The font size must be 11 points. The body text must be left aligned, double spaced, and presented in one column. The left, right, and bottom margins must be 3 cm, but the top margin must be 3.5 cm.
- Page numbers must be indicated in Arabic numerals in the middle of the bottom margin, starting from the abstract page.
- A complete title page should be submitted separately from the main document file, and the latter should contain no information that identifies the author or the author’s institutional affiliation.
- All manuscripts must be written in clearly understandable English. Authors whose first language is not English are requested to have their manuscripts checked for grammatical and linguistic correctness before submission. Correct medical terminology should be used, and jargon should be avoided.
- The use of abbreviations should be minimized and restricted to those that are generally recognized. When using an abbreviated word, it should be spelled out in full on first usage in the manuscript, followed by the abbreviation in parentheses.
- Numbers should be written in Arabic numerals, but must be spelled out when placed at the beginning of a sentence.
- Drugs and chemicals should be referred to using standard chemical or generic terms. The names and locations (city, state, and country only) of manufacturers of equipment and non-generic drugs should be given.
- Measurements should be described using the metric system, and hematologic and biochemical markers using the International System of Units. All units must be preceded by one space, except for the following symbols: percentage (%), temperature (°C), and degree (°).

All authors of a manuscript must have agreed to its submission and are responsible for its content, including appropriate citations and acknowledgements; they must also have agreed that the corresponding author has the authority to act on their behalf on all matters pertaining to the publication of the paper. By publishing in this journal, the authors agree that the Korean Geriatrics Society
has the right to protect the manuscript from misappropriation. Illustrations in published articles will not be returned to the authors.

**Reporting Guidelines for Specific Study Designs**

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

**Composition of Manuscripts**

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

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

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

AGMR, Annals of Geriatric Medicine and Research.

a)Maximum number of words is exclusive of the abstract, references, tables, and figure legends.

b)Background, methods, results, and conclusion.

**Title Page**

The Title Page should include only the following information:

- Title: The title and the running title should be 25 or less and 10 or less words, respectively. Please consider the title very carefully, as these are often used in information-retrieval systems. Please use a concise and informative title (avoiding abbreviations where possible). The title should be written in sentence case (capitalize only the first word of the title and proper nouns).
- Author names and affiliations in the correct order: Where the family name may be ambiguous (e.g., a double name), please indicate this clearly. Present the authors’ affiliation (where the actual work was done) below the names. Indicate all institutional affiliations, including the city and country, using lower-case superscript letters immediately after the author's name and in front of the appropriate address.
- Corresponding author: Clearly indicate who will handle correspondence at all stages of the refereeing and publication process and after publication. Provide the full postal address, including the city and country and, if available, the e-mail address of each author. When stating the author's degree, do not place periods within “MD” and “PhD”. The e-mail address and ORCID of the corresponding author should be placed in the title page. Contact details must be kept up-to-date by the corresponding author. ORCID (Open Researcher and Contributor ID) identifier must be also addressed. If the corresponding author does not have an ORCID identifier, it can be obtained through the ORCID website (https://orcid.org).
- Acknowledgments: This section is for the Conflicts of Interest, Funding, Author Contributions, ORCID, Additional Contributions, and Previous Presentations.
- Conflicts of Interest Disclosures: Please include the authors’ potential conflicts of interest that could possibly influence their interpretation of data. If no conflict exists, please state the following: “The researcher(s) claim(s) no conflicts of interest.”
- Funding: For each source of funds, both the research funder and the grant number should be listed in this section.
- Author Contributions: The contributions of all authors must be described using the CRediT (https://www.casrai.org/credit.html) Taxonomy of author roles.

Sample:

| Conceptualization, GDH; Data curation, JHK; Funding acquisition, GDH; Investigation, JHK, SSL; Methodology, AGK; Project administration, GDH; Supervision, GDH; Writing–original draft, JHK, SSL; Writing–review & editing, GDH, AGK |

- ORCID: We recommend that the open researcher and contributor ID (ORCID) of all authors be provided. In order to obtain an ORCID, authors should register in the ORCID website: http://orcid.org/. Registration is free to every researcher in the world.
- Additional Contributions: All persons who have made substantial contributions, but who have not met the criteria for authorship, are acknowledged here.
- Previous Presentation: Please inform any previous presentation of the material. Provide the exact data and location of the meeting.
Abstract & Keywords
A concise and factual abstract is required. The abstract should not be more than 250 words (150 words for case reports and reviews). Abstracts should include the following headings: Background, Methods, Results, and Conclusion. Author(s) should specify the number of study participants. The abstract’s conclusion should emphasize clinical relevance. Do not use vague phrases such as “We believe that …” or “We suppose that ….” Non-standard or uncommon abbreviations should be avoided, but if essential, must be defined the first time they are mentioned in the abstract. After the abstract, list 3-5 keywords to be used for indexing. The keywords are from medical subject headings (MeSH; https://www.ncbi.nlm.nih.gov/mesh). Editorials and Letters to the editor do not require an abstract. An abstract is often presented separately from the article, and therefore must be able to stand alone.

Guidelines for the Main Body
• Introduction: State the objectives of the work and provide adequate background, avoiding a detailed literature survey or summary of the results.
• Materials and Methods: Authors of empirical papers are expected to provide full details of the research methods used, including study location(s), sampling procedures, date(s) of data collection, research instruments, and data analysis techniques. Methods already published should be indicated in a reference; only relevant modifications should be described. For Case Reports, the case history or case description replaces the Methods section, as well as the Results section. Any study using human subjects or materials should be approved by the Institutional Review Board, as well through patient consent. Affiliation name of Institutional Review Board and approval number must be clearly stated as the following: “This study was approved by the Institutional Review Board of [Name of Affiliation] (Approval Number)”. Any study using animals should state the Institutional Animal Care approval and number. Any other ethics approvals should also be listed. If no ethical approvals were achieved or required, please state the reason (e.g., “In this study, the Institutional Review Board of [Name of Affiliation] approved the exemption and allowed authors to review the patient’s records with no need for the informed consents.”). Ensure correct use of the terms sex (when reporting biological factors) and gender (identity, psychosocial or cultural factors), and, unless inappropriate, report the sex and/or gender of study participants, the sex of animals or cells, and describe the methods used to determine sex and gender. If the study was done involving an exclusive population, for example in only one sex, authors should justify why, except in obvious cases (e.g., prostate cancer).
• Results: Results should be clear and concise. Excessive repetition of table or figure content should be avoided.
• Discussion: This should explore the significance of the findings, rather than repeating them. Avoid extensive citations or a discussion of published literature. The main conclusions of the study may be presented in a short Conclusion section, which may stand alone or form a subsection of the Discussion section.

References
The citation of references in the text should be made using consecutive numbers in parentheses (Vancouver style). They should be listed in the text in the order of citation, with consecutive numbering in this separate section. The style for papers in periodicals is as follows: the name and initials of all authors, the full title of article, the journal name abbreviated in accordance with Index Medicus, the year and volume, and the first and last page numbers. If there are more than 7 authors, write the names of the first 6 authors, followed by “et al.”. The style for a book chapter is as follows: author and title of the chapter, editor of the book, title of the book, edition, volume, place, publisher, year, and first and last page numbers. The style for a book is as follows: author, title of the book, edition, place of publication, publisher, and year of publication. The style for a website is as follows: title of the website, the book, edition, volume, place, publisher, and year of publication. The style for a website is as follows: title of the website, the book, edition, volume, place, publisher, and year of publication.

Reference Style
• Journal article:
• Book:
• Book chapter:
  4. Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh...
Tables and Figures

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

- Table: Please submit tables as editable text and not as images. Avoid using vertical rules. Tables should be simple and should not duplicate information already presented in figures. Title all tables and number them using Arabic numerals in the order of their citation. Tables should be double-spaced, with each table on a separate sheet. Describe all abbreviations using footnotes. Footnotes are followed by the source notes, other general notes, abbreviation, notes on specific parts of the table (a), (b), (c), (d)…), and notes on level of probability (*, **, *** for p-values). Each column and row should have an appropriate heading. The first letter of the first word in each column and row should be capitalized. Use Arabic numerals after “Table” in accordance with the order of citation, with a space between “Table” and the Arabic number. Mean and standard deviation (mean ± SD) and numbers of subjects are included and the significance of results is indicated through appropriate statistical analysis. The p-value should be provided to 3 decimal places and the letter "p" in “p-value” written in lower case. Table footnotes should be indicated with superscript markings. All units of measurement and concentration should be designated. Exponential terminology is discouraged. The table should be drawn in MS word and not as an image file (JPG, GIF, TIFF, etc.).

- Figure: Electronic art should be created/scanned and saved and submitted as either a TIFF (tagged image file format) or an EPS (encapsulated postscript) file. Figures must be cited in the text and numbered in order of first mention. Make sure to mark the figure number clearly on the figure or part of the electronic file name (i.e., Figure 1.tif). Line art must have a resolution of at least 1,200 dpi (dots per inch), and electronic photographs, radiographs, CT scans, and scanned images must have a resolution of at least 300 dpi. Images should be supplied at a size that approximates the final figure size in the print journal. If fonts are used in the artwork, they must be converted to paths or outlines, or embedded in the files. Color images must be created/scanned, saved, and then submitted as CMYK files. Please note that artwork generated using office suite programs such as Corel Draw or MS Word, as well as artwork downloaded from the Internet (JPEG or GIF files), cannot be used. Color photographs will be published if the editor considers them absolutely necessary. The expense of reproducing color photographs/designs will be passed on to the author. The author is responsible for submitting prints that are of sufficient quality to permit accurate reproduction, and for approving the final color galley proof.

- Figure legend: All of the figure legends should be typewritten and double-spaced. Use a separate sheet for each legend. Figure legends should describe briefly the data shown, explain any abbreviations or reference points in the photographs, and identify all units, mathematical expressions, abscissas, ordinates, and symbols.

Other Manuscript Formats

General guidelines are same as for original articles.

- Review Articles: The text is structured in the following order: Title page, Introduction, Main text, Conclusion, and References, which should not exceed 100. Unstructured abstracts should contain no more than 150 words. Review article does not necessarily need to be reviewed by an Institutional Review Board.

- Case Reports

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

- A case report is an academic/educational activity that does not meet the definition of “research”, which is: “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” Therefore, the activity does not necessarily need to be reviewed by an Institutional Review Board. However, patients have a right to privacy that should not be infringed without an informed consent. Identifying information, including patients’ names, initials, or hospital numbers, should...
not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written informed consent for publication. Informed consent for this purpose requires that a patient who is identifiable be shown the manuscript to be published. Complete anonymity is difficult to achieve, however, an informed consent should be obtained if there is any doubt. For example, masking the eye region in photographs of patients is inadequate protection of anonymity. If identifying characteristics are altered to protect anonymity, such as in genetic pedigrees, authors should provide assurance that alterations do not distort scientific meaning and editors should so note.

- Editorials are an invited comment on a recently published manuscript. Editorial offers broader view of raised issues, balanced interpretation, and a link to further questions. Manuscript limitations are 1,200 words and 15 references.
- Letters to the editor: Letters to the editor comment on papers published in this journal or on other relevant matters and do not require an abstract. Manuscripts may be no longer than 1,200 words, with 15 or less references and may include only 1 figure or table. Subtitles should not be used, and any acknowledgements should be included in the body of the letter. Writing a letter is an academic/educational activity that does not meet the definition of “research”, which is: “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” Therefore, the activity does not necessarily need to be reviewed by an Institutional Review Board.

Supplemental Data
Additional data, including Methods, Results, References, Tables, Figures, and video, that are difficult to be inserted in the main body can be submitted in the form of Supplemental Data. Supplemental Data submitted by the author will be published online together with the main body without going through a separate editing procedure. All supplemental data, except video materials, are to be submitted in a single file, and the manuscript title, authors’ name, organization, and corresponding author’s contact information must be specified in the first page.

FINAL PREPARATION FOR PUBLICATION

Final Version
After the paper has been accepted for publication, the author(s) should submit the final version of the manuscript. The names and affiliations of the authors should be double-checked, and if the originally submitted image files were of poor resolution, higher resolution image files should be submitted at this time. Symbols (e.g., circles, triangles, squares), letters (e.g., words, abbreviations), and numbers should be large enough to be legible on reduction to the journal’s column widths. All symbols must be defined in the figure caption. If references, tables, or figures are moved, added, or deleted during the revision process, renumber them to reflect such changes so that all tables, references, and figures are cited in numeric order.

Manuscript Corrections
Before publication, the manuscript editor will correct the manuscript such that it meets the standard publication format. The author(s) must respond within 2 days when the manuscript editor contacts the corresponding author for revisions. If the response is delayed, the manuscript’s publication may be postponed to the next issue.

Gallery Proof
The author(s) will receive the final version of the manuscript as a PDF file. Upon receipt, the author(s) must notify the Editorial Office (or printing office) of any errors found in the file within 2 days. Any errors found after this time are the responsibility of the author(s) and will have to be corrected as an erratum.

Errata and Corrigenda
To correct errors in published articles, the corresponding author should contact the journal’s Editorial Office with a detailed description of the proposed correction. Corrections that profoundly affect the interpretation or conclusions of the article will be reviewed by the editors. Corrections will be published as corrigenda (corrections of the author’s errors) or errata (corrections of the publisher’s errors) in a later issue of the journal.

ARTICLE PROCESSING CHARGES

There are no article submission charges or article processing charges for AGMR. Only reprinting cost will be charged to the authors. Reprints may be ordered directly from the publisher. An order form for reprints will be sent with the proofs to the corresponding author. Reprints are available in quantities of 50.
Before submitting the manuscript, please complete the author’s checklist below and send it to the editorial office using online submission system (http://www.e-agmr.org).

General Guideline
☐ The content of the manuscript is original.
☐ The contact information (address, ORCID, e-mail address) of the corresponding author is indicated.

Abstract and Keywords
☐ The abstract is 250 words or less.
☐ The abstract is presented in the order of background, methods, results, and conclusion.
☐ The keywords are from medical subject headings (MeSH) (see https://www.ncbi.nlm.nih.gov/mesh).

References
☐ References are listed in accordance with the “submission guidelines”.
☐ The number of references is appropriate.
☐ One or more articles are cited from the “Annals of Geriatric Medicine and Research”.

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

Author’s checklist

Date: __________________________________________

No. of Manuscript: AGMR- __________________________________________

Title of Manuscript: __________________________________________

Corresponding Author

Print Name

Signature

www.e-agmr.org
Copyright transfer form

*Must be signed and returned to the editor-in-chief of the journal before the manuscript can be considered for publication

YOUR STATUS
I am the author signing on behalf of all co-authors of the manuscript
Name/Title/Institution/Signature: _______________________________________________________________
E-mail address: _________________________________________________________________________

I have read and agree to the terms of the License Agreement [ ]

Author(s) hereby certify that:
1. The Author(s) are the sole authors of and sole owners of the copyright in the Contribution.
2. If the Contribution includes materials of others, the Author(s) certify that they have obtained written permission for the use of text, tables, and/or illustrations from any copyrighted source(s), and agree to supply such written permission(s) to the Korean Geriatrics Society (KGS) upon request.
3. In consideration of publication of the Contribution in the Annals of Geriatric Medicine and Research (AGMR), the Author(s) hereby grants to KGS for the full term of copyright and any extensions thereto the sole and exclusive, irrevocable license to publish, reproduce, distribute, transmit, display, store, translate, create derivative works from and otherwise use the Work in any language or in any form, manner, format, or medium now known or hereafter developed without limitation throughout the world, and to permit and/or license others to do any or all of the above. In the event that AGMR decides not to publish the Contribution, this license shall be terminated and all rights revert to the author(s). And I agree to the AGMR Open Access license agreement: Creative Commons Attribution Noncommercial license.

AUTHORS RIGHTS

Ownership of copyright remains with the Authors, and provided that, when reproducing the Contribution or extracts from it, they acknowledge first and reference publication in the Journal. Authors also retain the following nonexclusive rights:
* To reproduce the Contribution in whole or in part in any printed volume (book or thesis) of which they are the author(s).
* They and any academic institution where they work at the time may reproduce the Contribution for the purpose of course teaching.
* To post a copy of the Contribution as accepted for publication after peer review (in Word or Text format) on the Authors’ own web site or institutional repository or the Author's funding body’s archive, after publication of the printed or online edition of the Journal, provided that they also give a hyperlink from the Contribution to the Journal's web site.
* To reuse figures or tables created by them and contained in the Contribution in other works created by them.

USERS RIGHTS: SUMMARY OF CREATIVE COMMONS LICENCES

CREATIVE COMMONS ATTRIBUTION-NON-COMMERCIAL LICENCE
Users are free to share (copy, distribute and transmit) and remix (adapt) the contribution under the following conditions (read full legal code at https://creativecommons.org/licenses/by-nc/4.0/legalcode):
* Attribution: Users must attribute the contribution in the manner specified by the author or licensor (but not in any way that suggests that they or their use of the contribution is endorsed by the author or licensor).
* Noncommercial: Users may not use this work for commercial purposes.
* For any reuse or distribution, users must make clear to others the license terms of this work, preferably using a link to the Creative commons webpage (http://creativecommons.org/licenses/)
* Any of the above conditions can be waived if users get permission from the copyright holder.
AUTHOR REPRESENTATIONS / ETHICS AND DISCLOSURE

I affirm the Author Representations noted below, and confirm that I have reviewed and complied with the relevant Instructions to Authors.

Author representations
The Article I have submitted to the journal for review is original, has been written by the stated authors and has not been previously published.
The Article was not submitted for review to another journal while under review by this journal and will not be submitted to any other journal.
The Article and the Supplemental Materials do not infringe any copyright, violate any other intellectual property, privacy or other rights of any person or entity, or contain any libelous or other unlawful matter.
I have obtained written permission from copyright owners for any excerpts from copyrighted works that are included and have credited the sources in the Article or the Supplemental Materials. Except as expressly set out in this License Agreement, the Article is not subject to any prior rights or licenses and, if my or any of my co-authors’ institution has a policy that might restrict my ability to grant the rights required by this License Agreement (taking into account the Author Rights permitted hereunder, including Internal Institutional Use), a written waiver of that policy has been obtained.
If I am using any personal details or images of patients, research subjects or other individuals, I have obtained all consents required by applicable law and complied with the publisher’s policies relating to the use of such images or personal information. If the Article or any of the Supplemental Materials were prepared jointly with other authors, I have informed the coauthor(s) of the terms of this License Agreement and that I am signing on their behalf as their agent, and I am authorized to do so.
The Korean Geriatrics Society Board of Trustees

President
Yong Kyun Roh, Hallym University

Chairperson
Seok Yeon Kim, Seoul Medical Center

Honorary Committee
Haeng Il Koh, Mirea ING
In Soon Kwon, Korea Medical Dispute Mediation and Arbitration Agency
Cheol Ho Kim, Seoul National University
Jong Chun Park, Chonnam National University
Hyun Wook Baik, Bundang Jesaeng Hospital
Seok Whan Shin, Health Insurance Review & Assessment Service (Inchon)
Jun Hyun Yoo, Sungkyunkwan University
Hyung Joon Yoo, CM Hospital
Sang Yun Kim, Seoul National University
Young-Soo Lee, Ulsan University
Jung Ae Rhee, Chonnam National University
Hong Soon Lee, Inje University
Hak Chul Jang, Seoul National University
Kyung Hwan Cho, Korea University
Young Soo Jin, Honorary professor, Ulsan University
Hyun Rim Choi, Good Morning Hospital
Chang Won Won, Kyung Hee University
Il Woo Han, Yong-in Hyoja Geriatric Hospital

Vice-President
Kang Seo Park, Eulji University
Min Ho Chun, Ulsan University

Secretary General
Young Jung Cho, National Medical Center

Treasurer
Su Hyun Kim, Seoul Medical Center

Director, Academic Affairs
Kwang-II Kim, Seoul National University

Director, Board Exam Committee
Eun Ju Lee, Ulsan University

Director, Publication Committee, Editor-in-chief
Jae-Young Lim, Seoul National University

Director, Scientific Committee
Ki Young Son, Ulsan University

Director, Big Data Research TFT
Cheol Min Shin, Seoul National University

Director, Ethics Committee
Nam-Jong Bail, Seoul National University

Director, Committee of Strategic Planning
Yong Deuk Jeon, National Medical Center
Yong Kyun Roh, Hallym University

Director, Medical Policy Planning Committee
Dong-Woo Lee, Inje University
Jae Kyung Choi, Konkuk University

Director, Training Committee
Chang-Oh Kim, Yonsei University

Director, Education Committee
Dae Yul Kim, Ulsan University

Director, Public Relations and Informational Committee
Heewon Jung, Ulsan University

Director, Collaborative Policy Committee of Geriatric Long-term Care Hospital
Hang Suk Cho, Yonsei Noble Hospital

Director, External Cooperation Committee
Il-Young Jang, Ulsan University

Director, Medical Insurance Policy
Hyuk Ga, Incheon Eun-Hye Hospital

Director, Legislation Committee
Be Long Cho, Seoul National University

Director, Nursing and community care TFT
Yong Kyun Roh, Hallym University

Director, Age Friendly Hospital TFT
Jong Min Lee, Konkuk University

Director, Smart Healthcare TFT
Chul Jun Kim, Daejeon Wellness Hospital

Director, International Cooperation Committee
Chang Won Won, Kyung Hee University

Auditor
Sung Hee Hwang, Hallym University
Hwan Sik Hwang, Hanyang University

Special Appointment Director
Young-Kyu Park, OMC Bundang Jesaeng Hospital
Jae Won Ri, Gwanggye Hospital
Yong-Chan Ha, Seoul Bumin Hospital
Yu Hea-Min, Eulji University
Yoon-He Choi, Sungkyunkwan University
Doo Soo Jeon, Catholic University of Korea
Yun Hwan Lee, Aju University
Jae-Geun Lee, Jeju Hospital
Hyeng Kue Park, Chonnam National University

Jan 2022–Dec 2023