pISSN 2508-4798
eISSN 2508-4909

AGMR

Annals of Geriatric Medicine and Research

June 2020 Vol. 24, No. 2

The Korean Geriatrics Society

The Korean Society for Gerontology

www.e-agmr.org

AGMR Annals of Geriatric Medicine and Research

Vol. 24, No. 2, Page 59-153, June 2020

The Korean Geriatrics Society

AGMR
Annals of Geriatric Medicine and Research

AGMR
Annals of Geriatric Medicine and Research

pISSN 2508-4798
eISSN 2508-4909

June 2020 Vol. 24, No. 2

Aims and Scope

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

General Information

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

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. The Korean Geriatrics Society regularly published about 300 copies of printed journals.

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

Printed on June 30, 2020
Published on June 30, 2020
Publisher The Korean Geriatrics Society
Editor-in-Chief Jae-Young Lim

Editorial office
The Korean Geriatrics Society (Ann Geriatr Med Res)
#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

Printing office
M2community Co.
8th FL, DreamTower, 66 Seongsui-ro, Seongdong-gu, Seoul 04784, Korea
Tel: +82-2-2190-7300 Fax: +82-2-2190-7333 E-mail: journal@m2community.co.kr

AGMR
Annals of Geriatric Medicine and Research

Editorial board

AGMR
Annals of Geriatric Medicine and Research

Contents

June 2020 Vol. 24, No. 2

Special Contribution

Invited Review

Review Article

Original Articles

AGMR
Annals of Geriatric Medicine and Research

Contents

June 2020 Vol. 24, No. 2

Case Report

Letter to the Editor

AGMR
Annals of Geriatric Medicine and Research

Special Contribution
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):59-61
https://doi.org/10.4235/agmr.20.0031

The Korean Geriatrics Society COVID-19 Strategy for Older Adults

Hyuk Ga[1], Chang Won Won[2], Eunju Lee[3], Chang Oh Kim[4], Il-Young Jang[3,5], Hak Chul Jang[6], Hang-Suk Cho[7], Sun-wook Kim[8]

[1]Institute of Geriatric Medicine, Incheon Eun-Hye Hospital, Incheon, Korea
[2]Elderly Frailty Research Center, Department of Family Medicine, Kyung Hee University School of Medicine, Seoul, Korea
[3]Division of Geriatrics, Asan Medical Center, Seoul, Korea
[4]Division of Geriatrics, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea
[5]Pyeongchang Health Center & Country Hospital, Gangwon-do, Korea
[6]Department of Internal Medicine, Seoul National University Bundang Hospital and Seoul National University College of Medicine, Seongnam, Gyunggi-do, Korea
[7]Yonsei Noble Hospital, Seoul, Korea
[8]Department of Hospital Medicine, Seoul National University Bundang Hospital, Seongnam, Gyunggi-do, Korea

As of May 16, 2020, the World Health Organization (WHO) reported a total of 4,434,653 confirmed cases of coronavirus disease 2019 (COVID-19) worldwide, including 302,169 COVID-19-related deaths.[1] Since the first case of COVID-19 was reported on January 20, 2020, Korea has extensively tested all contacts, with an emphasis on identifying individuals with respiratory illness, tracing, and testing for severe respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes COVID-19.[2] Older adults are vulnerable to COVID-19; moreover, residents of long-term care facilities (LTCFs) are extremely frail, which is associated with high mortality.[3-6] One of the goals of establishing the Korean Geriatrics Society (KGS) is to make "Recommendations on healthcare for the aged to organizations and institutions".[7] Accordingly, the authors representing the KGS composed a COVID-19 preventive strategy for older adults and posted it to the KGS website on March 13, 2020 (Table 1).[8] The strategies employed the following principles: (1) two separate guidelines for older adults residing in community and LTCFs, respectively, reflecting the unique differences in their health conditions and environments; (2) strategies for LTCF health workers because their roles are crucial in LTCF infection control; (3) written in an easily comprehensible manner so that it can be clearly followed; (4) to follow general recommendations from international organizations such as the WHO and the Centers for Disease Control and Prevention (CDC), with modifications according to domestic policies as stipulated by the Korean Centers for Disease Control and Prevention (KCDC); and (5) to encourage indoor activities to prevent frailty, depression, and enhance resilience.[9-11]

Our guidelines have some unique features. First, we included strategies for long-term care hospitals (LTCHs) among those for LTCFs. LTCHs are a wide-spread unique form of hospitals for frail and activities of daily living (ADL)-dependent older people in Korea; however, we assumed that the strategies for LTCHs are similar to those for LTCFs (nursing homes).[12,13] Second, we emphasized the importance of wearing facemasks regularly even in encounters with older adults or healthcare workers without respiratory symptoms, as 5% to 75% of positive cases are reportedly asymptomatic SARS-CoV-2 carriers.[14] Third, we divided the LTCF strategies into three parts; namely, blocking spread INTO, WITHIN, and BETWEEN facilities. In addition, the Korean Ministry of Health and Welfare issued a temporary regulation that permits telephone-based consultation and prescription and covers half of the expenses for COVID-19 testing for all new inpatients of LTCHs.[11]

On May 2, 2020, the KCDC announced zero positive cases from randomly-screened samples from among 6,544 residents and care assistants of 46 LTCHs in the Seoul area.[15] However, new outbreaks have occurred since then and even tertiary transmission of COVID-19 has been reported in communities;[16] therefore, we believe our recommendations should be strictly followed until these conditions resolve, with revision of these guidelines as needed.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The author claims no conflicts of interest.

Table 1. Preventive strategies for coronavirus disease (COVID-19) infection in older adults

For community-dwelling older adults

A. Wash your hands frequently. Rub your hands with soap and water for 20 seconds or more, especially after nose-blowing, coughing, and visiting public places.
B. Hand sanitizers containing 60% alcohol can be used instead of soap and water.
C. Try to avoid touching your face, nose, and eyes with your bare hands.
D. Stay at home and avoid visiting crowded or enclosed spaces.
E. When going out, wear facemasks for the safety of yourselves and others.
F. Keep yourselves healthy with indoor exercise, regular eating, and sun exposure.
G. When prescribed medicines whose stocks are low, ask healthy family for prescription.

For residents and health-care workers in long-term care facilities

A. Blocking spread INTO facilities
1. Managing visitors
- Regulation of interviewers: communication with residents via video-telephoning is recommended
- Minimizing work experience of trainees and strict education regarding infection control
- Minimizing volunteer activities
2. Post signs at the entrances requesting that visitors not enter if they have one of the respiratory symptoms or signs: fever 37.5°C or more, coughing, or dyspnea.
3. Educate healthcare workers to stay at home if they have respiratory symptoms.
4. Educate healthcare workers to abstain from joining external meetings and dining together and to wear facemasks if they should meet people.
5. Check all incoming inpatients for respiratory symptoms. Refer to local public healthcare centers for COVID-19 tests if they have any of them.

B. Blocking spread WITHIN facilities
1. Check all residents and healthcare workers for fever or respiratory symptoms.
2. All healthcare workers should wear facemasks and wash hands before and after contacting residents. Especially, care assistants should wash their hands and discard gloves every time they change residents in their care.
3. Make clear to residents and workers the actions required to protect against COVID-19 infection.
4. Suspected COVID-19 patients should be reported to public healthcare centers, isolated from others, and tested for infection.

C. Blocking spread BETWEEN facilities
1. Minimize transfers to other facilities unless the residents have respiratory symptoms or emergency state.
2. Phone calls should precede transfer other facilities if the residents have respiratory symptoms.

REFERENCES

1. World Health Organization. Coronavirus disease (COVID-2019) situation reports [Internet]. Geneva, Switzerland: World Health Organization; c2020 [cited 2020 May 31]. Available: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.
2. Black JR, Bailey C, Przewrocka J, Dijkstra KK, Swanton C. COVID-19: the case for health-care worker screening to prevent hospital transmission. Lancet 2020;395:1418-20.
3. Na S, Cho Y, Lim TH, Kang H, Oh J, Ko BS. (2019). Risk factors and causes of short-term mortality after emergency department discharge in older patients: using nationwide health insurance claims data. Ann Geriatr Med Res 2019;23:133-40.
4. Kojima G. Prevalence of frailty in nursing homes: a systematic review and meta-analysis. J Am Med Dir Assoc 2015;16:940-5.
5. Ga H, Won CW, Jung HW. Use of the frailty index and FRAIL-NH scale for the assessment of the frailty status of elderly individuals admitted in a long-term care hospital in Korea. Ann Geriatr Med Res 2018;22:20-5.
6. Comas-Herrera A, Zalakain J, Litwin C, Hsu AT, Lane N, Fernandez JL. Mortality associated with COVID-19 outbreaks in care homes: early international evidence [Internet]. London, UK: International Long Term Care Policy Network; 2020 [cited 2020 May 31]. Available: https://ltccovid.org/2020/04/12/mortality-associated-with-covid-19-outbreaks-in-care-homes-early-international-evidence/.
7. The Korean Geriatrics Society. History of the Korean Geriatrics Society [Internet]. Seoul, Korea: The Korean Geriatrics Society; c2014 [cited 2020 May 31]. Available from: http://www.geriatrics.or.kr/eng/organ/organ01.html.
8. The Korean Geriatrics Society. Preventive strategies for coronavirus disease (COVID-19) infection in older adults [Internet]. Seoul, Korea: The Korean Geriatrics Society; 2020 [cited 2020 May 31]. Available from: http://www.geriatrics.or.kr/board/list.html?num=2215&start=10&sort=top%20desc,num%20desc&code=notice&key=&keyword=.
9. Centers for Disease Control and Prevention. Preparing for

COVID-19 in Nursing Homes [Internet]. Atlanta, GA: Centers for Disease Control and Prevention; c2020 [cited 2020 May 31]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/long-term-care.html.
10. Korea Centers for Disease Control and Prevention. Maneuver for COVID-19 Combat for local government (version 7-1). Sejong: Korea Centers for Disease Control and Prevention; 2020.
11. Lim WS, Liang CK, Assantachai P, Auyeung TW, Kang L, Lee WJ, et al. COVID-19 and older people in Asia: AWGS calls to actions. Geriatr Gerontol Int 2020;May 4;[Epub]. http://doi.org/10.1111/ggi.13939.
12. Sanford AM, Orrell M, Tolson D, Abbatecola AM, Arai H, Bauer et al. An international definition for "nursing home". J Am Med Dir Assoc 2015;16:181-4.
13. Ga H, Won CW. Perspective on long term care hospitals in Korea. J Am Med Dir Assoc 2013;14:770-2.
14. Heneghan C, Brassey J, Jefferson T. COVID-19: What proportion are asymptomatic? [Internet]. Oxford, UK: Centre for Evidence-Based Medicine; c2020 [cited 2020 May 31]. Available from: https://www.cebm.net/covid-19/covid-19-what-proportion-are-asymptomatic/.
15. Lim S. 6544 samples from 46 long-term care hospitals in Seoul area were reported all negative [Internet]. Seoul, Korea: Medigate News; 2020 [cited 2020 May 31]. Available from: https://www.medigatenews.com/news/1106529578.
16. Ock H. From Itaewon to Hongdae, coronavirus spread through karaoke rooms [Internet]. Seoul, Korea: The Korea Herald; 2020 [cited 2020 May 31]. Available from: http://www.koreaherald.com/view.php?ud=20200515000724.

Corresponding Author: Chang Won Won, Elderly Frailty Research Center
Department of Family Medicine, Kyung Hee University School of Medicine, Kyungheedae-ro, Dongdaemun-gu, Seoul, Korea [02447]
Tel : +82-2-958-8700
Fax : +82-2-958-8699
E-mail: chunwon62@naver.com
ORCID: https://orcid.org/0000-0002-6429-4461

Received: May 19, 2020 ; Revised: May 26, 2020; Accepted: June 17, 2020

AGMR
Annals of Geriatric Medicine and Research

Invited Review
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):62-74
https://doi.org/10.4235/agmr.20.0002

Measuring Frailty in Health Care Databases for Clinical Care and Research

Dae Hyun Kim

Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife, Boston, MA, USA
Division of Gerontology, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA
Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA
Harvard Medical School, Boston, MA, USA

Corresponding Author:
Dae Hyun Kim, MD, MPH, ScD
Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife, Boston, MA 02131, USA
Email: daehyunkim@hsl.harvard.edu
ORCID:
https://orcid.org/0000-0001-7290-6838

Received: January 22, 2020
Revised: February 10, 2020
Accepted: March 16, 2020

Considering the increasing burden and serious consequences of frailty in aging populations, there is increasing interest in measuring frailty in health care databases for clinical care and research. This review synthesizes the latest research on the development and application of 21 frailty measures for health care databases. Frailty measures varied widely in terms of target population (16 ambulatory, 1 long-term care, and 4 inpatient), data source (16 claims-based and 5 electronic health records [EHR]-based measures), assessment period (6 months to 36 months), data types (diagnosis codes required for 17 measures, health service codes for 7 measures, pharmacy data for 4 measures, and other information for 9 measures), and outcomes for validation (clinical frailty for 7 measures, disability for 7 measures, and mortality for 16 measures). These frailty measures may be useful to facilitate frailty screening in clinical care and quantify frailty for large database research in which clinical assessment is not feasible.

Key Words: Frailty, Healthcare administrative claims, Electronic health records

INTRODUCTION

Frailty is a clinical state resulting from age-related changes in multiple physiologic systems and accumulation of diseases that reduces patient ability to maintain homeostasis in response to stressors.[1] Frailty is common in older adults, affecting one in every 10 community-dwellers[2,3] and one in every two nursing home residents,[4] and is associated with increased risks of death (relative risk [RR], 1.6–6.0), disability (RR, 1.8–2.8), institutionalization (RR, 2.6–24.0), and falls (RR, 1.2–2.4).[1] Health care costs for older adults with frailty increase by up to 2-fold compared to those in their non-frail counterparts,[5,6] mainly due to inpatient care, post-acute care, and care for potentially preventable conditions.[7,8] Given the considerable clinical and societal consequences of frailty in the ever-growing aging population, assessment of frailty in clinical and population settings offers valuable opportunities for prevention and treatment through efficient use of evidence-based interventions and resources.[9-11]

Several validated tools are available to measure frailty,[12-15] which can be selected based on the purpose (screening, diagnosis, or monitoring response to interventions), setting (emergency department, inpatient, outpatient, or public health), and available resources (trained staff to perform self-report vs. objective assessment).[16] Although simple clinical assessment tools[17-19] and online calculators are available,[20] frailty assessment typically requires clinical assessment in the form of a survey[21-23] or objective assessments of physical performance[24-27] conducted by a clinician (e.g., geriatrician) or trained health care professional. However, routine adoption of the frailty concept for clinical care or public health practice is variably slow across health systems in different countries,[11] in part due to a lack of time and resources for assessment.[28,29] To overcome these barriers, there is a growing interest in the measurement of frailty using ubiquitous health care databases such as administrative claims data and electronic health records (EHRs), which are by-products of health care encounters and transactions between health care providers and health plans. Admin-

istrative claims data contain diagnosis codes, health service codes, and prescription drug data obtained from a large population of health plan members but lack detailed clinical information such as vital signs, physical examination findings, and diagnostic test results. In contrast, EHR provide clinical information not available in administrative claims data; however, much of the information is unstructured (e.g., narrative clinical notes) and may be discontinuous due to patients receiving care at multiple health systems using different EHR systems.[30] Nonetheless, frailty scores derived from health care databases ("database-derived frailty measures") hold promise for population-level frailty screening as well as health services and outcomes research in frail older adults who are under-represented in clinical trials.[31]

This review summarizes the latest advances in frailty measurement in health care databases, mainly administrative claims data and EHR, as well as the potential applications for clinical care and research. Frailty measures requiring in-person surveys or evaluations are beyond the scope of this review. The outline is as follows: (1) literature search; (2) general approaches to frailty measurement in health care data; (3) frailty measurement in administrative claims data; (4) frailty measurement in EHR; (5) considerations in developing a database-derived frailty measure; (6) potential applications of database-derived frailty measures; (7) areas of uncertainty; and (8) conclusions.

LITERATURE SEARCH

A literature search was conducted in PubMed using the Medical Subject Headings, "frailty" AND ("administrative claims, healthcare" OR "electronic health records" OR "Medicare"), and their variations in the title field. Additional filters were applied, including publication date, January 1, 2001, to December 31, 2019, and "aged, 65+ years". This search yielded 50 articles. Risk scores derived from health care databases that aimed to predict mortality or hospitalization were not considered as frailty measures, although they may also be correlated with frailty.[32,33] From the search results, 10 reviews or commentaries; 9 articles using frailty measures not derived from health care databases; and 8 articles not reporting development, validation, or application of database-derived frailty measures were excluded. The initial search was supplemented by an additional 29 articles from the references of the included articles. Finally, 52 articles informed this review.

GENERAL APPROACHES TO FRAILTY MEASUREMENT IN HEALTH CARE DATA

Health care databases generated primarily for health care service administration, care quality assessment, and clinical care delivery generally do not contain sufficient information to derive clinically validated measures of frailty.[12-15] Therefore, frailty measures[24-27] requiring clinical assessment (e.g., gait speed, grip strength, physical activity, or cognitive function) cannot be directly calculated. In the absence of sufficient clinical information, researchers attempted to measure frailty using demographic information, diagnosis codes, or health service codes available in health care databases. The approach to developing a frailty measure depended on the availability of a dataset containing a reference standard measure of frailty and methods to select diagnosis and health service codes in health care databases (Fig. 1).

Clinical Knowledge-Driven Selection

Health care providers and researchers with expertise in aging and frailty select diagnosis codes or health service codes based on prior research and clinical knowledge. These codes may include diseases (e.g., pressure ulcer, failure to thrive, or history of falls), symptoms or signs (e.g., fatigue, muscle weakness, abnormality of gait), and health services (e.g., hospital beds, walking aids, or transportation services) commonly reported or used by older adults with frailty.[31] Frailty has been defined as the presence of any code within a pre-specified period (e.g., 12 months), while its absence assumes that the condition does not exist. This approach is straightforward and does not require a dataset containing a reference standard measure of frailty. It generally offers high specificity and low sensitivity but underestimates frailty prevalence. Alternatively, researchers have quantified frailty by counting the number of different codes in a pre-specified period and deriving a deficit-accumulation frailty index[34] using these codes as health deficits. For example, a person with 10 of 40 pre-specified codes within a 12-month period is assigned a frailty index of 0.25 (= 10/40). The deficit-accumulation approach allows measurement of severity rather than all-or-none classification and choice of a threshold to achieve high sensitivity or high specificity depending on the purpose. Notably, a deficit-accumulation frailty index calculated mainly from diagnosis codes seems to have a narrower range of values (99th percentile 0.4–0.5)[35] than that for a frailty index calculated from clinical assessment (99th percentile 0.6–0.7).[36]

Data-Driven Selection without a Reference Standard

When a dataset with a reference standard frailty measure is not available, researchers have tried to define frail individuals in the dataset by cluster analysis.[37] Cluster analysis is an unsupervised learning technique that classifies individuals into groups of similar nature in terms of measured characteristics in the dataset such as diagnosis codes, hospital days, and total costs during a pre-specified period. After examining the characteristics of the groups derived from cluster analysis, one of the groups (i.e., the group with a

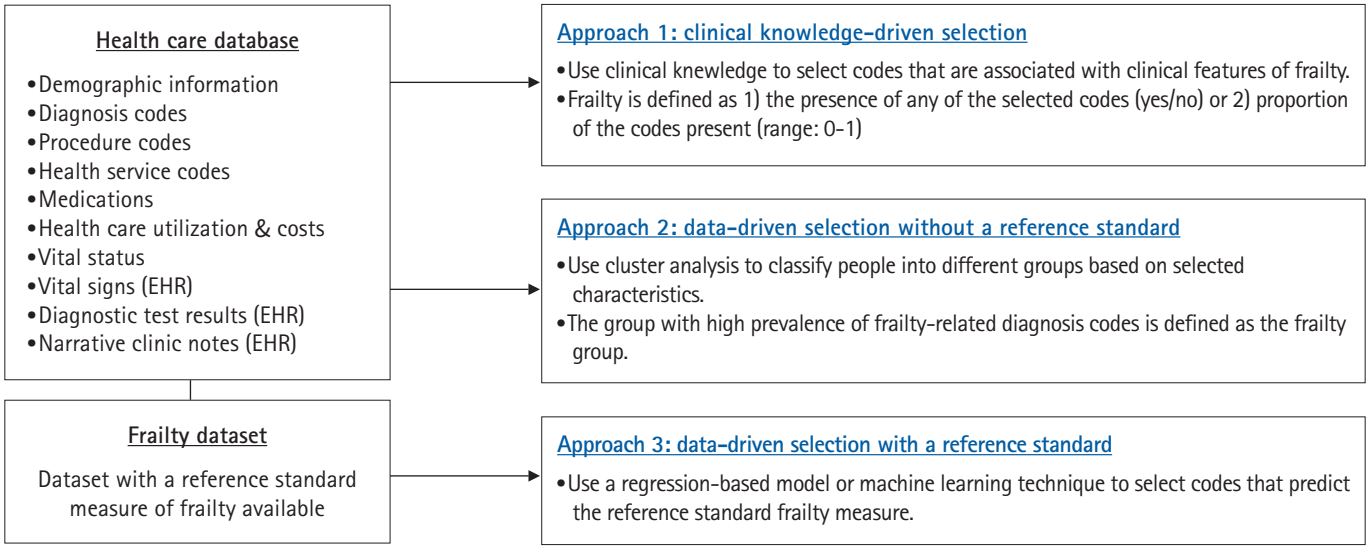

Fig. 1. Approaches to developing a frailty measure in health care databases. Prior research applied three general approaches to develop a frailty measure for health care databases. When a dataset containing information on a reference standard measure of frailty was not available, frailty was measured using diagnosis and health service codes selected based on clinical knowledge (approach 1) or cluster analysis using diagnosis codes, hospital days, and total costs (approach 2). When a dataset with a reference standard measure of frailty was available, a variable selection method (e.g., penalized regression or machine learning technique) was used to select diagnosis and health service codes to measure frailty (approach 3). EHR, electronic health records.

high number of diagnoses indicative of frailty) can be designated as the frailty group. However, cluster analysis can be computing-intensive for large datasets and may not yield the same grouping in different datasets. Gilbert et al.[37] tried to overcome this limitation by conducting cluster analysis in a subset of a large hospital administrative dataset and developing a logistic regression model to predict frailty group membership based on diagnosis codes. The predicted probability from this logistic model can be used to assign individuals to the frailty group from the entire dataset. While this approach identifies frail individuals without requiring a dataset with a reference standard frailty measure, determining the number of groups in the cluster analysis and designating a single frailty group may be subject to interpretation. Moreover, frail individuals may not be classified exclusively into a single group (e.g., frail people with cancer and frail people with heart disease may be classified into different groups despite similar levels of frailty).[38]

Data-Driven Selection with a Reference Standard

If a population-based dataset containing information on a reference standard frailty measure (e.g., frailty phenotype or deficit-accumulation frailty index) and administrative claims data is avaiable, specific codes can be selected against the reference frailty measure (also known as supervised learning). Several variable selection algorithms have been applied— e.g., stepwise regression,[39,40] penalized regression,[39,41] or tree-based algorithms.[39] More flexible "black-box" machine learning algorithms such as random forest and gradient boosting, provide limited or marginal advantages over regression-based algorithms in predictive performance.[39] Under this approach, the first step is variable selection and estimation of weights (in regression models) to optimize predictive performance against a reference standard measure of frailty in a training dataset. The model derived from the training dataset is evaluated in a hold-out testing dataset or via cross-validation. This method can select codes that are positively (e.g., degenerative disease of the central nervous system) or negatively (e.g., vaccination) associated with frailty. It provides better predictive performance of frailty and adverse health outcomes than counting the number of codes or calculating a deficit-accumulation frailty index directly from the codes.[41]

FRAILTY MEASUREMENT IN ADMINISTRATIVE CLAIMS DATA

Table 1 summarizes 16 frailty measures for administrative claims data. Of these, 12 measures were developed for the United States Medicare[8,39-48] or Veterans Affairs[49,50] claims databases, including two proprietary measures; namely, the Johns Hopkins Adjusted Clinical Groups Frailty Indicators[43] and JEN-Frailty Index,[45,46] two were developed for the Canadian claims databases,[51,52] and two were developed for the United Kingdom hospital claims data-

Table 1. Frailty measures for administrative claims data

	Author (y)	Database/population (study year)	Outcomes		Predictors
			Development	Validation	
Clinical knowledge-driven selection	Lunney et al.[42] (2002)	Medicare database (USA) - Medicare 0.1% sample (1993–1998)[42]	Not applicable	None	Presence (yes/no) of any of 11 conditions based on ICD diagnosis codes
	Abrams et al.[43] (2003)	Medicare database (USA)[43] - HMO in Israel (2008)[54] - Major non-cardiac surgery, emergency general surgery, orthopedic surgery patients in Canada (2002–2014)[80-83]	Not applicable	Vulnerable Elders Survey Mortality Complications Discharge disposition Costs	Presence (yes/no) of any of 10 conditions based on ICD diagnosis codes (Johns Hopkins Adjusted Clinical Groups)
	Chrischilles et al.[44] (2014)	Medicare database (USA) - Acute MI patients (2007–2008)[44] - Kidney cancer patients (2000–2009)[84]	Not applicable	Mortality Cardiac catheterization Complications Costs	Presence (yes/no) of any or ≥ 2 of 16 conditions based on ICD diagnosis and HCPCS codes
	JEN Associates[45,46] (2008)	Medicare database (USA)[45,86] - Spouses of AD patients (2001–2005)[85] - National Long-Term Care Survey (2004)[60] - Medicare 5% sample (2011–2014)[61]	Not applicable	Mortality NH admission Costs Disability	Count of the number of 13 conditions present based on ICD diagnosis codes (JEN-Frailty Index)
	Hope et al.[47] (2015)	Medicare database (USA) - ICU patients (2004–2008)[47]	Not applicable	Mortality	Presence (yes/no) of nursing facility claims or 11 conditions based on ICD diagnosis codes
	Soong et al.[53,87] (2015)	Inpatient claims database, England - HES database (2005–2013)[53,87]	Not applicable	Mortality Discharge disposition Readmission	Presence (yes/no) of any of 9 conditions based on ICD diagnosis codes
	Joynt et al.[8] (2017)	Medicare database (USA) - Medicare 20% sample (2011–2012)[7,8]	Not applicable	Costs	Presence (yes/no) of ≥ 2 of 12 conditions based on ICD diagnosis codes and HCPCS codes (specified by Kim and Schneeweiss)[31]
	Orkaby et al.[49] (2018)	VA claims database (USA) - National sample (2002–2012)[49]	Not applicable	Mortality	Proportion of 31 health deficits present based on ICD diagnosis, CPT, and HCPCS codes
	McIsaac et al.[51] (2019)	Administrative claims database (Canada) - Major non-cardiac surgery (2002–2015)[51,88]	Not applicable	Mortality Discharge disposition	Proportion of 30 health deficits present based on ICD diagnosis codes, drugs, assistive device codes, and living environment (preoperative Frailty Index)
Data-driven selection without a reference standard	Gilbert et al.[37] (2018)	Inpatient claims database, England - HES database (2005–2013)[37] - Hospital cohorts[37]	Frailty cluster (from cluster analysis)	Mortality Prolonged hospitalization Readmission Frailty phenotype Deficit-accumulation FI	Includes 109 ICD diagnosis variables
Data-driven selection with a reference standard	Rosen et al.[50] (2000)	VA claims database (USA) - Long-term care (1996–1997)[50,89]	Disability	Disability	Includes 13 conditions based on ICD diagnosis codes
Data-driven selection with a reference standard	Dubois et al.[52] (2010)	Prescription claims database (Canada) - PRISMA cohort (2001–2005)[52]	Functional status score	Mortality Disability Hospitalization NH admission	Includes 11 prescription drug categories
	Davidoff et al.[40] (2013)	Medicare database (USA) - MCBS cohort (2001-2005)[40] - HRS cohort (2008-2010)[56] - SEER-Medicare cohort (1999–2007)[90,91]	Disability	Mortality Disability Frailty phenotype Deficit-accumulation FI	Includes sex, Medicaid enrollment, number of office visits, 8 health care visit types, 3 health care services, 9 procedures, 6 DMEs, and 2 imaging tests based on CPT and HCPCS codes, and geographical regions

(Continued to the next page)

Table 1. Continued

Author (y)	Database/population (study year)	Outcomes		Predictors
		Development	Validation	
Faurot et al.[48] (2015)	Medicare database (USA) - MCBS cohort (2006)[48] - Medicare beneficiaries with or without influenza vaccination (2007–2008)[62] - ARIC cohort (2011–2013)[58] - MarketScan Medicare (2013)[63] - HRS cohort (2008-2010)[56]	Disability	Mortality Disability Falls Mobility impairment Frailty phenotype Deficit-accumulation FI Costs	Includes age, sex, race, and 23 conditions based on ICD diagnosis, CPT, or HCPCS codes
Segal et al.[39,55] (2017)	Medicare database (USA) - CHS cohort (1992–1993/1997)[39] - NHATS cohort (2000)[55] - Medicare TAVR cohort (2011-2015)[64] - HRS cohort (2008-2010)[56]	Frailty phenotype	Mortality Disability Hospitalization Fracture NH admission Frailty phenotype Deficit-accumulation FI	Includes age, sex, race, Charlson Comorbidity Index, past hospitalization, and 16 conditions based on ICD diagnosis codes
Kim et al.[41] (2018)	Medicare database (USA) - MCBS cohort (2006–2007/2011–2012)[41] - HRS cohort (2008–2010)[56,57]	Deficit-accumulation FI	Mortality Disability Hospitalization SNF stay NH admission Falls Frailty phenotype Deficit-accumulation FI	Includes 52 ICD diagnosis variables, 25 CPT variables, and 16 HCPCS variables

AD, Alzheimer disease; ARIC, Atherosclerosis Risk in Communities; CHS, Cardiovascular Health Study; CPT, Current Procedural Terminology; DME, durable medical equipment; FI, frailty index; HCPCS, Healthcare Common Procedure Coding System; HES, Hospital Episode Statistics; HMO, health maintenance organization; HRS, Health and Retirement Study; ICD, International Classification of Diseases; ICU, intensive care unit; MCBS, Medicare Current Beneficiary Survey; MI, myocardial infarction; NH, nursing home; NHATS, National Health and Aging Trends Study; PRISMA, Program of Research to Integrate Services for the Maintenance of Autonomy; SEER, Surveillance, Epidemiology, and End Results; TAVR, transcatheter aortic valve replacement; VA, Veterans Affairs.

base.[37,53] Database-derived frailty measures varied widely in terms of development approaches (clinical knowledge in nine measures, cluster analysis in one measure, and reference standard measures in six measures), number of variables included (nine to 109 variables), target populations (general vs. specific disease populations), and validation outcomes (clinical frailty assessment, functional status, mortality, health care utilization, or costs). Only seven of 16 measures have been compared against a clinical frailty assessment[37,54-59] and seven measures have been tested for disability[50,52,56,57,60] or nursing home admission.[45,52,57,60]

The comparative performance of database-derived frailty measures has not been well studied. In an analysis of Medicare Current Beneficiary Survey data, implementation of a deficit-accumulation frailty index using commonly used diagnosis codes or health service codes showed lower correlation with a reference standard frailty index and was less predictive of mortality than a frailty measure developed using a least absolute shrinkage and selection operator (LASSO) regression.[41] A recent study compared four Medicare claims-based frailty measures—Davidoff index,[40] Faurot index,[48] Segal index,[39] and Kim index[41]—for the ability to measure frailty phenotype, deficit-accumulation frailty index, and activities-of-daily-living dependency (requiring another person's help to perform daily activities). Of the four measures, the Kim index showed higher C statistic for frailty phenotype (0.78 vs. 0.73–0.74) after age and sex adjustment, as well as age and sex-adjusted partial correlation with a deficit-accumulation frailty index from clinical assessment (0.55 vs. 0.18–0.32).[56]

These frailty measures have been applied to define population subgroups by frailty levels,[61] reduce confounding by frailty in examining the association between influenza vaccination and mortality,[62] estimate health care costs attributed to frailty,[63] and improve mortality prediction after transcatheter aortic valve replacement.[64]

FRAILTY MEASUREMENT IN EHR

Table 2 summarizes five frailty measures for EHR. Four measures were developed for three United States regional EHR systems[65-68] or the Veterans Affairs EHR database,[69] while the e-Frailty Index was developed for the United Kingdom primary care practices,[35] which was later implemented in a primary care EHR system in Australia.[59] Clinical knowledge-based selection was used for four mea-

Table 2. Frailty measures for electronic health records

	Author (y)	Database/population (study year)	Outcomes		Predictors
			Development	Validation	
Clinical knowledge-driven selection	Clegg et al.[35] (2016)	Primary care EHR database (UK) - ResearchOne database (2008–2016)[35,70,75] - THIN database (2008–2013)[35,73] - CPRD database (2001–2009)[71,72] Primary care EHR database, Australia - A primary care clinic[59]	Not applicable	Mortality Hospitalization NH admission Fracture Frailty phenotype	Proportion of 36 health deficits present based on Read codes (codes for diagnosis, procedure, disability, and social circumstances) and polypharmacy
	Lekan et al.[65] (2017)	A tertiary-care hospital EHR database (USA) - Inpatients (2010–2011)[65,66]	Not applicable	Mortality Readmission SNF stay	Includes 16 biopsychosocial factors including 4 laboratory tests
	Anzaldi et al.[67] (2017)	A regional health system EHR database (USA) - Medicare ACO enrollees (2011–2013)[67]	Not applicable	Geriatric syndromes identified using diagnosis codes and text phrases	Mention of "frailty" in clinical notes
	Pajewski et al.[68] (2019)	A regional health system EHR database (USA) - Medicare ACO enrollees (2014–2016)[68]	Not applicable	Mortality Falls Health care utilization	Includes 54 health deficits based on diagnosis codes, smoking status, vital signs, laboratory tests, and functional status
Data-driven selection without a reference standard	Shao et al.[69] (2017)	VA EHR database (USA) - Heart failure patients (2010)[69]	Topics generated from clinical notes	Mortality Hospitalization	Includes 53 topics generated from clinical notes

ACO, accountable care organization; CPRD, Clinical Practice Research Datalink; EHR, electronic health records; NH, nursing home; SNF, skilled nursing facility; THIN, The Health Improvement Network; VA, Veterans Affairs.

sures while data-driven selection without a reference standard was used for one measure. A natural language processing method to explore unstructured clinic notes was applied for two measures.[67,69]

Of these measures, the e-Frailty Index has been most widely used in the United Kingdom primary care EHR database to describe frailty trajectories before dying,[70] examine the effect measure modification of systolic blood pressure and mortality relationship by frailty,[71] predict fractures and mortality after fractures,[72] and assess de-intensification for diabetes and hypertension treatment regimens among older adults with frailty.[73]

CONSIDERATIONS IN DEVELOPING A DATABASE-DERIVED FRAILTY MEASURE

Database-derived frailty measures use different types of data (e.g., diagnosis, procedure, and health service codes) collected over a pre-specified period, ranging from 6[39] to 36[49] months. Because some claims datasets record information according to a unique coding system specific to each country (e.g., Current Procedural Terminology codes and Healthcare Common Procedure Coding System codes in the United States and Read codes in the United Kingdom), the choice of datasets can affect the transportability of the frailty measures. The length of the assessment period during which codes are measured may affect the accuracy of capturing certain chronic conditions. Chronic conditions that are less likely recognized or coded by general practitioners (e.g., dementia and incontinence) may require a longer assessment period than acute conditions (e.g., acute myocardial infarction) or well recognized chronic conditions (e.g., hypertension and diabetes). A longer assessment period to calculate a frailty measure reduces the amount of follow-up data available for the main analysis.

Frailty measures developed from health care databases tend to rely on diagnoses, whereas clinical frailty assessment relies more on functional status and physical performance, factors rarely available in health care databases. Health service codes indicating clinical encounter types (e.g., home visits) and use of durable medical equipment (e.g., hospital beds or wheelchairs) seem to be important to capture functional impairment or poor physical perfor-

mance, which differentiates frailty measures from comorbidity indices.[57] However, including demographic characteristics in the frailty model lessens its ability to explain variation in frailty beyond demographic variables.[56]

Once a frailty measure is developed, the key step is its validation against a reference standard measure of frailty. Given the lack of consensus on frailty definitions,[12] prevalent activities-of-daily-living dependency can be used as an alternative outcome for validation.[40,48,56,60] However, information on a reference standard frailty measure or activities-of-daily-living dependency is not always available. Many database-derived frailty measures were tested for mortality prediction rather than for frailty itself. Although frailty is associated with mortality, it is unclear how these frailty measures can be differentiated from mortality prediction models.

Another consideration is that coding systems or coding practices may change over time or vary across geographical regions. In the United States, the International Classification of Disease system transitioned from the 9th to 10th revisions in October 2015. New billing codes are generated for new procedures and health care services and some codes are retired each year. Coding practice may be influenced by the likelihood of reimbursement for health care services, which may differ across health care systems or countries. Therefore, the performance of claims-based frailty measures should be evaluated periodically in more contemporary datasets and before application to a different health care system or country.

Lastly, the development of a frailty measure from EHR may require restricting the population to those with high rates of data completeness within an EHR system to avoid bias due to health information outside the EHR system.[30] A predictive algorithm is available to identify those with high rates of completeness.[74]

POTENTIAL APPLICATIONS OF DATABASE-DERIVED FRAILTY MEASURES

Frailty measures calculated from health care databases can be useful to measure frailty and study health outcomes of older adults with frailty in clinical care and research (Table 3).

Clinical Care

Database-derived frailty measures can be used to screen older adults for frailty in a health care system or a health plan. Because database-derived frailty scores generally have C statistics ranging from 0.65 to 0.75 for frailty phenotype and correlation coefficients of 0.2 to 0.6 against a deficit-accumulation frailty index,[37,39,56] they are unlikely to replace bed-side clinical frailty assessments. Frailty measures are useful to predict adverse health outcomes. In particular, the Kim index performed better than a comorbidity index for the prediction of disability, mobility impairment, recurrent falls, and skilled nursing facility days in the Medicare population.[41,57] However, an e-Frailty Index >0.19, a threshold for frailty, had a positive predictive value of 0.11 for death in the next 3 months among primary care patients in the United Kingdom. These results suggest that, although a database-derived frailty measure may be a strong predictor in a population, it cannot be interpreted deterministically for an individual (this issue also exists for a clinical frailty assessment).[75] Nonetheless, they can be useful as a routine screening test to identify individuals requiring additional detailed assessment and individualized care management.[76] A cut-off point for positive screening can be determined according to percentile distributions (e.g., top 5% percent), sensitivity and specificity for frailty state (e.g., 90% sensitivity to detect frailty phenotype), or pre-defined clinically relevant thresholds (e.g., ≥ 0.20 according to a deficit-accumulation frailty index) after considering clinical contexts (e.g., outpatient, inpatient, or preoperative screening) and available resources for detailed assessment and care management.

Research

Database-derived frailty measures provide vast opportunities for clinical research in older populations. These measures can be used to efficiently screen individuals for enrollment in a clinical trial of interventions for frailty. In database studies to evaluate treatment effects in older adults, treated individuals may differ in frailty levels from untreated individuals, which leads to confounding. Such bias can be reduced by adjusting for a frailty measure, although residual confounding may persist.[62] In choosing a frailty measure for confounding adjustment, a measure that does not include demographic variables may be more effective than a measure that includes them.[56] Moreover, frailty can be an effect measure modifier. The benefits and risks of a treatment may vary by frailty status—e.g., a hypnotic drug increases the risk of hip fracture more in less frail older adults than frailer ones who are totally dependent.[77] Evaluation of treatment effect heterogeneity by frailty in health care databases may provide real-world evidence to guide individualized treatment choice based on frailty assessment in older adults who are typically excluded from clinical trials. In some clinical trials that enrolled frail individuals yet lacked frailty assessment, frailty levels at trial baseline can be estimated by linking trial data to administrative claims data or EHR and applying database-derived frailty measures. Such secondary analyses of existing clinical trial data may generate hypotheses for future trials.

AREAS OF UNCERTAINTY

Few studies to date used a database-derived frailty measure as an

Table 3. Potential applications of database-derived frailty measures and areas for future research

Areas	Applications	Caveats/areas for future research
Clinical care	Screen for frail individuals requiring detailed evaluation and care management in a health care system or health plan Predict the risk of adverse health outcomes (frailty measures are more useful than comorbidity measures for the prediction of disability, mobility impairment, falls, and SNF days).	Database-derived frailty measures are acceptable yet imperfect; thus, they are unlikely to replace clinical assessment. Seeking health care during acute illness or functional decline may lead to overestimation of the frailty level (informed presence bias). Further improvement in frailty measurement may be possible by including clinical assessment datasets (e.g., MDS or OASIS in the United States Medicare database) or EHR clinic notes.
Research	Efficiently screen for frail individuals to enroll in a clinical trial Adjust for case-mix (confounding) by frailty in evaluating the effect of medical treatment or outcomes among health care systems Evaluate the treatment effect heterogeneity by frailty in analysis of health care databases or clinical trial datasets (by linking clinical trial data to claims data for estimation of frailty level)	Responsiveness and MCID of database-derived frailty measures remain to be investigated. The assessment period used to calculate a frailty measure ranges from 6 to 36 months. The optimal period is not known. Residual confounding may exist even after adjusting for case-mix by using a database-derived frailty measure. Usefulness of EHR data may depend on the health information technology infrastructure and completeness of documentation.

EHR, electronic health records; MCID, minimal clinically important difference; MDS, Minimum Data Set; OASIS, Outcome and Assessment Information Set; SNF, skilled nursing facility.

outcome (i.e., change in frailty level over time) to evaluate the treatment effect. The responsiveness of a frailty measure to improvement or deterioration of health status and the minimal clinically important change have not been well studied. Diagnosis codes, which comprise a large proportion of the database-derived frailty measures, tend to be carried over visits and accumulate over time in administrative claims data or EHR, causing increased frailty score. Since older adults are more likely to seek medical care during acute illness or functional decline (informed presence bias[78]), the estimated frailty level may be affected by the effect of acute illness and frailty progression may be recorded more often than improvement. Furthermore, in health care databases, the information needed to estimate frailty is obtained over time as opposed to clinical trials wherein information is obtained from a discrete assessment visit (e.g., baseline or follow-up visit). Therefore, the assessment periods may overlap between outcome frailty and baseline frailty, making the two measures highly collinear. For these reasons, the utility of a database-derived frailty measure as a treatment outcome remains uncertain.

Information on functional status or physical performance is often recorded in health care databases. In United States Medicare data, the Minimum Data Set records clinicians' assessments of functional status among nursing home patients. The Outcome and Assessment Information Set contains information on patient outcomes for individuals receiving home care. In EHR, cognitive function and physical function are documented in clinical notes by primary care physicians, specialists (e.g., geriatricians, neurologists, and psychiatrists), physical therapists, or occupational therapists. In the absence of routine assessment, these documentations tend to be inconsistently available or for a subset of patients in specific clinical contexts (e.g., after a fall event, hospitalization, or major surgery), which may not represent an individual's usual state of health. A recent study by Kharrazi et al.[79] showed that the prevalence of geriatric syndromes was underestimated when only claims and structured EHR data were analyzed; natural language processing of unstructured EHR data substantially improved detection by 1.5-fold for dementia, 3.2-fold for falls, 18.0-fold for malnutrition, and 455.9-fold for lack of social support. While these findings are promising, the contribution of unstructured EHR data for case identification depends on the health information technology infrastructure and completeness of documentation by health care providers.[79] How to best combine clinical information with administrative claims data or structured EHR data requires further investigation.

CONCLUSIONS

The use of a database-derived frailty measure offers new opportunities to facilitate frailty screening in clinical care and quantify frailty for large population-based database research in which clinical assessment is not feasible. Several database-derived frailty measures have been validated for use in administrative claims data and EHR, with some key differences (Fig. 2): target population (16 ambulatory, 1 long-term care, and 4 inpatient), data source (16 claims-based and 5 EHR-based measures), length of the assessment period (6 to 36 months), data types required for calculation (diagnosis codes required for 17 measures, health service codes for 7 measures, pharmacy data for 4 measures, and other additional

Frailty Measure by Health Care Database	Population	Data Source	Assessment Period (Months)	Types of Data Needed for Calculation				Existing Data on Validation		
				Diagnosis	Health Services	Pharmacy	Others	Clinical frailty	Disability	Mortality
US Medicare										
Lunney (2002)	Ambulatory	Claims	12	X						
Abrams (2003)	Ambulatory	Claims	12	X				X		X
Chrischilles (2013)	Ambulatory	Claims	12	X	X			X		
Davidoff (2013)	Ambulatory	Claims	12		X		X	X	X	X
JEN Associates (2014)	Ambulatory	Claims	12	X					X	X
Hope (2015)	Ambulatory	Claims	12	X				X		
Faurot (2015)	Ambulatory	Claims	8	X	X		X	X	X	X
Joynt (2017)	Ambulatory	Claims	12	X						
Segal (2017)	Ambulatory	Claims	6	X			X	X	X	X
Lekan (2017)	Inpatient	EHR	12	X			X	X		
Anzaldi (2017)	Ambulatory	EHR	24	X						
Kim (2018)	Ambulatory	Claims	12	X	X			X	X	X
Pajewski (2019)	Ambulatory	EHR	24	X		X	X	X		
US Veterans Affairs										
Rosen (2000)	Long-term care	Claims	6	X				X		
Shao (2017)	Ambulatory	EHR	12	X				X		
Orkaby (2018)	Ambulatory	Claims	36	X	X			X		
UK/England										
Soong(2015)	Inpatient	Claims	24	X				X		
Clegg (2016)	Ambulatory	EHR	12	X	X	X	X	X		X
Gilbert (2018)	Inpatient	Claims	24	X				X		X
Canada										
Dubois (2010)	Ambulatory	Claims	6	X				X		
McIsaac (2019)	Inpatient (surgical)	Claims	36	X	X	X	X	X		

Fig. 2. Considerations in choosing a database-derived frailty measure. EHR, electronic health records.

information for 9 measures), and outcomes against which a frailty measure was validated (clinical frailty assessment for 7 measures, disability for 7 measures, and mortality for 16 measures). This summary can serve as a guide to choosing a database-derived frailty measure that suits specific objectives and databases at hand.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The author provides paid consultative services to Alosa Health, a nonprofit educational organization with no relationship to any drug or device manufacturers.

FUNDING

The author is supported by R01AG062713 from the National Institute on Aging (NIA). The funding sources had no role in the data design, collection, analysis, or interpretation or the decision to submit the manuscript for publication.

REFERENCES

1. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet 2013;381:752-62.
2. Collard RM, Boter Soc 2012;60:1487-92.
3. Kim KJ, Shin J, Choi J, Won CW. Discrepancies in the prevalence of known frailty scales: Korean Frailty and Aging Cohort Study. Ann Geriatr Med Res 2018;22:137-44.
4. Kojima G. Prevalence of frailty in nursing homes: a systematic review and meta-analysis. J Am Med Dir Assoc 2015;16:940-5.
5. Hajek A, Bock JO, Saum KU, Matschinger H, Brenner H, Holleczek B, et al. Frailty and healthcare costs-longitudinal results of a prospective cohort study. Age Ageing 2018;47:233-41.
6. Comans TA, Peel NM, Hubbard RE, Mulligan AD, Gray LC, Scuffham PA. The increase in healthcare costs associated with frailty in older people discharged to a post-acute transition care program. Age Ageing 2016;45:317-20.
7. Figueroa JF, Joynt Maddox KE, Beaulieu N, Wild RC, Jha AK. Concentration of potentially preventable spending among high-cost medicare subpopulations: an observational study. Ann In-

tern Med 2017;167:706-13.
8. Joynt KE, Figueroa JF, Beaulieu N, Wild RC, Orav EJ, Jha AK. Segmenting high-cost Medicare patients into potentially actionable cohorts. Healthc (Amst) 2017;5:62-7.
9. Buckinx F, Rolland Y, Reginster JY, Ricour C, Petermans J, Bruyere O. Burden of frailty in the elderly population: perspectives for a public health challenge. Arch Public Health 2015;73:19.
10. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP. Frailty: implications for clinical practice and public health. Lancet 2019;394:1365-75.
11. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD. Management of frailty: opportunities, challenges, and future directions. Lancet 2019;394:1376-86.
12. Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, et al. Frailty consensus: a call to action. J Am Med Dir Assoc 2013;14:392-7.
13. Buta BJ, Walston JD, Godino JG, Park M, Kalyani RR, Xue QL, et al. Frailty assessment instruments: systematic characterization of the uses and contexts of highly-cited instruments. Ageing Res Rev 2016;26:53-61.
14. Aguayo GA, Donneau AF, Vaillant MT, Schritz A, Franco OH, Stranges S, et al. Agreement between 35 published frailty scores in the general population. Am J Epidemiol 2017;186:420-34.
15. Theou O, Squires E, Mallery K, Lee JS, Fay S, Goldstein J, et al. What do we know about frailty in the acute care setting? A scoping review. BMC Geriatr 2018;18:139.
16. Dent E, Morley JE, Cruz-Jentoft AJ, Woodhouse L, Rodriguez-Manas L, Fried LP, Woo J, et al. Physical frailty: ICFSR international clinical practice guidelines for identification and management. J Nutr Health Aging 2019;23:771-87.
17. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-95.
18. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging 2012;16:601-8.
19. Theou O, Andrew M, Ahip SS, Squires E, McGarrigle L, Blodgett JM, et al. The pictorial fit-frail scale: developing a visual scale to assess frailty. Can Geriatr J 2019;22:64-74.
20. Beth Israel Deaconess Medical Center. Senior health calculator: for providers - online tool to calculate Frailty Index (FI) [Internet]. Boston, MA: Beth Israel Deaconess Medical Center; c2020 [cited 2020 Feb 1]. Available from: https:// www.bidmc.org/research/research-by-department/medicine/gerontology/calculator.
21. Saliba D, Elliott M, Rubenstein LZ, Solomon DH, Young RT, Kamberg CJ, et al. The Vulnerable Elders Survey: a tool for identifying vulnerable older people in the community. J Am Geriatr Soc 2001;49:1691-9.
22. Mitnitski AB, Song X, Rockwood K. The estimation of relative fitness and frailty in community-dwelling older adults using self-report data. J Gerontol A Biol Sci Med Sci 2004;59:M627-32.
23. Schuurmans H, Steverink N, Lindenberg S, Frieswijk N, Slaets JP. Old or frail: what tells us more? J Gerontol A Biol Sci Med Sci 2004;59:M962-5.
24. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-56.
25. Jones DM, Song X, Rockwood K. Operationalizing a frailty index from a standardized comprehensive geriatric assessment. J Am Geriatr Soc 2004;52:1929-33.
26. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. Age Ageing 2006;35:526-9.
27. Gobbens RJ, van Assen MA, Luijkx KG, Wijnen-Sponselee MT, Schols JM. The Tilburg Frailty Indicator: psychometric properties. J Am Med Dir Assoc 2010;11:344-55.
28. Nicosia FM, Spar MJ, Steinman MA, Lee SJ, Brown RT. Making function part of the conversation: clinician perspectives on measuring functional status in primary care. J Am Geriatr Soc 2019;67:493-502.
29. Walston J, Bandeen-Roche K, Buta B, Bergman H, Gill TM, Morley JE, et al. Moving frailty toward clinical practice: NIA intramural frailty science symposium summary. J Am Geriatr Soc 2019;67:1559-64.
30. Lin KJ, Schneeweiss S. Considerations for the analysis of longitudinal electronic health records linked to claims data to study the effectiveness and safety of drugs. Clin Pharmacol Ther 2016;100:147-59.
31. Kim DH, Schneeweiss S. Measuring frailty using claims data for pharmacoepidemiologic studies of mortality in older adults: evidence and recommendations. Pharmacoepidemiol Drug Saf 2014;23:891-901.
32. Ruiz JG, Priyadarshni S, Rahaman Z, Cabrera K, Dang S, Valencia WM, Mintzer MJ. Validation of an automatically generated screening score for frailty: the care assessment need (CAN) score. BMC Geriatr 2018;18:106.
33. Ruiz JG, Rahaman Z, Dang S, Anam R, Valencia WM, Mintzer MJ. Association of the CAN score with the FRAIL scale in community dwelling older adults. Aging Clin Exp Res 2018;30:1241-5.
34. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A

standard procedure for creating a frailty index. BMC Geriatr 2008;8:24.
35. Clegg A, Bates C, Young J, Ryan R, Nichols L, Ann Teale E, et al. Development and validation of an electronic frailty index using routine primary care electronic health record data. Age Ageing 2016;45:353-60.
36. Rockwood K, Mitnitski A. Limits to deficit accumulation in elderly people. Mech Ageing Dev 2006;127:494-6.
37. Gilbert T, Neuburger J, Kraindler J, Keeble E, Smith P, Ariti C, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet 2018;391:1775-82.
38. Shi SM, Kim DH. The challenges of using the Hospital Frailty Risk Score. Lancet 2019;392:2692.
39. Segal JB, Chang H-Y, Du Y, Walston JD, Carlson MC, Varadhan R. Development of a claims-based frailty indicator anchored to a well-established frailty phenotype. Med Care 2017;55:716-22.
40. Davidoff AJ, Zuckerman IH, Pandya N, Hendrick F, Ke X, Hurria A, et al. A novel approach to improve health status measurement in observational claims-based studies of cancer treatment and outcomes. J Geriatr Oncol 2013;4:157-65.
41. Kim DH, Schneeweiss S, Glynn RJ, Lipsitz LA, Rockwood K, Avorn J. Measuring frailty in medicare data: development and validation of a claims-based frailty index. J Gerontol A Biol Sci Med Sci 2018;73:980-7.
42. Lunney JR, Lynn J, Hogan C. Profiles of older medicare decedents. J Am Geriatr Soc 2002;50:1108-12.
43. Abrams C, Lieberman R, Weiner JP. Development and evaluation of the Johns Hopkins University Risk adjustment models for Medicare+Choice plan payment. Baltimore, MD: Johns Hopkins University Press; 2003.
44. Chrischilles E, Schneider K, Wilwert J, Lessman G, O'Donnell B, Gryzlak B, et al. Beyond comorbidity: expanding the definition and measurement of complexity among older adults using administrative claims data. Med Care 2014;52 Suppl 3:S75-84.
45. JEN Associates Inc. MassHealth SCO program evaluation pre-SCO enrollment period CY2004 and post-SCO enrollment period CY2005 nursing home entry rate and frailty level comparisons. Cambridge, MA: JEN Associates Inc.; 2008.
46. JEN Associates Inc. JEN Frailty Index (JFI) [Internet]. Cambridge, MA: JEN Associates Inc.; c2019 [cited 2020 Feb 1]. Available from: https://www.jen.com/jfi2.
47. Hope AA, Gong MN, Guerra C, Wunsch H. Frailty before critical illness and mortality for elderly medicare beneficiaries. J Am Geriatr Soc 2015;63:1121-8.
48. Faurot KR, Jonsson Funk M, Pate V, Brookhart MA, Patrick A, Hanson LC, et al. Using claims data to predict dependency in activities of daily living as a proxy for frailty. Pharmacoepidemiol Drug Saf 2015;24:59-66.
49. Orkaby AR, Nussbaum L, Ho YL, Gagnon D, Quach L, Ward R, et al. The burden of frailty among U.S. veterans and its association with mortality, 2002-2012. J Gerontol A Biol Sci Med Sci 2019;74:1257-64.
50. Rosen A, Wu J, Chang BH, Berlowitz D, Ash A, Moskowitz M. Does diagnostic information contribute to predicting functional decline in long-term care? Med Care 2000;38:647-59.
51. McIsaac DI, Wong CA, Huang A, Moloo H, van Walraven C. Derivation and validation of a generalizable preoperative frailty index using population-based health administrative data. Ann Surg 2019;270:102-8.
52. Dubois MF, Dubuc N, Kroger E, Girard R, Hebert R. Assessing comorbidity in older adults using prescription claims data. J Pharm Health Serv Res 2010;1:157-65.
53. Soong J, Poots AJ, Scott S, Donald K, Woodcock T, Lovett D, et al. Quantifying the prevalence of frailty in English hospitals. BMJ Open 2015;5:e008456.
54. Sternberg SA, Bentur N, Abrams C, Spalter T, Karpati T, Lemberger J, et al. Identifying frail older people using predictive modeling. Am J Manag Care 2012;18:e392-7.
55. Segal JB, Huang J, Roth DL, Varadhan R. External validation of the claims-based frailty index in the national health and aging trends study cohort. Am J Epidemiol 2017;186:745-7.
56. Kim DH, Patorno E, Pawar A, Lee H, Schneeweiss S, Glynn RJ. Measuring frailty in administrative claims data: comparative performance of four claims-based frailty measures in the united states medicare data. J Gerontol A Biol Sci Med Sci 2019.
57. Kim DH, Glynn RJ, Avorn J, Lipsitz LA, Rockwood K, Pawar A, et al. Validation of a claims-based frailty index against physical performance and adverse health outcomes in the health and retirement study. J Gerontol A Biol Sci Med Sci 2019;74:1271-6.
58. Cuthbertson CC, Kucharska-Newton A, Faurot KR, Sturmer T, Jonsson Funk M, Palta P, et al. Controlling for frailty in pharmacoepidemiologic studies of older adults: validation of an existing medicare claims-based algorithm. Epidemiology 2018;29:556-61.
59. Ambagtsheer RC, Beilby J, Dabravolskaj J, Abbasi M, Archibald MM, Dent E. Application of an electronic Frailty Index in Australian primary care: data quality and feasibility assessment. Aging Clin Exp Res 2019;31:653-60.
60. Kinosian B, Wieland D, Gu X, Stallard E, Phibbs CS, Intrator O. Validation of the JEN frailty index in the National Long-Term Care Survey community population: identifying functionally impaired older adults from claims data. BMC Health Serv Res

2018;18:908.
61. Yao NA, Ritchie C, Cornwell T, Leff B. Use of home-based medical care and disparities. J Am Geriatr Soc 2018;66:1716-20.
62. Zhang HT, McGrath LJ, Wyss R, Ellis AR, Stürmer T. Controlling confounding by frailty when estimating influenza vaccine effectiveness using predictors of dependency in activities of daily living. Pharmacoepidemiol Drug Saf 2017;26:1500-6.
63. Simpson KN, Seamon BA, Hand BN, Roldan CO, Taber DJ, Moran WP, et al. Effect of frailty on resource use and cost for Medicare patients. J Comp Eff Res 2018;7:817-25.
64. Kundi H, Valsdottir LR, Popma JJ, Cohen DJ, Strom JB, Pinto DS, et al. Impact of a claims-based frailty indicator on the prediction of long-term mortality after transcatheter aortic valve replacement in medicare beneficiaries. Circ Cardiovasc Qual Outcomes 2018;11:e005048.
65. Lekan DA, Wallace DC, McCoy TP, Hu J, Silva SG, Whitson HE. Frailty assessment in hospitalized older adults using the electronic health record. Biol Res Nurs 2017;19:213-28.
66. Lekan DA, McCoy TP. Frailty risk in hospitalised older adults with and without diabetes mellitus. J Clin Nurs 2018;27:3510-21.
67. Anzaldi LJ, Davison A, Boyd CM, Leff B, Kharrazi H. Comparing clinician descriptions of frailty and geriatric syndromes using electronic health records: a retrospective cohort study. BMC Geriatr 2017;17:248.
68. Pajewski NM, Lenoir K, Wells BJ, Williamson JD, Callahan KE. Frailty screening using the electronic health record within a medicare accountable care organization. J Gerontol A Biol Sci Med Sci 2019;74:1771-7.
69. Shao Y, Mohanty AF, Ahmed A, Weir CR, Bray BE, Shah RU, et al. Identification and use of frailty indicators from text to examine associations with clinical outcomes among patients with heart failure. AMIA Annu Symp Proc 2017;2016:1110-8.
70. Stow D, Matthews FE, Hanratty B. Frailty trajectories to identify end of life: a longitudinal population-based study. BMC Med 2018;16:171.
71. Ravindrarajah R, Hazra NC, Hamada S, Charlton J, Jackson SHD, Dregan A, et al. Systolic blood pressure trajectory, frailty, and all-cause mortality >80 years of age: cohort study using electronic health records. Circulation 2017;135:2357-68.
72. Ravindrarajah R, Hazra NC, Charlton J, Jackson SHD, Dregan A, Gulliford MC. Incidence and mortality of fractures by frailty level over 80 years of age: cohort study using UK electronic health records. BMJ Open 2018;8:e018836.
73. McAlister FA, Lethebe BC, Lambe C, Williamson T, Lowerison M. Control of glycemia and blood pressure in British adults with diabetes mellitus and subsequent therapy choices: a comparison across health states. Cardiovasc Diabetol 2018;17:27.
74. Lin KJ, Singer DE, Glynn RJ, Murphy SN, Lii J, Schneeweiss S. Identifying patients with high data completeness to improve validity of comparative effectiveness research in electronic health records data. Clin Pharmacol Ther 2018;103:899-905.
75. Stow D, Matthews FE, Barclay S, Iliffe S, Clegg A, De Biase S, et al. Evaluating frailty scores to predict mortality in older adults using data from population based electronic health records: case control study. Age Ageing 2018;47:564-9.
76. Rockwood K. Screening for grades of frailty using electronic health records: where do we go from here? Age Ageing 2016;45:328-9.
77. Berry SD, Lee Y, Cai S, Dore DD. Nonbenzodiazepine sleep medication use and hip fractures in nursing home residents. JAMA Intern Med 2013;173:754-61.
78. Weiskopf NG, Rusanov A, Weng C. Sick patients have more data: the non-random completeness of electronic health records. AMIA Annu Symp Proc 2013;2013:1472-7.
79. Kharrazi H, Anzaldi LJ, Hernandez L, Davison A, Boyd CM, Leff B, et al. The value of unstructured electronic health record data in geriatric syndrome case identification. J Am Geriatr Soc 2018;66:1499-507.
80. McIsaac DI, Bryson GL, van Walraven C. Association of frailty and 1-year postoperative mortality following major elective noncardiac surgery: a population-based cohort study. JAMA Surg 2016;151:538-45.
81. McIsaac DI, Beaule PE, Bryson GL, Van Walraven C. The impact of frailty on outcomes and healthcare resource usage after total joint arthroplasty: a population-based cohort study. Bone Joint J 2016;98-B:799-805.
82. McIsaac DI, Moloo H, Bryson GL, van Walraven C. The association of frailty with outcomes and resource use after emergency general surgery: a population-based cohort study. Anesth Analg 2017;124:1653-61.
83. McIsaac DI, Wijeysundera DN, Huang A, Bryson GL, van Walraven C. Association of the hospital volume of frail surgical patients cared for with outcomes after elective, major noncardiac surgery: a retrospective population-based cohort study. Anesthesiology 2017;126:602-13.
84. Tan HJ, Shirk JD, Chamie K, Litwin MS, Hu JC. Patient function and the value of surgical care for kidney cancer. J Urol 2017;197:1200-7.
85. Gilden DM, Kubisiak JM, Kahle-Wrobleski K, Ball DE, Bowman L. Using U.S. Medicare records to evaluate the indirect health effects on spouses: a case study in Alzheimer's disease patients. BMC Health Serv Res 2014;14:291.
86. De Jonge KE, Jamshed N, Gilden D, Kubisiak J, Bruce SR, Taler

G. Effects of home-based primary care on Medicare costs in high-risk elders. J Am Geriatr Soc 2014;62:1825-31.
87. Soong J, Poots AJ, Scott S, Donald K, Bell D. Developing and validating a risk prediction model for acute care based on frailty syndromes. BMJ Open 2015;5:e008457.
88. Hui Y, van Walraven C, McIsaac DI. How do common comorbidities modify the association of frailty with survival after elective noncardiac surgery? A Population-Based Cohort Study. Anesth Analg 2019;129:1699-706.
89. Rosen A, Wu J, Chang BH, Berlowitz D, Rakovski C, Ash A, et al. Risk adjustment for measuring health outcomes: an application in VA long-term care. Am J Med Qual 2001;16:118-27.
90. Davidoff AJ, Gardner LD, Zuckerman IH, Hendrick F, Ke X, Edelman MJ. Validation of disability status, a claims-based measure of functional status for cancer treatment and outcomes studies. Med Care 2014;52:500-10.
91. Feliciano J, Gardner L, Hendrick F, Edelman MJ, Davidoff A. Assessing functional status and the survival benefit of chemotherapy for advanced non-small cell lung cancer using administrative claims data. Lung Cancer 2015;87:59-64.

AGMR
Annals of Geriatric Medicine and Research

Review Article
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):75-82
https://doi.org/10.4235/agmr.20.0023

Utility of Frailty Screening Tools in Older Surgical Patients

Alicia Wan Yan Poh, Shyh Poh Teo

Department of Internal Medicine, Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital, Brunei Darussalam

Corresponding Author:
Shyh Poh Teo, FRACP
Department of Internal Medicine, Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital, Bandar Seri Begawan BA 1710, Brunei Darussalam
E-mail: shyhpoh.teo@moh.gov.bn
ORCID:
https://orcid.org/0000-0002-6117-5774

Received: April 10, 2020
Revised: May 22, 2020
Accepted: May 28, 2020

Frailty is a loss of functional reserve that compromises a person's ability to cope with stressors such as surgery. Identifying and quantifying frailty may enable intensive rehabilitation interventions, caregiver support, or consideration of palliative care before surgery. This study describes the characteristics of five frailty screening tools, namely the Geriatric 8, Vulnerable Elders Survey-13, the Groningen Frailty Indicator, Edmonton Frailty Scale (EFS), and Clinical Frailty Scale. We further propose an approach incorporating a frailty scale into preoperative assessment, wherein older patients undergoing elective general surgery are screened using EFS, and frail patients are offered comprehensive geriatric assessment. The expected outcome is an individualized patient-centered care plan that will reduce frailty and optimize the patient's condition before surgery.

Key Words: Aged, Diagnosis, Frailty, General surgery, Risk assessment

INTRODUCTION

The international report "An Aging World: 2015" predicted that the number of people aged 65 years and above will increase from 617 million in 2015 to 1.6 billion by 2050, with two-thirds of the world's total older population living in Asia by 2050.[1] This older population will require planning for the provision of medical treatment, including surgery. Aging is a physiologic process in which there is deterioration in terms of cellular homeostasis, organ mass, and functional reserve. This loss of functional reserve varies among individuals and compromises their ability to cope with stressors such as surgery.[2] Thus, it is important to quantify this variability or frailty to identify individuals at a significant risk of developing disability despite initial independence.[3]

The vulnerability of a frail person is obvious when comparing their functional capacity to that of a non-frail person after physiological stress. For example, after minor surgery, an older person is expected to recover to their baseline function. However, a frail older person may experience a significant decline in function with increasing dependence or require rehabilitation to regain this function.[4]

An observational study showed a poor prognosis for functional recovery among older patients hospitalized for acute medical illness and discharged with a new or additional disability. Identifying these patients early enables clinicians to provide intensive rehabilitation interventions, caregiver support, or consideration of palliative care.[5] For example, before surgical intervention, identifying frailty may facilitate early rehabilitation to improve the likelihood of recovery. It may also be appropriate to counsel frail patients against surgery or offer palliation if there is a high risk of complications, including dependence and mortality.

This paper provides an overview of frailty and frailty screening tools and suggests an approach that incorporates a frailty scale in preoperative assessments for older surgical patients to identify those who may benefit from early intervention and rehabilitation.

FRAILTY

The Asia-Pacific Clinical Practice Guideline indicates that frailty can be identified through three approaches, namely the Fried

physical phenotype, the Rockwood and Mitnitski deficit accumulation model, and mixed physical and psychosocial models.[6] Using the Fried phenotype, frailty is diagnosed when at least three of the following physical criteria are met: slow gait, low grip strength, weight loss, self-reported exhaustion, and low physical activity. While this approach is suitable for clinical settings, it requires time and equipment to assess grip strength and walking speed.[6] Another approach to quantify frailty is through calculating a frailty index based on cumulative health deficits from among at least 30 variables in multiple domains such as physical function, multi-morbidities, cognition, and psychosocial factors.[6,7] Both approaches for identifying frailty are predictive of disability, falls, functional decline, hospitalization, and risk with surgery,[6-9] implying flexibility in the choice of frailty model applied to older people. However, the frailty index may have a better ability to discriminate at the lower to middle end of the frailty continuum.[9]

Patients with chronic diseases at increased risks of surgical complications and decline in organ function. Quantifying frailty can a useful biomarker to predict surgical outcome and survival after surgery.[10-13] However, frailty indices do not differently weight specific comorbidities associated with worse surgical outcomes. For example, a retrospective study of 6,729 patients showed that chronic kidney disease, acute myocardial infarction, and intracerebral hemorrhage were the comorbidities most likely to be associated with post-anesthetic mortality.[14] The most common postoperative complications are delirium, pulmonary, and cardiac issues; which are mostly attributable to previous cardiovascular and cerebrovascular disease.[15,16] In addition, the relationship between age-related change in the immune system, inflammation and anemia leads to progressive loss of functional organ reserve and, eventually, frailty.[17]

A patient's social circumstances are also important to consider, as social frailty significantly affects physical and cognitive frailty. Living alone, economic hardship, and limited social participation are associated with a decline in activities of daily living (ADL) and increased risk of disability.[18] A hybrid approach including both physical and psychosocial models was recently adopted and incorporated into screening tools.[6]

The gold standard for frailty assessment is comprehensive geriatric assessment (CGA); it is usually performed by geriatricians and can take more than 1 hour to complete. Practically, it is more appropriate to screen using an assessment tool and request CGA for those who screen positive for frailty. Identifying frailty should result in a comprehensive care plan, addressing polypharmacy and contributors to weight loss, sarcopenia, and exhaustion in addition to a multi-component physical activity program and protein supplementation for malnourished patients.[19] Frailty screening tools are described briefly in the following section.

FRAILTY SCREENING TOOLS

Table 1 summarizes the main characteristics of five frailty screen-

Table 1. Frailty screening tools

	Screening tests				
	G8	VES-13	GFI	EFS	CFS
Total number of items	8	13	15	17	N/A
Dimensions included in the tests	Food intake Weight loss Mobility Neuropsychological problems Body mass index Drugs Health status Age	Reported health status Reported activities of daily living Age	Mobility Vision Hearing Nutrition Comorbidity Cognition Psychosocial Reported physical fitness	Cognition General health status Functional independence Social support Medication use Nutrition Mood Continence Functional performance	N/A
Score range/categories	0–17	0–10	0–15	0-17	1–9 categories
Cut-off value	≤ 14: frail	≥ 3: increased risk of death within 2 years	≥ 4: moderate or severe frailty	> 7: increased risk of postoperative complications < 4: lower risk of complications	Category 5: mild frailty Category 9: terminally ill
Time to complete (min)	≤ 5	5	5	≤ 5	< 5

VES-13, Vulnerable Elders Survey-13; GFI, Groningen Frailty Indicator; EFS, Edmonton Frailty Scale; CFS, Clinical Frailty Scale.

ing tools, namely the Geriatric 8 (G8), Vulnerable Elders Survey-13 (VES-13), Groningen Frailty Indicator (GFI), Edmonton Frailty Scale (EFS), and Clinical Frailty Scale (CFS). While these tools were mainly developed for community-dwelling older people, they may also be applicable in screening older surgical patients. The five frailty screening tools were identified through a literature search and shortlisted according to those that seemed practically applicable in the preoperative clinic assessment setting.

G8

The G8 was initially developed from the Mini-Nutritional Assessment–Short Form questionnaire specifically for patients with cancer. Two systematic reviews evaluating screening tools for frailty in older patients with cancer showed that compared with other screening tools, the G8 had the highest sensitivity but at the expense of specificity.[20,21] The high sensitivity of ≥ 80% was identified in six of eight studies using 14 points as a cut-off.

The G8 was modified to increase its specificity by adding 14 new items to the original questionnaire. The additional variables were asthenia, risk of fall, the Eastern Cooperative Oncology Group-Performance Status, urinary or fecal incontinence, heart failure or chronic heart disease, complete arrhythmia with atrial fibrillation, hypertension, diabetes mellitus, and chronic kidney disease. This improved the G8 specificity from 57.7% to 79% with a cutoff value of ≥ 6 (or 88.4% with a cutoff value of ≥ 7), while maintaining high specificity (87.2% in the original G8 compared with 89.2% in the modified G8 with a cutoff value of ≥ 6 or 85.8% with a cutoff value of ≥ 7). Compared with the original G8, the modified G8 was predictive of chemotherapy-related toxicity in cancers, including hematological cancers.[22]

VES-13

The VES-13 was developed to screen community-dwelling older adults at risk of functional deterioration. It comprises 13 items, mainly regarding self-reported functional health. Generally, the VES-13 has better specificity than sensitivity, implying it may not be useful as a screening tool. Its sensitivity ranged from 39%–88%, with > 80% in 2 of 11 studies, whereas its specificity ranged from 62%–100%, with 100% in three of 11 studies.[20,21] The sensitivity and specificity can also be improved by using both the VES-13 and G8 screening tools concomitantly.[21]

GFI

The GFI was designed for older adults in hospital, residential care, and community settings. Similar to the VES-13, the GFI has higher specificity (86%–87%) than sensitivity (39%–66%). Both sensitivity (87%) and specificity (70%) were increased by lowering the standard cutoff value from ≥ 4 to ≥ 3. A cohort study found that frailty identified using the GFI was only associated with subjective postoperative reported limitations in terms of "daily activities" and "health problems".[23] Another study found that frail adults classified according to GFI required more assistance in ADLs, were more complex patients with higher comorbidities, and experienced lower satisfaction and quality of life.[24] However, these results of these studies were consistent with those of a systematic review reporting that neither VES-13 nor GFI was associated with postoperative morbidity and mortality.[21]

EFS

The EFS is another frailty screening tool for older people that can be completed rapidly. Unlike other screening tools, it incorporates functional performance using the Timed Up and Go (TUG) test, social support, and cognition screening with the clock-drawing test. These components may be used to identify important issues that need to be addressed through CGA. Higher TUG predicted the risk of early mortality in oncology patients receiving chemotherapy, postoperative complications, and morbidity.[21,25,26] TUG also assesses balance, gait, and (indirectly) risk of falls, which may identify patients who would benefit from preoperative rehabilitation.[27]

Surgical complications may result in negative psychosocial effects that are associated with prolonged wound healing and impaired immune function. Limited postoperative social support for older people may affect their recovery.[28,29] Cognitive screening using the clock-drawing test predicted patients who were likely to develop postoperative delirium and mortality.[30] A study screening for frailty in community-dwelling older adults showed that the clock-drawing test component of the EFS had high sensitivity (82.6%, specificity 36.9%) in identifying cognitive impairment.[31] Overall, EFS score > 7 was associated with postoperative complications and increased hospital stay.[15,22]

CFS

The CFS is used to provide a common language among health professionals to define frailty. This tool describes frailty with scores ranging from 1 (very fit) to 7 (completely dependent). It was initially developed from a prospective cohort study, the Canadian Study of Health and Aging, and validated in patients followed up over 5 years. Additional categories were added subsequently for a

total of seven to differentiate terminally ill but independent patients from those dependent on others for ADLs.[32]

Overall, CFS is an easy and quick test that does not require physical performance tests such as TUG or hand grip. It is also predictive of the duration of hospital stay and risk of death.[33] However, the CFS requires subjective clinical judgment, which may lead to problems with inter-rater reliability. The frailty scores are also heavily weighted on a person's ability to perform basic and instrumental ADLs and do not cover other aspects such as cognition and psychosocial assessment that may impact preoperative management.

FRAILTY IN OLDER SURGICAL PATIENTS

Studies on older surgical patients have also consistently shown the association between frailty and poor surgical outcomes. Thus, frailty screening may be useful as a risk-stratification tool specifically in older surgical patients. For example, frailty screening using a modified frailty index for elective total shoulder arthroplasty showed that frailty was more predictive of postoperative complications, readmission, reoperation, and increased length of stay than age alone.[34]

A cohort study of non-cardiac surgical patients used a novel operative stress score to quantify physiologic stress for surgical procedures. Using the Risk Analysis Index for frailty screening, the study found that frail patients had higher rates of complications and 30-day mortality, which continually increased at 90 and 180 days regardless of physiological stress scores, where even low- to moderate-stress procedures such as cystoscopy were high-risk in frail patients.[35]

A study comparing the diagnostic accuracy of six screening instruments for frailty, including the VES-13, G8, and GFI, in older patients undergoing emergency abdominal surgery found that these screening tools were predictive of postoperative outcomes, with the VES-13 showing the highest sensitivity and negative predictive value for postoperative morbidity and mortality.[36] Another study on emergency abdominal surgery combined the Surgical Apgar Score, which predicts postoperative mortality based on estimated blood loss, blood pressure, and heart rate, with the G8 for frailty screening. This study reported that both measures were independent predictors of postoperative adverse events and proposed the use of both scores to predict outcomes.[37]

The application of the GFI to older patients undergoing vascular surgery showed higher complication rates, 30-day mortality, and discharge to residential care in frail patients.[38] Frailty identified using the modified frailty index and GFI was also consistently associated with poor outcomes in terms of length of stay, mortality, complications, and discharge to residential care for head and neck surgery.[39]

Retrospective analyses of prospective databases of elective spine surgery also confirmed positive correlations between frailty and mortality, postoperative complications, and length of stay. While the modified frailty index was recommended, the researchers suggested the use of more comprehensive frailty indices specific for spinal surgery, such as the Adult Spinal Deformity frailty index, and consideration of adding clinical, radiographic, and laboratory measures to improve outcome predictions.[40] Another study that recalibrated and validated the Risk Analysis Index using a national surgical registry reported that the revision improved its discriminatory ability to predict mortality.[41]

Based on currently available studies on older surgical patients, frailty screening appears to discriminate and identify high-risk patients regardless of screening tool and type of surgery. The ability to predict outcomes may be improved by combining frailty screening tools with other tools (such as the Surgical Apgar Score), adding more variables to achieve a more comprehensive frailty index, or adapting and validating available frailty tools to individual surgical interventions or clinical settings.

However, in terms of feasibility and practical implementation of frailty screening for older surgical patients, it is more appropriate to integrate a common frailty screening tool for surgical patients that can be applied during pre-assessment in clinics.

JOURNEY FROM REFERRAL TO SURGERY

While the referral pathway to surgery may vary depending on clinical settings, it generally begins when patients are provided the option of surgery at the time of diagnosis in the clinic. For most elective surgical interventions, patients attend preoperative assessments by anesthetists 1–2 weeks before surgery. When issues are identified, the patients may be referred to organ-specific specialists for consultation. This limited engagement between patients and doctors and the possible need for interventions to optimize the patient's condition before surgery tends to be done within a limited time, with occasional consequent postponement of surgery. This is consistent with the literature, suggesting it can take up to 50 days from a general practitioner referral to the first formal assessment, which may be 2–14 days before the day of surgery.[42]

The preoperative assessment pathway has two main roles: first, to ensure discussion and appropriate decision-making regarding surgery, and second, to ensure the patient is as prepared as possible to maximize their resilience to the psychological stresses of surgery. From the anesthetist's perspective, this pathway can be re-engineered so that risk stratification occurs through simple screening

tools, then staged early using cardiopulmonary tests as an objective physiological assessment, with interventions if necessary before surgery.[42] Similarly, for older patients undergoing elective surgery, screening tools may be utilized to identify frailty and such patients can be referred preoperatively for interventions to optimize their recovery.

SUGGESTED APPROACH: PREOPERATIVE ASSESSMENT INCORPORATING A FRAILTY SCALE

A suggested approach for preoperative assessment incorporating a frailty scale is summarized in Fig. 1. In this approach, all patients aged 65 years and older undergoing elective general abdominal surgery are screened using the EFS during the surgical consultation, as soon as a decision for surgery is made. This should be done at least 3 months before surgery to allow sufficient time for interventions. The EFS is multi-domain; hence, it can be used to identify areas that require further assessment. Moreover, the assessment can be performed quickly in clinics by non-geriatricians.

Although most of the frailty tools appear to be predictive of poor surgical outcomes, with some differences in sensitivity and specificity, the EFS was preferred over the other tools as it incorporates objective cognitive and functional performance through the TUG and clock-drawing tests within the short time required to complete the tool. These objective measures may avoid potential variability in self-reporting among older surgical patients.

Patients with EFS scores >7 should be referred for CGA. As there is usually limited time before the date of surgery, coordina-

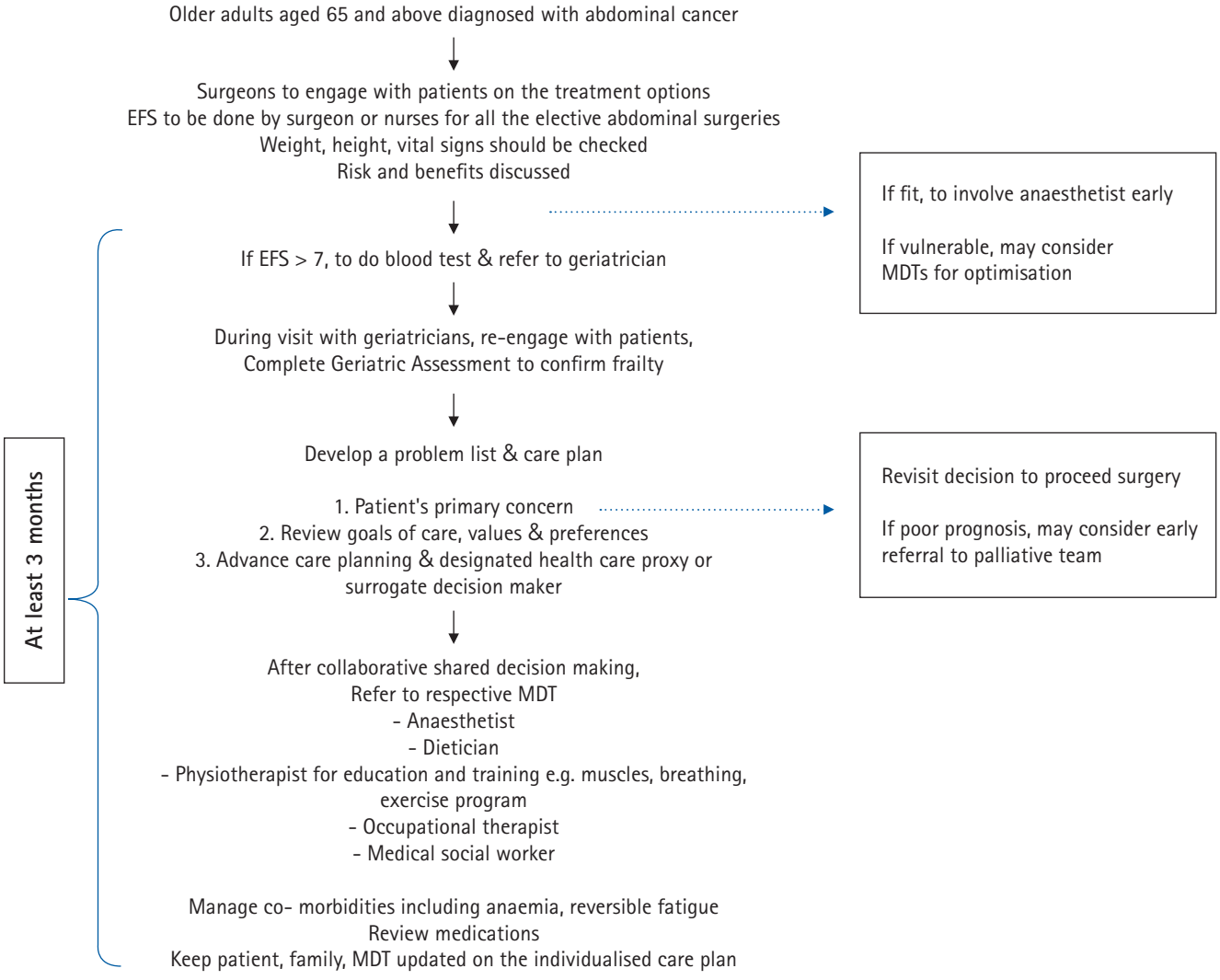

Fig. 1. A suggested approach for preoperative assessment incorporating a frailty scale. EFS, Edmonton frailty scale; MDT, multidisciplinary team

tion of assessment and treatment by a multidisciplinary team is required. This team should comprise surgeons, geriatricians, organ-specific physicians, anesthetists, physiotherapists, occupational therapists, dietitians, social workers, nurses, and patients. For patients with a poor prognosis, early referral to palliative teams for supportive care is warranted. The main outcome is individualized patient-centered care plans that are actionable and feasible and which consider the patient's personal treatment goals and preferences. Nutritional, physical, cognitive, and combination interventions can significantly reduce frailty in older people, which is beneficial preoperatively.[43]

The possible postoperative recovery trajectories should be discussed and understood by patients and families to allow proactive planning for potential care needs on discharge. Advance care planning should also be discussed, and a designated decisionmaker or health care proxy may need to be documented in patients' medical records.[44]

CONCLUSION

Frailty is associated with complications, prolonged recovery after surgery, and mortality. Frailty screening tools are available to identify frail patients that may benefit from CGA and individualized management plans to optimize patient conditions before surgery. We have proposed an algorithm for frailty screening that appears to be feasible to implement in preoperative assessment clinics. Further research is required to assess whether this approach will improve outcomes in older people.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

AUTHOR CONTRIBUTIONS

Conceptualization, AWP, SPT; Data curation, AWP, SPT; Investigation, AWP, SPT; Writing–original draft, AWP, SPT; Writing–review & editing, AWP, SPT.

REFERENCES

1. He W, Goodkind D, Kowal P. An aging world: 2015 (International Population Reports). Washington, DC: U.S. Government Publishing Office; 2016.
2. Nigam Y, Knight J, Bhattacharya S, Bayer A. Physiological changes associated with aging and immobility. J Aging Res 2012;2012:468469.
3. Biganzoli L, Mislang AR, Di Donato S, Becheri D, Biagioni C, Vitale S, et al. Screening for frailty in older patients with early-stage solid tumors: a prospective longitudinal evaluation of three different geriatric tools. J Gerontol A Biol Sci Med Sci 2017;72:922-8.
4. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet 2013;381:752-62.
5. Boyd CM, Landefeld CS, Counsell SR, Palmer RM, Fortinsky RH, Kresevic D, et al. Recovery of activities of daily living in older adults after hospitalization for acute medical illness. J Am Geriatr Soc 2008;56:2171-9.
6. Dent E, Lien C, Lim WS, Wong WC, Wong CH, Ng TP, et al. The Asia-Pacific clinical practice guidelines for the management of frailty. J Am Med Dir Assoc 2017;18:564-75.
7. Rockwood K, Blodgett JM, Theou O, Sun MH, Feridooni HA, Mitnitski A, et al. A frailty index based on deficit accumulation quantifies mortality risk in humans and in mice. Sci Rep 2017;7:43068.
8. Li G, Thabane L, Ioannidis G, Kennedy C, Papaioannou A, Adachi JD. Comparison between frailty index of deficit accumulation and phenotypic model to predict risk of falls: data from the global longitudinal study of osteoporosis in women (GLOW) Hamilton cohort. PLoS One 2015;10:e0120144.
9. Blodgett J, Theou O, Kirkland S, Andreou P, Rockwood K. Frailty in NHANES: Comparing the frailty index and phenotype. Arch Gerontol Geriatr 2015;60:464-70.
10. Kristjansson SR, Nesbakken A, Jordhoy MS, Skovlund E, Audisio RA, Johannessen HO, et al. Comprehensive geriatric assessment can predict complications in elderly patients after elective surgery for colorectal cancer: a prospective observational cohort study. Crit Rev Oncol Hematol 2010;76:208-17.
11. Ommundsen N, Wyller TB, Nesbakken A, Jordhoy MS, Bakka A, Skovlund E, et al. Frailty is an independent predictor of survival in older patients with colorectal cancer. Oncologist 2014;19:1268-75.
12. Robinson TN, Wu DS, Pointer L, Dunn CL, Cleveland JC Jr, Moss M. Simple frailty score predicts postoperative complications across surgical specialties. Am J Surg 2013;206:544-50.
13. Makary MA, Segev DL, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, et al. Frailty as a predictor of surgical outcomes in older patients. J Am Coll Surg 2010;210:901-8.
14. Chu CL, Chiou HY, Chou WH, Chang PY, Huang YY, Yeh HM. Leading comorbidity associated with 30-day post-anesthetic mortality in geriatric surgical patients in Taiwan: a retrospective study from the health insurance data. BMC Geriatr 2017;17:245.
15. Dasgupta M, Rolfson DB, Stolee P, Borrie MJ, Speechley M.

Frailty is associated with postoperative complications in older adults with medical problems. Arch Gerontol Geriatr 2009;48:78-83.
16. Sieber FE, Barnett SR. Preventing postoperative complications in the elderly. Anesthesiol Clin 2011;29:83-97.
17. Rohrig G. Anemia in the frail, elderly patient. Clin Interv Aging 2016;11:319-26.
18. Makizako H, Tsutsumimoto K, Shimada H, Arai H. Social frailty among community-dwelling older adults: recommended assessments and implications. Ann Geriatr Med Res 2018;22:3-8.
19. Dent E, Morley JE, Cruz-Jentoft AJ, Woodhouse L, Rodriguez-Manas L, Fried LP, et al. Physical frailty: ICFSR International clinical practice guidelines for identification and management. J Nutr Health Aging 2019;23:771-87.
20. Hamaker ME, Jonker JM, de Rooij SE, Vos AG, Smorenburg CH, van Munster BC. Frailty screening methods for predicting outcome of a comprehensive geriatric assessment in elderly patients with cancer: a systematic review. Lancet Oncol 2012;13:e437. -44.
21. Decoster L, Van Puyvelde K, Mohile S, Wedding U, Basso U, Colloca G, et al. Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendations. Ann Oncol 2015;26:288-300.
22. Martinez-Tapia C, Canoui-Poitrine F, Bastuji-Garin S, Soubeyran P, Mathoulin-Pelissier S, Tournigand C, et al. Optimizing the G8 screening tool for older patients with cancer: diagnostic performance and validation of a six-item version. Oncologist 2016;21:188-95.
23. Bras L, Peters TT, Wedman J, Plaat BE, Witjes MJ, van Leeuwen BL, et al. Predictive value of the Groningen Frailty Indicator for treatment outcomes in elderly patients after head and neck, or skin cancer surgery in a retrospective cohort. Clin Otolaryngol 2015;40:474-82.
24. Peters LL, Boter H, Buskens E, Slaets JP. Measurement properties of the Groningen Frailty Indicator in home-dwelling and institutionalized elderly people. J Am Med Dir Assoc 2012;13:546-51.
25. Soubeyran P, Fonck M, Blanc-Bisson C, Blanc JF, Ceccaldi J, Mertens C, et al. Predictors of early death risk in older patients treated with first-line chemotherapy for cancer. J Clin Oncol 2012;30:1829-34.
26. Huisman MG, van Leeuwen BL, Ugolini G, Montroni I, Spiliotis J, Stabilini C, et al. "Timed Up & Go": a screening tool for predicting 30-day morbidity in onco-geriatric surgical patients? A multicenter cohort study. PLoS One 2014;9:e86863.
27. Kronzer VL, Jerry MR, Ben Abdallah A, Wildes TS, Stark SL, McKinnon SL, et al. Preoperative falls predict postoperative falls, functional decline, and surgical complications. EBioMedicine 2016;12:302-8.
28. Pinto A, Faiz O, Davis R, Almoudaris A, Vincent C. Surgical complications and their impact on patients' psychosocial well-being: a systematic review and meta-analysis. BMJ Open 2016;6:e007224.
29. Kiecolt-Glaser JK, Page GG, Marucha PT, MacCallum RC, Glaser R. Psychological influences on surgical recovery: perspectives from psychoneuroimmunology. Am Psychol 1998;53:1209-18.
30. Long LS, Shapiro WA, Leung JM. A brief review of practical preoperative cognitive screening tools. Can J Anaesth 2012;59:798-804.
31. Fabricio-Wehbe SC, Schiaveto FV, Vendrusculo TR, Haas VJ, Dantas RA, Rodrigues RA. Cross-cultural adaptation and validity of the 'Edmonton Frail Scale - EFS' in a Brazilian elderly sample. Rev Lat Am Enfermagem 2009;17:1043-9.
32. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-95.
33. Juma S, Taabazuing MM, Montero-Odasso M. Clinical frailty scale in an acute medicine unit: a simple tool that predicts length of stay. Can Geriatr J 2016;19:34-9.
34. Holzgrefe RE, Wilson JM, Staley CA, Anderson TL, Wagner ER, Gottschalk MB. Modified frailty index is an effective risk-stratification tool for patients undergoing total shoulder arthroplasty. J Shoulder Elbow Surg 2019;28:1232-40.
35. Shinall MC Jr, Arya S, Youk A, Varley P, Shah R, Massarweh NN, et al. Association of preoperative patient frailty and operative stress with postoperative mortality. JAMA Surg 2019;155:e194620.
36. Kenig J, Zychiewicz B, Olszewska U, Barczynski M, Nowak W. Six screening instruments for frailty in older patients qualified for emergency abdominal surgery. Arch Gerontol Geriatr 2015;61:437-42.
37. Kenig J, Mastalerz K, Lukasiewicz K, Mitus-Kenig M, Skorus U. The Surgical Apgar Score predicts outcomes of emergency abdominal surgeries both in fit and frail older patients. Arch Gerontol Geriatr 2018;76:54-9.
38. Visser L, Banning LBD, El Moumni M, Zeebregts CJ, Pol RA. The effect of frailty on outcome after vascular surgery. Eur J Vasc Endovasc Surg 2019;58:762-9.
39. Fu TS, Sklar M, Cohen M, de Almeida JR, Sawka AM, Alibhai SMH, et al. Is frailty associated with worse outcomes after head and neck surgery? A narrative review. Laryngoscope 2020;130:1436-42.
40. Simcox T, Antoku D, Jain N, Acosta F, Hah R. Frailty syndrome

and the use of frailty indices as a preoperative risk stratification tool in spine surgery: a review. Asian Spine J 2019;13:861-73.
41. Arya S, Varley P, Youk A, Borrebach JA, Perez S, Massarweh NN, et al. Recalibration and external validation of the risk analysis index: a surgical frailty assessment tool. Ann Surg 2019;Mar 19;[Epub]. http://doi.org/10.1097/SLA.0000000000003276.
42. Grocott MPW, Plumb JOM, Edwards M, Fecher-Jones I, Levett DZH. Re-designing the pathway to surgery: better care and added value. Perioper Med (Lond) 2017;6:9.
43. Ng TP, Feng L, Nyunt MS, Feng L, Niti M, Tan BY, et al. Nutritional, physical, cognitive, and combination interventions and frailty reversal among older adults: a randomized controlled trial. Am J Med 2015;128:1225-36.
44. Mohanty S, Rosenthal RA, Russell MM, Neuman MD, Ko CY, Esnaola NF. Optimal perioperative management of the geriatric patient: a best practices guideline from the American College of Surgeons NSQIP and the American Geriatrics Society. J Am Coll Surg 2016;222:930-47.

AGMR
Annals of Geriatric Medicine and Research

Original Article
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):83-90
https://doi.org/10.4235/agmr.20.0017

Importance of Geriatric Syndrome Screening within 48 Hours of Hospitalization for Identifying Readmission Risk: A Retrospective Study in an Acute-Care Hospital

Jinyoung Shin[1,2], Seol-Heui Han[2,3], Jaekyung Choi[1,2], Yoon-Sook Kim[2,4], Jongmin Lee[2,5]

[1]Department of Family Medicine, Konkuk University Medical Center, Konkuk University School of Medicine, Seoul, Korea
[2]Research Institute on Healthy Aging, Konkuk University Medical Center, Seoul, Korea
[3]Department of Neurology, Konkuk University Medical Center, Seoul, Korea
[4]Department of Quality Improvement, Konkuk University Medical Center, Seoul, Korea
[5]Department of Rehabilitation Medicine, Konkuk University Medical Center, Konkuk University School of Medicine, Seoul, Korea

Corresponding Author:
Jongmin Lee, MD, PhD
Department of Rehabilitation Medicine, Konkuk University Medical Center, 120-1 Neungdong-ro, Gwangjin-gu, Seoul 05030, Korea
E-mail: leej@kuh.ac.kr
ORCID:
https://orcid.org/0000-0001-8718-0099

Received: March 24, 2020
Revised: April 20, 2020
Accepted: May 1, 2020

Background: Given the association between geriatric syndrome and hospital readmission, we evaluated the suitability of geriatric syndrome screening for care (GSC) in identifying readmission risk and suggested the appropriate time for GSC. **Methods:** GSC considering cognitive impairment, depression, polypharmacy (five or more medications), functional mobility, dysphagia, malnutrition, pain, and incontinence was performed among 2,663 general ward inpatients aged 65 years or older within 48 hours after admission and again before discharge between November 2016 and October 2017. From each patient, fall events, pressure ulcers, potentially inappropriate medication use, and delirium were assessed at admission. Patients were divided into two groups on the basis of readmission within 1 year after the first admission. According to the screening period (at admission and before discharge) and in-hospital decline, we applied receiver operating characteristic curve analysis to compare the prevalence of clinical concerns between the readmission and no-readmission groups. We also used multiple logistic regression analysis to evaluate the risk of readmission according to the presence of geriatric syndrome and clinical outcomes. **Results:** The 782 readmitted patients (29.4%) showed a higher rate of poor GSC than those who were not readmitted. Polypharmacy at admission was significantly correlated with readmission risk (area under the receiver operating characteristic curve=0.602). Fall events (odds ratio [OR]=4.36; 95% confidence interval [CI], 2.36–8.05), urinary incontinence (OR=4.21; 95% CI, 3.28–5.39), and depressive mood (OR=3.88; 95% CI, 2.69–5.59) at admission were risk factors for readmission. **Conclusion:** Geriatric syndromes assessed by GSC at admission was associated with an increased risk of readmission.

Key Words: Patient readmission, Aged, Geriatric assessment, Risk assessment

INTRODUCTION

Readmission is an important quality and safety issue in healthcare research and is also a tremendous burden on patients and their families.[1)] The cost of unplanned readmissions among Medicare patients in the United States was as high as $26 billion in 2014.[2)] The older population, for whom medical expenditures and rates of hospital readmission are higher relative to those among individuals of other age groups, is growing in Korea.[3)] The risk factors for readmission have been evaluated widely and include both patient-related factors such as demographic characteristics, diagnosis, comorbidities, and healthcare utilization as well as provider and health system-related factors such as hospital location and healthcare costs.[3,4)] A risk-stratified approach has recently been proposed for

identifying patients at high risk of readmission for transitional care interventions, which includes assessments of disease severity, hospital-acquired complications, and stability on discharge.[5]

The Korean Framework for Senior-Friendly Hospitals[6] was developed with reference to the Taiwanese[7] and Canadian[8] systems and was first implemented to address the need for healthcare assessment tools for older Korean inpatients in our acute-care hospital in 2016. Since May 2016, geriatric syndrome screening for care (GSC) has been performed for all older inpatients aged 65 years or older both at admission and before discharge. For further diagnostic assessment, patients with clinical issues are referred to a multidisciplinary team consisting of medical doctors specializing in neurology, rehabilitation medicine, family medicine, internal medicine, and psychology; nurse practitioners; dieticians; pharmacists; and quality improvement facilitators. Further, patients may receive personalized and comprehensive consultations throughout their hospital stay based on the GSC results. All steps are logged in each patient's electronic health record (EHR) and shared with the attending medical staff.

Although readmission risk assessment throughout older patients' hospitalization is important,[6-8] continuous evaluation of patients in busy in-patient units can be cumbersome. Unfortunately, exactly when it is appropriate to assess the risk of readmission remains unclear.

Therefore, the present study aimed to identify the appropriate time for readmission risk assessment and confirmed a simple comprehensive screening approach for the assessment of readmission risk by GSC in older patients.

MATERIALS AND METHODS

Study Participants

We retrospectively enrolled 3,570 patients aged 65 years or older who were admitted to the general ward of a tertiary hospital with 800 beds located in Seoul, South Korea between November 2016 and October 2017. After excluding patients with 1-day hospitalization (n = 668; 18.7% of enrolled patients), localized disease such as ophthalmological conditions (n = 163; 4.6%), and incomplete records on the factors evaluated (n = 76; 2.1%), the remaining 2,663 patients were finally examined. Study population was divided into two groups on the basis of readmission within 1 year regardless of diagnosis. The readmission group was defined as patients with more than one hospitalization during the observation period, whereas the no-readmission group was defined as patients who experienced only one hospitalization during the same period.

The Institutional Review Board of the Clinical Research Ethics Committee of Konkuk University Medical Center approved the exemption for this study and allowed the authors to review the patients' records (No. 11701347). The need for informed consent was also waived.

Demographics and Comorbidities

We obtained data on age, sex, health insurance status, body mass index (BMI), smoking status (current smoker, nonsmoker, or former smoker), alcohol intake (no alcohol intake, less than once per week, or more than once per week), duration of hospital stay, marital status (married/with a partner or divorced/without a partner), route for hospitalization (scheduled from an outpatient clinic or abruptly from an emergency visit), and reason for admission (e.g., surgery) from the EHRs. Comorbidities were defined as hypertension, diabetes mellitus, stroke, cardiovascular disease, cancer, respiratory disease, mental disorder, or other according to the attending physician's diagnosis or prescription. We counted the number of comorbidities per patient.

Assessment of geriatric syndrome

Geriatric syndrome was assessed not only within 48 hours of admission but also before discharge. An attending nurse designated at admission assessed the following nine GSC domains in each patient: cognitive impairment,[9] depressive mood,[10] polypharmacy (five or more medications),[11] functional immobility,[12,13] dysphagia,[14] malnutrition,[15] urinary incontinence,[16] fecal incontinence,[17] and pain.[18] A multidisciplinary team trained the nurses who conducted this assessment through face-to-face training and monitored all GSC results. The GSC questionnaire is shown in Supplementary Table S1. Functional mobility was categorized as "independent", "requires assistance", or "unable to perform" regarding climbing stairs, walking to a toilet, and transferring from a bed to a chair or a wheelchair. Patients categorized as "requires assistance" or "unable to perform" were considered to have functional immobility. The dysphagia screening test was performed using a simplified dysphagia symptom questionnaire.[14] Malnutrition was defined as a score of more than two for the sum of the responses to weight loss in the last 6 months (yes = 1, no = 0) and decreased appetite (yes = 1, no = 0).[15] The other screening questions, including the presence of cognitive impairment, depressive mood, polypharmacy (five or more medications), incontinence in the last month, and pain score (≥ 4 points), were relevant when participants responded "yes". The attending nurses were able to complete this survey for each patient within 5 minutes since the GSC can be done simply using EHRs.

Assessment of Other Clinical Outcomes

An attending nurse also surveyed fall events, the presence of pres-

sure ulcers, potentially inappropriate medication use, and delirium risk within 48 hours of admission. A fall event was defined as at least one fall within 90 days before the day of admission.[9] Pressure ulcers were defined as partial skin loss, deep craters in the skin, a skin break exposing muscle or bone, or necrotic ulcer.[9] Potentially inappropriate medication use was defined according to the updated 2012 American Geriatrics Society Beers Criteria.[19] On the basis of these criteria, two pharmacists categorized patients who were taking more than one medication into the inappropriate medication use group. Delirium risk was evaluated using the Nursing Delirium Screening Scale, which consists of five items: disorientation, inappropriate behavior, inappropriate communication, illusion or hallucinations, and psychomotor retardation.[20] Each domain was scored as 1 (yes) or 0 (no) point(s). We considered patients with total scores of more than 2 points to be at risk for delirium.

Statistical Analysis

Descriptive statistics were expressed as mean ± standard deviation for continuous variables and as numbers (proportions) for categorical variables. These data were compared between the readmission and no-readmission groups using Student t-test and chi-square test. In-hospital decline was defined as any aggravation of assessment findings between admission and discharge. Patients with no change or with an improvement in these findings were categorized into the "no in-hospital decline" group. The prevalence of readmission was compared according to the time of assessment (at admission or before discharge) and in-hospital decline using chi-square test. Receiver operating characteristic (ROC) curves were used to test the ability to predict the readmission risk. An area under the ROC curve (AUC) value of 0.5 represents a variable with no discriminating ability, whereas an AUC of 1.0 represents a variable with perfect discrimination.[21]

We evaluated the odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of readmission according to the presence of geriatric syndrome and other clinical outcomes using a multiple logistic regression analysis after adjusting for age, sex, BMI, marital status, smoking, alcohol intake, number of comorbidities, duration of hospital stay, reason for admission, route for hospitalization, and type of health insurance. Additionally, we performed stratified analysis according to sex and the 75th percentile of hospital stay (< 13 days and ≥ 13 days). As an increased risk of readmission in female patients has been reported,[3] we confirmed that similar findings were apparent in our study. We examined the statistical significance of the modifying effects of sex and the duration of hospital stay using a generalized linear model after adjusting for confounding factors. All analyses were performed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Among the 2,663 participants, 782 (29.4%) were readmitted (Table 1) during the observation period. Age, sex, smoking status,

Table 1. Baseline characteristics of the study population.

Variable	No readmission (n = 1,881)	Readmission (n = 782)	p-value
Age (y)	75.1 ± 6.9	75.2 ± 6.7	0.486
Sex			0.176
Male	884 (47.0)	390 (49.9)	
Female	997 (53.0)	392 (50.1)	
Smoking			0.774
Current	177 (9.4)	74 (9.5)	
Never/former	1,704 (90.6)	708 (90.5)	
Alcohol intake			0.341
Never/less than one time per week	1,637 (87.0)	674 (86.2)	
More than one time per week	244 (13.0)	108 (13.8)	
Body mass index (kg/m^2)	23.9 ± 3.7	23.7 ± 4.0	0.003
Hospital stay (day)	11.2 ± 13.9	12.7 ± 14.3	0.153
Reason for admission			< 0.001
Surgery	813 (43.2)	224 (28.6)	
Others	1,068 (56.8)	558 (71.4)	
Marital status			0.966
Married/with partner	1,824 (97.0)	741 (94.8)	
Unmarried/without partner	57 (3.0)	41 (5.2)	
Comorbidity			0.096
None	238 (12.7)	97 (12.4)	
Hypertension	733 (39.0)	289 (37.0)	
Diabetes mellitus	207 (11.0)	85 (10.9)	
Stroke	32 (1.7)	11 (1.4)	
Cardiovascular disease	122 (6.5)	58 (7.4)	
Cancer	68 (3.6)	46 (5.9)	
Respiratory disease	55 (2.9)	35 (4.5)	
Mental disorder	14 (0.7)	4 (0.5)	
Others	412 (21.9)	157 (20.1)	
Type of health insurance			0.180
National health insurance	1,744 (92.7)	734 (93.9)	
Medical aid program	137 (7.3)	48 (6.1)	
Route for hospitalization			0.830
Scheduled from outpatient clinic	1,233 (65.6)	516 (66.0)	
Abruptly from emergency visit	648 (34.4)	266 (34.0)	
Fall events	20 (1.1)	38 (4.9)	< 0.001
Pressure ulcer	123 (6.5)	90 (11.5)	< 0.001
Inappropriate medication use (≥ 1)	129 (6.9)	101 (12.9)	< 0.001
Nursing delirium screening scale (≥ 2)	109 (5.8)	63 (8.1)	0.154

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

Table 2. Prevalence of clinical concerns by GSC according to readmission measured at admission and before discharge

Variable	At admission				Before discharge				In-hospital decline[a]			
	Noreadmission (n = 1,881)	Readmission (n = 782)	p-value	AUC	No readmission (n = 1,881)	Readmission (n = 782)	p-value	AUC	No readmission (n = 1,881)	Readmission (n = 782)	p-value	AUC
Cognitive impairment, yes	146 (7.8)	121 (15.5)	< 0.001	0.539[d]	85 (4.5)	30 (3.8)	0.430	0.497	15 (0.8)	12 (1.5)	0.084	0.504
Depressive mood, yes	60 (3.2)	91 (11.6)	< 0.001	0.542[d]	54 (2.9)	42 (5.4)	0.002	0.513	24 (1.3)	19 (2.4)	0.031	0.506
Polypharmacy, ≥ 5	380 (20.2)	318 (40.7)	< 0.001	0.602[d]	557 (29.6)	339 (43.2)	< 0.001	0.569[d]	218 (11.6)	98 (12.5)	0.493	0.501
Functional immobility[b]												
Transferring from bed to chair/wheelchair	350 (18.6)	256 (32.7)	< 0.001	0.569[d]	463 (24.6)	251 (32.1)	< 0.001	0.535[d]	158 (8.4)	63 (8.1)	0.770	0.498
Walking to a toilet	368 (19.6)	273 (34.9)	< 0.001	0.575[d]	482 (25.6)	260 (33.2)	< 0.001	0.537[d]	157 (8.3)	67 (8.6)	0.851	0.501
Climbing upstairs	427 (22.7)	303 (38.7)	< 0.001	0.580[d]	579 (30.8)	307 (39.3)	< 0.001	0.539[d]	209 (11.1)	79 (10.1)	0.445	0.495
Dysphagia, yes	71 (3.8)	66 (8.4)	< 0.001	0.523	71 (3.8)	66 (8.4)	< 0.001	0.515	41 (2.2)	30 (3.8)	0.016	0.508
Malnutrition, ≥ 2[c]	213 (11.3)	224 (28.6)	< 0.001	0.560[d]	171 (9.1)	110 (14.1)	< 0.001	0.531[d]	117 (6.2)	76 (9.7)	0.001	0.514
Fecal incontinence, yes	61 (3.3)	74 (9.5)	< 0.001	0.531[d]	85 (4.5)	68 (8.7)	< 0.001	0.521	39 (2.1)	29 (3.7)	0.015	0.508
Urinary incontinence, yes	158 (8.4)	213 (27.2)	< 0.001	0.594[d]	112 (6.0)	78 (10.0)	< 0.001	0.520	40 (2.1)	27 (3.5)	0.047	0.507
Pain, yes	269 (14.3)	194 (24.8)	< 0.001	0.553[d]	28 (1.5)	16 (2.0)	0.001	0.518	105 (5.6)	42 (5.4)	0.772	0.499

Values are presented as number (%).
GSC, geriatric syndrome screening for care; AUC, area under the receiver operating characteristic curve.
[a]Values in the in-hospital decline group indicated cases with deterioration compared to admission and discharge.
[b]Functional immobility was defined as "requires assistance" or "impossible".
[c]Malnutrition was defined both weight loss in the last 6 months (yes=1, no=0) and decreased appetite (yes=1, no=0).
[d]$p<0.05$.

alcohol intake, marital status, comorbidities, health insurance type, route for hospitalization, and duration of hospital stay did not differ between the readmission and no-readmission groups. Patients in the readmission group showed a lower BMI value and admission rate for surgery but higher frequencies of fall events, pressure ulcers, and inappropriate medication use than those in the no-readmission group. However, there was no difference in delirium scale scores between the two groups.

Table 2 shows the prevalence of clinical concerns observed during GSC at admission, before discharge, and during in-hospital decline. The readmission group showed a higher frequency of clinical concerns by GSC at admission than that in the no-readmission group (all $p < 0.001$). However, the difference in cognitive impairment between the readmission and no-readmission groups disappeared before discharge ($p = 0.430$). We observed significant differences in the number of patients who experienced in-hospital decline relating to depressive mood, dysphagia, malnutrition, and fecal and urinary incontinence between the readmission and no-readmission groups (all $p < 0.05$). Polypharmacy, functional immobility, and the presence of pain showed similar rates of decline during hospitalization in both groups. Screening for geriatric syndromes at admission showed a higher AUC value than the GSC recorded before discharge or the GSC of in hospital decline group. Polypharmacy (five or more medications per day) and urinary incontinence at admission were significantly associated with readmission (AUC = 0.602 and 0.594, respectively).

The risks of readmission according to the presence of geriatric syndromes and other clinical outcomes assessed within 48 hours after admission are shown in Table 3. After adjusting for confounding factors, we found that all measured variables increased the risk of readmission. The ORs were highest for fall events (OR = 4.36; 95% CI, 2.36–8.05), urinary incontinence (OR = 4.21; 95% CI, 3.28–5.39), and depressive mood (OR = 3.88; 95% CI, 2.69–5.59). In stratified subgroup analysis, delirium in men, and cognitive impairment, dysphagia, and delirium in patients with hospital stays of longer than 13 days did not increase the OR of readmission. Furthermore, pressure ulcers in patients with hospital stays of < 13 days did not increase the OR of readmission, whereas a hospital stay of ≥ 13 days did (OR = 4.89, 95% CI, 2.92–8.18) (p-interaction < 0.001). Hospital stays of < 13 days tended to be associated with

Table 3. Comparison of readmission according to the geriatric syndrome and clinical outcomes

Variable	Total[a]	Male[b]	Female[b]	Hospital stay[c]	
				≥ 13 days	< 13 days
Cognitive impairment	2.46 (1.84–3.29)	2.17 (1.43–3.30)	2.80 (1.86–4.22)	1.44 (0.85–2.45)	3.19 (2.25–4.53)
Depressive mood	3.88 (2.69–5.59)	4.17 (2.34–7.41)	3.74 (2.32–6.05)	3.54 (1.80–6.99)	4.04 (2.62–6.24)
Polypharmacy	2.63 (2.15–3.22)	3.17 (2.38–4.22)	2.20 (1.64–2.95)	2.64 (1.81–3.85)	2.67 (2.10–3.40)
Functional immobility					
Transferring from a bed to a chair/wheelchair	2.58 (2.03–3.28)	2.55 (1.80–3.61)	2.63 (1.88–3.68)	1.79 (1.20–2.67)	3.11 (2.30–4.21)
Walking to a toilet	2.60 (2.05–3.30)	2.72 (1.93–3.83)	2.51 (1.80–3.49)	1.83 (1.23–2.72)	3.07 (2.28–4.14)
Climbing up stairs	2.47 (1.94–3.03)	2.54 (1.84–3.49)	2.33 (1.70–3.20)	1.80 (1.22–2.66)	2.72 (2.07–3.59)
Dysphagia	2.65 (1.78–3.94)	2.69 (1.55–4.69)	2.62 (1.47–4.68)	1.34 (0.73–2.47)	4.56 (2.64–7.87)
Malnutrition	3.32 (2.61–4.22)	4.05 (2.88–5.71)	2.77 (1.96–3.91)	3.10 (1.99–4.83)	3.23 (2.41–4.34)
Incontinence					
Fecal	3.39 (2.25–5.10)	3.82 (2.09–6.97)	3.36 (1.89–5.95)	2.32 (1.19–4.53)	4.59 (2.71–7.77)
Urinary	4.21 (3.28–5.39)	4.06 (2.81–5.87)	4.54 (3.23–6.39)	3.85 (2.46–6.04)	4.42 (3.27–5.96)
Pain	2.06 (1.64–2.60)	2.21 (1.58–3.09)	1.98 (1.44–2.73)	2.08 (1.37–3.14)	2.07 (1.56–2.73)
Fall events	4.36 (2.36–8.05)	4.07 (1.73–9.61)	4.70 (1.93–11.45)	6.21 (2.40–16.01)	3.14 (1.37–7.17)
Pressure ulcers[d]	1.92 (1.35–2.73)	2.01 (1.23–3.29)	2.00 (1.19–3.38)	4.89 (2.92–8.18)	0.93 (0.56–1.56)
Inappropriate medication use, ≥ 1	1.90 (1.41–2.58)	2.00 (1.31–3.05)	1.79 (1.15–2.80)	2.16 (1.26–3.70)	1.84 (1.27–2.67)
Nursing delirium screening scale, ≥ 2[d]	1.62 (1.08–2.44)	1.44 (0.81–2.58)	1.91 (1.07–3.41)	1.01 (0.56–1.82)	2.81 (1.56–5.04)

Values are presented as odds ratio (95% confidence interval). All variables were measured within 48 hours after admission.

[a]Multiple logistic regression analysis after adjusting for age, sex, body mass index (BMI), marital status, smoking, alcohol intake, number of comorbidities, duration of hospital stay, reason for admission, route for hospitalization, and type of health insurance.

[b]Multiple logistic regression analysis after adjusting for age, BMI, marital status, smoking, alcohol intake, number of comorbidities, duration of hospital stay, reason for admission, route for hospitalization, and type of health insurance.

[c]Multiple logistic regression analysis after adjusting for age, sex, BMI, marital status, smoking, alcohol intake, number of comorbidities, reason for admission, route for hospitalization, and type of health insurance. Hospital stay was divided into the 75th percentile of duration (13 days).

[d]p-interaction <0.05 which was only analyzed according to the hospital stay.

an increased risk of delirium in older inpatients hospitalized for acute care (p-interaction < 0.05).

DISCUSSION

In this study of Korean older inpatients, geriatric syndromes were associated with an increased risk of readmission in an acute-care hospital. The presence of geriatric syndromes assessed by GSC at admission, rather than before discharge or the occurrence of in-hospital decline, was associated with the risk of readmission. Polypharmacy at admission showed the highest discriminating ability for readmission. Among the GSC criteria and other clinical outcomes, a fall event before hospitalization was a significant risk factor for readmission among Korean older patients.

GSC was developed for administration by medical staff, caregivers, or patients in both clinical and nonclinical settings. GSC is a multidimensional and interdisciplinary screening tool encompassing medical, psychological, and functional domains. Therefore, it can be extended to transitional care settings even when the medical staff is not adequately trained or is too occupied to manage complex geriatric needs.[18] Delirium, cognitive impairment, depressive mood, and inappropriate medication use are often not recognized in older patients, a fact that underscores the need for better geriatric care.[18] Therefore, an easily administered tool is important to promptly evaluate inpatients for the presence of geriatric syndromes. In this context, our study confirmed the effectiveness of screening using GSC within 48 hours of hospitalization rather than before discharge or assessing in-hospital decline to determine the readmission risk. Although in-hospital decline and stability at discharge in older patients with pneumonia are considered good predictors of readmission risk,[22] only one study has reported this correlation; thus, it had low generalizability, in addition to other limitations such as incomplete ascertainment of readmission and a lack of validation.[5] The study was further limited by including only pneumonia patients.

Similar to the results of our study, a study in the United States found that polypharmacy (six or more medicines) at admission predicted the risk of 30-day readmission.[23] Polypharmacy was also a major risk factor for readmission in a prospective study of older Italian inpatients, with similar OR and 95% CI values (2.72; 1.48–4.99).[24] While potentially inappropriate medication use did not increase the risk of readmission in the Italian study, the results of the present study confirmed an increased risk of readmission. This difference could be attributed to the fact that the previous study assessed readmission during a 6-month period in contrast to the 1-year period in our study.[24] The previous study may not have observed an association between readmission and potentially inappropriate medication during the short-term observation period.

The results of our study confirmed that fall events before hospitalization increased the risk of readmission. In addition, long-term hospitalization (> 13 days) was associated with the presence of pressure ulcers, which is a common problem in older inpatients.[9] However, relatively short-term hospitalization conferred a higher risk of delirium than did longer hospital stay, although the difference was not statistically significant. Therefore, delirium, which develops or is aggravated by acute environmental changes, requires attention during the care of older patients.[25]

A systematic review of 12 studies including 3,590 patients reported that in-hospital geriatric assessment and co-management had no overall effect on readmission within 30 days (OR = 1.28; 95% CI, 0.71–2.31; n = 695) and within 12 months (OR = 0.91; 95% CI, 0.64–1.29; n = 601). Unfortunately, limited reduction in the length of hospital stay (pooled mean difference = −1.88 days; 95% CI, −2.44 to −1.33) and in-hospital mortality (pooled OR = 0.72; 95% CI, 0.50–1.03) after geriatric assessment and co-management were reported, with low-quality evidence.[26] Although we did not administer any interventions based on the GSC finding, our results suggest that a long hospital stay related to pressure ulcers could mediate the risk of readmission; thus, it may confer an effect modification, as shown previously.[5,26]

Among GSC variables, dysphagia alone did not provide an acceptable AUC (p > 0.05). Dysphagia can cause respiratory complications, including aspiration pneumonia and malnutrition.[27] One explanation for this finding is the lower prevalence of dysphagia in our participants, including those in the readmission group (8.4%), relative to those among acute-care older inpatients in Spain (47.4%)[28] and Denmark (50%).[29]

Compared to the GSC results at admission, pain, cognitive impairment, and urinary impairment improved on the assessment before discharge. Whereas pain is thought to have been controlled after hospitalization, the other factors may not be improved with short hospitalization. This change may be due to positive responses by the participants to the medical staff's questions that has been treated, resulting in a response bias in the before-discharge questionnaire, which may have reduced the relevance of the findings to readmission.[30] In contrast, the prevalence of polypharmacy, functional immobility, and fecal incontinence before discharge increased compared to that at admission, possibly due to the treatment process.

Logging all care processes in EHRs and sharing records with attending physicians play a specialized and comprehensive role in consultation in the hospital setting.[31] Furthermore, EHRs facilitate communication among medical staff and organizations and provide structured coordination and documentation of the medi-

cal services provided.[32] Therefore, GSC performed within 48 hours of hospitalization using the EHRs of all inpatients aged 65 years or older is expected to be efficient.

Still, the present study has some limitations. First, it was conducted in a single institution; thus, the findings cannot be generalized to other hospital settings without further review. However, screening for geriatric syndromes by GSC within 48 hours can provide information on patients at high risk of readmission in similar institutions. Second, instead of assessing the exact cause of hospitalization in the current study, we adjusted for whether the hospitalization was for surgery based on the EHR. Additionally, we could not confirm whether the causes of readmission were related to previous admissions or to other hospitals, or to pre-admission residence. Since the various associations between geriatric syndromes and individual diagnoses were not significant in this study and could be confounded by detection bias, we simplified the participant-related variables. Additionally, comorbidities and medication use were assessed based on self-reports rather than medical record review, which might have caused bias toward positive answers because of social desirability.[30] Unfortunately, we could not assess all medical records of all participants as they were not shared between different medical institutions. The no-readmission group may have included patients who were admitted to other hospitals, as we did not consider visits or admission to other hospitals in this analysis.

In conclusion, geriatric syndromes assessed by GSC was associated with an increased risk of readmission. The results of our study support the importance of an integrated approach regarding readmission in older inpatients. Further research is needed to determine the efficacy of GSC related to transitional care or other hospital settings.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

This study was supported by Konkuk University in 2020.

AUTHOR CONTRIBUTIONS

Conceptualization, JS, SHH, JC, YSK, JL; Data curation, SJ, JC, YSK; Investigation, JS, JC, YSK; Methodology, JS, SHH; Project administration, SHH, JL; Supervision, SHH; Writing original draft, JS, JL; Review and editing, SHH, JC, YSK.

Supplementary Materials

Supplementary materials can be found via https://doi.org/10.4235/agmr.20.0017.

REFERENCES

1. Goldstein JN, Hicks LS, Kolm P, Weintraub WS, Elliott DJ. Is the care transitions measure associated with readmission risk? Analysis from a single academic center. J Gen Intern Med 2016;31:732-8.
2. Boozary AS, Manchin J 3rd, Wicker RF. The Medicare hospital readmissions reduction program: time for reform. JAMA 2015;314:347-8.
3. Robinson S, Howie-Esquivel J, Vlahov D. Readmission risk factors after hospital discharge among the elderly. Popul Health Manag 2012;15:338-51.
4. Wang YC, Chou MY, Liang CK, Peng LN, Chen LK, Loh CH. Post-acute care as a key component in a healthcare system for older adults. Ann Geriatr Med Res 2019;23:54-62.
5. Weinreich M, Nguyen OK, Wang D, Mayo H, Mortensen EM, Halm EA, et al. Predicting the risk of readmission in pneumonia: a systematic review of model performance. Ann Am Thorac Soc 2016;13:1607-14.
6. Kim YS, Lee J, Moon Y, Kim HJ, Shin J, Park JM, et al. Development of a senior-specific, citizen-oriented healthcare service system in South Korea based on the Canadian 48/6 model of care. BMC Geriatr 2020;20:32.
7. Chiou ST, Chen LK. Towards age-friendly hospitals and health services. Arch Gerontol Geriatr 2009;49 Suppl 2:S3-6.
8. Wong KS, Ryan DP, Liu BA. A system-wide analysis using a senior-friendly hospital framework identifies current practices and opportunities for improvement in the care of hospitalized older adults. J Am Geriatr Soc 2014;62:2163-70.
9. Lakhan P, Jones M, Wilson A, Courtney M, Hirdes J, Gray LC. A prospective cohort study of geriatric syndromes among older medical patients admitted to acute care hospitals. J Am Geriatr Soc 2011;59:2001-8.
10. Lachs MS, Feinstein AR, Cooney LM Jr, Drickamer MA, Marottoli RA, Pannill FC, et al. A simple procedure for general screening for functional disability in elderly patients. Ann Intern Med 1990;112:699-706.
11. Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. J Clin Epidemiol 2012;65:

989-95.
12. Tinetti ME. Performance-oriented assessment of mobility problems in elderly patients. J Am Geriatr Soc 1986;34:119-26.
13. Lee Y, Lee HH, Uhm KE, Jung HJ, Kim YS, Shin J, et al. Early Identification of Risk Factors for Mobility Decline Among Hospitalized Older Patients. Am J Phys Med Rehabil 2019;98:699-705.
14. Uhm KE, Kim M, Lee YM, Kim BR, Kim YS, Choi J, et al. The Easy Dysphagia Symptom Questionnaire (EDSQ): a new dysphagia screening questionnaire for the older adults. Eur Geriatr Med 2019;10:47-52.
15. Ferguson M, Capra S, Bauer J, Banks M. Development of a valid and reliable malnutrition screening tool for adult acute hospital patients. Nutrition 1999;15:458-64.
16. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology 2003;61:37-49.
17. Elsawy B, Higgins KE. The geriatric assessment. Am Fam Physician 2011;83:48-56.
18. Deschodt M, Van Grootven B, Jeuris A, Devriendt E, Dierckx de Casterle B, Dubois C, et al. Geriatric CO-mAnagement for Cardiology patients in the Hospital (G-COACH): study protocol of a prospective before-after effectiveness-implementation study. BMJ Open 2018;8:e023593.
19. American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2012;60:616-31.
20. Gaudreau JD, Gagnon P, Harel F, Tremblay A, Roy MA. Fast, systematic, and continuous delirium assessment in hospitalized patients: the nursing delirium screening scale. J Pain Symptom Manage 2005;29:368-75.
21. Hoo ZH, Candlish J, Teare D. What is an ROC curve? Emerg Med J 2017;34:357-9.
22. Capelastegui A, Espana Yandiola PP, Quintana JM, Bilbao A, Diez R, Pascual S, et al. Predictors of short-term rehospitalization following discharge of patients hospitalized with community-acquired pneumonia. Chest 2009;136:1079-85.
23. Logue E, Smucker W, Regan C. Admission data predict high hospital readmission risk. J Am Board Fam Med 2016;29:50-9.
24. Fabbietti P, Di Stefano G, Moresi R, Cassetta L, Di Rosa M, Fimognari F, Bambara V, Ruotolo G, Castagna A, Ruberto C, Lattanzio F, Corsonello A. Impact of potentially inappropriate medications and polypharmacy on 3-month readmission among older patients discharged from acute care hospital: a prospective study. Aging Clin Exp Res 2018;30:977-84.
25. Setters B, Solberg LM. Delirium. Prim Care 2017;44:541-59.
26. Van Grootven B, Flamaing J, Dierckx de Casterle B, Dubois C, Fagard K, Herregods MC, et al. Effectiveness of in-hospital geriatric co-management: a systematic review and meta-analysis. Age Ageing 2017;46:903-10.
27. Martin A, Ortega O, Roca M, Arus M, Clave P. Effect of a minimal-massive intervention in hospitalized older patients with oropharyngeal dysphagia: a proof of concept study. J Nutr Health Aging 2018;22:739-47.
28. Carrion S, Cabre M, Monteis R, Roca M, Palomera E, Serra-Prat M, et al. Oropharyngeal dysphagia is a prevalent risk factor for malnutrition in a cohort of older patients admitted with an acute disease to a general hospital. Clin Nutr 2015;34:436-42.
29. Melgaard D, Rodrigo-Domingo M, Morch MM. The prevalence of oropharyngeal dysphagia in acute geriatric patients. Geriatrics (Basel) 2018;3:15.
30. Paulhus DL. Measurement and control of response bias. In: Robinson JP, Shaver PR, Wrightsman LS, editors. Measures of personality and social psychological attitudes. St. Louis, MO: Academic Press; 1991. p. 17-59.
31. Shin J, Ko H, Kim JA, Song YM, An JS, Nam SJ, et al. Hospital cancer pain management by electronic health record-based automatic screening. Am J Manag Care 2018;24:e338-e343.
32. Tomoaia-Cotisel A, Farrell TW, Solberg LI, Berry CA, Calman NS, Cronholm PF, et al. Implementation of care management: an analysis of recent AHRQ research. Med Care Res Rev 2018;75:46-65.

AGMR
Annals of Geriatric Medicine and Research

Original Article
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):91-98
https://doi.org/10.4235/agmr.20.0028

Effects of Statin Use for Primary Prevention among Adults Aged 75 Years and Older in the National Health Insurance Service Senior Cohort (2002–2015)

Sunyoung Kim[1], Hangseok Choi[2], Chang Won Won[3]

[1]Department of Family Medicine, Kyung Hee University Medical Center, Seoul, Korea
[2]College of Pharmacy, Chung-Ang University, Seoul, Korea
[3]Elderly Frailty Research Center, Department of Family Medicine, College of Medicine, Kyung Hee University, Seoul, Korea

Corresponding Author:
Chang Won Won. MD, PhD
Elderly Frailty Research Center, Department of Family Medicine, College of Medicine, Kyung Hee University, 23 Kyungheedae-ro, Dongdaemun-gu, Seoul 02447, Korea
E-mail: chunwon@khmc.or.kr
ORCID:
https://orcid.org/0000-0002-6429-4461

Received: May 7, 2020
Revised: June 16, 2020
Accepted: June 17, 2020

Background: This study aimed to identify adverse events and mortality in adults aged 75 years and older who were initially prescribed statins for primary prevention. **Methods:** This retrospective study analyzed the data from the National Health Insurance Corporation–Senior Cohort from 2002 to 2015. An exact block matched model was constructed from statin user and statin non-user groups. **Results:** The study sample comprised 1,370 older adults (mean age, 78 years), with 685 statin non-users matched to 685 new statin users. Compared to non-users, the adjusted hazard ratios (HRs) of new statin users were 0.83 (p=0.04) for all-cause mortality, 1.24 (p=0.003) for major adverse cardiovascular events, and 1.18 (p=0.06) for new-onset diabetes mellitus. In a sub-analysis of statin use duration, longer statin use (>5 years) was associated with a significantly lower risk of all-cause mortality (HR=0.76, p=0.01) but not with major adverse cardiovascular events (HR=0.88, p=0.36) or new-onset diabetes mellitus (HR=0.95, p=0.78) after adjusting for age, sex, body mass index, diabetes mellitus, hypertension, aspirin use, and antiplatelet use. **Conclusion:** Our findings suggested that statins started for primary prevention in older adults aged 75 years and older had an advantageous effect on all-cause mortality only if used for at least 5 years.

Key Words: Aged, Cardiovascular disease, Hydroxymethylglutaryl-CoA reductase inhibitors, Mortality, Primary prevention

INTRODUCTION

Among countries with an aging global population, South Korea is the country with the fastest-aging population; with more than 14% of its population aged 65 years and older, South Korea officially became an aged society in 2017.[1)] Cardiovascular disease is the second leading cause of death among Koreans, and ischemic heart disease accounts for the majority of deaths.[2)]

High low-density lipoprotein cholesterol (LDL-C) level is a well-documented risk factor for cardiovascular disease because it is associated with progression from early-stage fatty streaks to advanced-stage, lipid-rich plaques.[3)] Hydroxymethylglutaryl-coenzyme A reductase inhibitors, are one of the best-established means for preventing and treating atherosclerotic cardiovascular disease.[4)] However, there is limited evidence to recommend statins for the primary prevention of cardiovascular disease in adults aged 75 years and over.[5,6)]

Since the American College of Cardiology/American Heart Association (ACC/AHA) guidelines published in 2013,[5)] five guidelines for statin use have been released:[7)] the UK National Institute for Health and Care Excellence (NICE-UK) in 2014,[8)] the Canadian Cardiovascular Society (CCS),[9)] the US Preventive Services Task Force,[6)] the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS)[10)] in 2016, and ACC/AHA in

2018.[11] However, of these guidelines, only the NICE-UK strongly recommends statins for primary prevention up to age 84; the ESC/EAS and the ACC/AHA recommend treatment to age 65 and 75, respectively. The Korean guideline for dyslipidemia in 2018 indicated that there is insufficient evidence regarding the effectiveness of statins for primary prevention of cardiovascular disease in older adult patients over 75 years of age without cardiovascular disease and diabetes and recommended to consider statin use for primary prevention only in case of diabetes.[12]

Previous studies reported increased risks of diabetes mellitus (DM)[13] and cognitive dysfunction due to statin use,[14] with concerns regarding statin prescriptions for older adults. However, few studies have evaluated the efficacy and safety of statins in people aged 75 years or older.

Furthermore, most studies were conducted in Western countries; thus, there is insufficient clinical evidence regarding the primary preventive effect or tolerability of statins in older Asian populations.

Therefore, we evaluated the efficacy, mortality, and adverse outcomes of statins in people aged over 75 years by analyzing National Health Insurance data.

MATERIALS AND METHODS

Data Background

The dataset was provided by the Korean National Health Insurance Service (NHIS), which was founded in 2000 as a single-insurer system. The NHIS has converted all medical records into the National Health Information Database containing personal information, demographic data, and medical treatment data for Korean citizens categorized as insured employees, insured self-employed individuals, or medical-aid beneficiaries. Within this dataset is the NHIS-Senior Cohort (NHIS-SC), which is a population-based cohort comprising 558,147 people who account for approximately 10% of the total 5,500,000 patients aged ≥ 60 years in 2002. The NHIS-SC database contains information on insurance membership and income, medical use history, medical checkups, and long-term care and provides data from medical health examinations that all older adult beneficiaries receive every 2 years, including blood pressure measurement, health behavior status (smoking, alcohol), and past medical history.[15,16]

Study Population

In this study, we included people aged 75 years and older who were enrolled in the NHIS-SC database between January 1, 2004, and December 31, 2005 (n = 159,015) and who received a health examination provided by the NHIS within 2 years of their first prescription day (n = 25,350). We included people with total cholesterol level of > 200 mg/dL on their health screening blood test. The exclusion criteria were: (1) having been prescribed statins from 2002–2003 or (2) having any of the following major or minor diagnostic codes on their medical records within the 2 years before enrollment -I20-25 (ischemic heart disease), I60-69 (cerebrovascular disease), and I73 (other peripheral vascular diseases). For comparison, the baseline cohort included patients with hypercholesterolemia (with claim codes or a total cholesterol level > 200 mg/dL) in the primary prevention cohort who were eligible for statin therapy but had no statin prescription history (n = 7,782). The medication possession ratio (MPR) was calculated by dividing the sum of prescription days by the total prescription period (between the first date of prescription and the final follow-up day during the index period; January 1, 2004 to December 31, 2005) using medication history extracted from each patient's medical record. Subjects with a statin MPR above 20% were assigned to the statin-user group (n = 767), while those who had never been exposed to statins were assigned to the statin non-user group (n = 15,637).[17,18] Because statin use was not randomly assigned, the effects of treatment-selection bias and potential confounding factors were mitigated by applying an exact block-matching approach. Exact block matching was determined using four blocks of sex, age (age groups within 2 years), total cholesterol (three categories; < 240, 240–300, and > 300 mg/dL), and incidence year, with each statin user matched to one control subject. The analyses finally included 685 pairs (n = 1,370) (Fig. 1).

Covariate Confounders

We considered the risk factors for adverse events, including underlying medication history, socio-demographic characteristics (age, sex, income), body mass index (BMI), and lifestyle (smoking, alcohol consumption), as potential confounders.

Outcomes

The primary outcome variables included the rates of all-cause death and major adverse cardiovascular events (MACE), which was defined as the composite of myocardial infarction (MI; I20-25), stroke (I60-69), and coronary revascularization (I46; percutaneous transluminal coronary angioplasty or coronary artery bypass grafting) from NHIS-SC records dated within the study period. The secondary outcomes were hospitalization for any cause (acute MI, ischemic cerebrovascular disease, chronic obstructive pulmonary disease, and malignant neoplasm), cancer, new-onset diabetes mellitus (NODM), liver toxicity, and myopathy.[19] NODM was recorded when antidiabetic drugs were first prescribed during follow-up and when diagnostic codes were claimed for the first time.

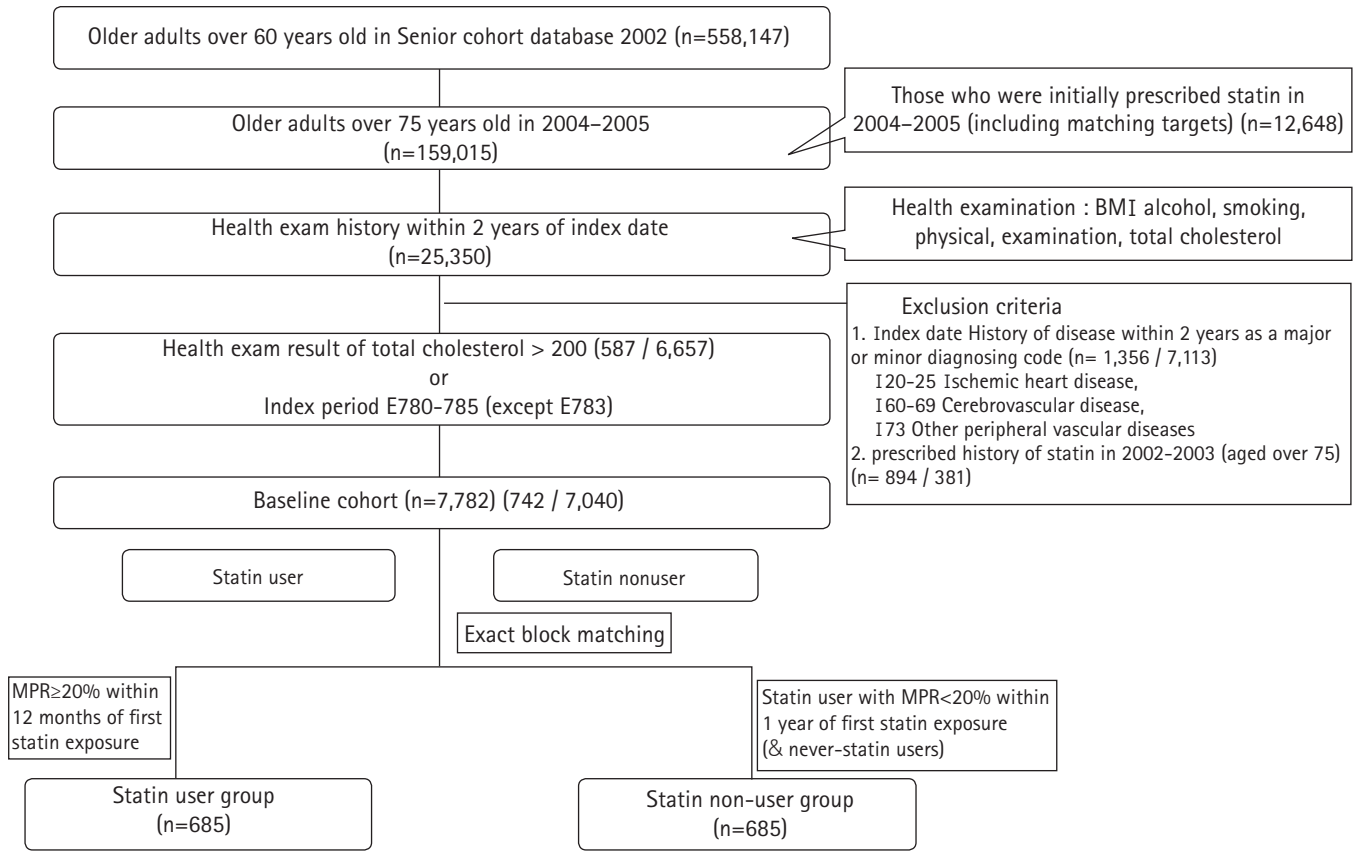

Fig. 1. Flow chart of study subjects. BMI, body mass index; MPR, medication possession ratio.

The DM diagnostic codes were taken from the 10th revision of the International Statistical Classification of Diseases as follows: E11 (non-insulin-dependent DM), E12 (malnutrition-related DM), E13 (other specified DM), or E14 (unspecified DM). The classes of antidiabetic drugs recognized for NODM diagnosis were sulfonylureas, biguanides, alpha-glucosidase inhibitors, thiazolidinediones, meglitinides, and insulin.[20] Incretin-based therapies (i.e., glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors) had not yet been introduced during the study period. Liver toxicity (K71, toxic liver disease) and myopathy (G71, drug-induced myopathy; M62.8, rhabdomyolysis) were considered attributable to statins if they occurred within 12 months of initiation.[21]

Ethics Statement

This study was approved by the Kyung Hee University Hospital Research Ethics Committee (No. KMC IRB 1601-09).

Statistical Analyses

We defined overall survival, one of the primary endpoints of this study, as the time from the enrollment date to the date of death from any cause. The baseline characteristics of the two groups are expressed as means and standard deviations for continuous variables and as percentages for categorical variables. We used Wilcoxon two-sample and Fisher exact tests for continuous and categorical variables, respectively. We performed log-rank tests and Cox proportional hazard regression to examine the differences between the statin user and non-user groups. Finally, we estimated the hazard ratios (HRs) adjusted for age, sex, BMI, DM, hypertension (HTN), aspirin, and antiplatelet use. All statistical analyses were conducted using R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria) and SAS version 9.3 (SAS Institute Inc., Cary, NC, USA) to explore and modify the large datasets.

RESULTS

General Characteristics

The average age of the 1,370 people who met the inclusion criteria was 78 years. The mean follow-up period was 8.7 years (statin users 8.7 years vs. statin non-users 8.6 years). We analyzed 685 pairs by propensity matching for sex, cholesterol level, and residential area. Statin users were more likely to have HTN and DM and to be

Table 1. Baseline characteristics

Variable	Exact matched cohort		
	Statin users (n = 685)	Statin non-users (n = 685)	p-value
Age (y)	78.0 ± 3.0	78.1 ± 3.2	0.900
Sex, women	450 (65.7)	450 (65.7)	1.000
HTN	548 (80.0)	267 (39.0)	< 0.001
Diabetes mellitus	241 (35.2)	90 (13.1)	< 0.001
Aspirin use	130 (19.0)	31 (4.5)	< 0.001
Antiplatelet use	185 (27.0)	39 (5.7)	< 0.001
HTN medication use	460 (67.2)	200 (29.2)	< 0.001
Alcohol drinker	51 (7.4)	44 (6.4)	0.520
Smoker	86 (12.6)	101 (14.7)	0.270
BMI (kg/m^2)	23.9 ± 3.3	23.2 ± 3.3	< 0.001
Physically active	130 (19.0)	108 (15.8)	0.130
Total cholesterol (mg/dL)	233.2 ± 44.0	237.7 ± 39.9	0.180

Values are presented as mean±standard deviation or number (%).
HTN, hypertension; BMI, body mass index.

taking aspirin or other antiplatelet. We observed no significant differences in age distribution, alcohol, smoking, or physical activity between the statin user and non-user groups (Table 1).

Outcomes according to Statin Use

During follow-up, significantly higher rates of MACE (HR = 1.51; p < 0.001), hospitalization (HR = 1.21, p < 0.001), and NODM (HR = 1.28, p = 0.002) were observed in the statin user group than in the non-user group. In addition, significantly higher rates of MI (HR = 1.25, p < 0.001) and stroke (HR = 1.21, p = 0.026) and a non-significantly higher rate of coronary revascularization (HR = 1.25, p = 0.750) were observed in the statin user group than in the non-user group (Supplementary Table S1). After adjusting for age, sex, BMI, DM (except for NODM), aspirin use, and antiplatelet use, the HRs were 0.83 (p = 0.040) for all-cause mortality, 1.24 (p = 0.030) for MACE, and 1.18 (p = 0.060) for NODM. The risks of hospitalization, cancer, myopathy, and hepatitis did not differ significantly according to statin use (Table 2).

Subgroup Analysis for Stain Use Duration

Our sub-analysis of duration showed a significant relationship between longer statin use (> 5 years) and all-cause mortality (HR = 0.76, p = 0.001) after adjusting for age, sex, BMI, DM, HTN, aspirin use, and antiplatelet use. The MACE risk was elevated among patients who used statins for < 3 years (HR = 1.5, p < 0.001), but MACE risk was lower among patients with statin use duration > 5 years (HR = 0.88, p = 0.360). Similarly, NODM risk was higher for < 3-year statin use duration (HR = 1.10, p = 0.190) but lower for > 5 years duration (HR = 0.95, p = 0.780). These results suggest that patients receiving statins for longer periods were less likely to experience adverse events, including all-cause mortality, MACE, and NODM (Table 3).

DISCUSSION

The most important finding in this study was that statin use for primary prevention in patients aged over 75 years was associated with a lower risk of all-cause mortality and higher risks of MACE and NODM. Longer statin use (> 5 years) resulted in a significantly lower risk of all-cause mortality and did not result in a significantly higher risk for NODM, hospitalization, or cancer compared to those for non-use. Finally, while the risk of MACE in long-term statin use was not statistically significant, it tended to decrease.

Advanced age is recognized as a definite and strong risk factor for cardiovascular disease.[22] The clinical benefit of statin use for secondary prevention, even in older adult patients, has been robustly demonstrated.[23] However, direct evidence of a benefit for primary prevention in patients aged 75 years and over is controversial.[24] Although the reason for this controversy is not clear, differences in sex, study design, participants, age range, and ethnic characteristics between studies may contribute to these differences.[25] The participants included in previous trials of primary prevention were required to have at least one cardiovascular risk factor, e.g., the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) trial[26] or elevated C-reactive protein level, e.g., Justification for the Use of statins in Primary prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial[27]. In contrast, the present study included patients with hypercholesterolemia without cardiovascular diseases irrespective of risk factors.

Although the secondary prevention effect on statin treatment in old age is clearly beneficial, the effect on primary prevention has

Table 2. Risks for outcomes in statin users compared to statin non-users by Cox proportional hazard regression test

Statin	Mortality			MACE			Hospitalization			NODM			Cancer			Myopathy			Hepatitis		
	HR	E	p-value	HR	E	p-value	HR	E	p-value	HR	E	p-value	HR	E	p-value	HR	E	p-value	HR	E	p-value
Non-user	1.00	1.00		1.00	1.00		1.00	1.00		1.00	1.00		1.00	1.00		1.00	1.00		1.00	1.00	
Model 1	0.92	1.31	0.280	1.51	1.99	< 0.001	1.21	1.54	< 0.001	1.28	1.66	0.002	1.03	1.17	0.780	1.42	1.87	0.480	1.08	1.30	0.710
Model 2	0.98	1.13	0.800	1.54	2.03	< 0.001	1.21	1.54	< 0.001	1.26	1.63	0.005	1.08	1.30	0.450	1.31	1.70	0.590	1.07	1.27	0.730
Model 3	0.83	1.53	0.030	1.29	1.67	< 0.001	1.11	1.36	0.090	1.18	1.49	0.060	1.06	1.25	0.640	1.25	1.61	0.680	0.83	1.53	0.400
Model 4	0.83	1.53	0.040	1.24	1.59	0.003	1.11	1.36	0.110	1.18	1.49	0.060	1.08	1.30	0.520	1.26	1.63	0.670	0.82	1.56	0.380

MACE, major adverse cardiovascular events; NODM, new-onset diabetes mellitus; HR, hazard ratio; BMI, body mass index; DM, diabetes mellitus; HTN, hypertension; Model 1, unadjusted; Model 2, adjusted for age, sex, BMI; Model 3, adjusted for age, sex, BMI, DM (except for NODM), HTN; Model 4, adjusted for age, sex, BMI, DM (except for NODM), HTN, aspirin use, antiplatelet use.

Table 3. Outcome risks according to statin use duration in a propensity-score matched cohort: comparison of 3 years vs. 5 years

	Duration (y)	Mortality			MACE			Hospitalization			NODM			Cancer			Myopathy			Hepatitis		
		HR	E	p	HR	E	p	HR	E	p	HR	E	p	HR	E	p	HR	E	p	HR	E	p
Non-user		1.00	1.00		1.00	1.00		1.00	1.00		1.00	1.00		1.00	1.00		1.00	1.00		1.00	1.00	
Model 1	< 3	1.12	1.38	0.520	1.85	2.43	< 0.001	1.37	1.79	< 0.001	1.47	1.94	< 0.001	1.08	1.30	0.580	1.35	1.76	0.700	1.49	1.96	0.230
	3–5	0.95	1.23	0.780	1.34	1.75	0.053	1.09	1.32	0.500	1.37	1.79	0.100	1.07	1.27	0.830	0.50	2.61	0.570	0.82	1.56	0.670
	> 5	0.85	1.48	0.110	1.07	1.27	0.620	0.94	1.26	0.590	0.96	1.20	0.810	0.95	1.23	0.760	2.42	3.07	0.290	0.93	1.28	0.820
Model 2	< 3	1.21	1.54	0.270	1.88	2.46	< 0.001	1.38	1.81	< 0.001	1.45	1.91	0.001	1.14	1.42	0.370	1.24	1.59	0.780	1.49	1.96	0.230
	3–5	1.03	1.17	0.890	1.36	1.78	0.040	1.10	1.34	0.490	1.36	1.78	0.110	1.13	1.40	0.680	0.47	2.75	0.530	0.81	1.58	0.640
	> 5	0.90	1.36	0.300	1.09	1.32	0.510	0.94	1.26	0.600	0.93	1.28	0.660	0.99	1.09	0.950	2.23	2.87	0.390	0.93	1.28	0.800
Model 3	< 3	1.02	1.13	0.920	1.57	2.07	< 0.001	1.27	1.64	0.003	1.10	1.34	0.170	1.11	1.36	0.510	1.19	1.51	0.820	1.16	1.45	0.680
	3–5	0.87	1.44	0.480	1.15	1.44	0.370	1.01	1.09	0.970	0.91	1.34	0.460	1.10	1.34	0.750	0.44	2.91	0.510	0.63	2.10	0.310
	> 5	0.76	1.71	0.010	0.89	1.39	0.410	0.86	1.46	0.270	0.95	1.23	0.770	0.97	1.17	0.860	2.12	2.74	0.380	0.72	1.82	0.290
Model 4	< 3	1.03	1.17	0.880	1.5	1.98	< 0.001	1.26	1.63	0.004	1.10	1.34	0.190	1.13	1.40	0.420	1.21	1.54	0.810	1.14	1.42	0.710
	3–5	0.88	1.41	0.510	1.11	1.36	0.480	1.00	1.00	0.980	0.92	1.31	0.470	1.13	1.40	0.690	0.45	2.86	0.520	0.62	2.13	0.300
	> 5	0.76	1.71	0.010	0.88	1.41	0.360	0.86	1.46	0.240	0.95	1.23	0.780	0.99	1.09	0.950	2.14	2.77	0.380	0.71	1.85	0.280

MACE, major adverse cardiovascular events; NODM, new-onset diabetes mellitus; HR, hazard ratio; BMI, body mass index; DM, diabetes mellitus; HTN, hypertension; Model 1, unadjusted; Model 2, adjusted for age, sex, BMI; Model 3, adjusted for age, sex, BMI, DM (except for NODM), HTN; Model 4, adjusted for age, sex, BMI, DM (except for NODM), HTN, aspirin use, antiplatelet use.

not been clear in randomized controlled trial studies. The PROSPER study was the first to investigate the effect of statin use in older adults without cardiovascular disease.[26] The results indicated a 15% decreased risk of cardiovascular disease in the pravastatin group than in the placebo group, but no reduction in all-cause mortality (HR = 0.85; 95% confidence interval [CI], 0.77–1.15). In the JUPITER study, the use of rosuvastatin did not significantly reduce mortality (HR = 0.8; 95% CI, 0.62–1.04) in those aged over 70 years without cardiovascular disease, with an LDL-C level < 130 mg/dL and high-sensitivity (hs)-CRP level of 2 mg/L or higher, but it did decrease cardiovascular disease incidence[27] (HR = 0.61; 95% CI, 0.46–0.82). In the Cholesterol Treatment Trialists, meta-analysis of subjects over 75 years of age did not prove the primary prevention effect[4] (HR = 0.92; 95% CI, 0.73–1.16).

The results of observational studies have suggested mixed and less obvious benefits of initiating statins in patients older than 75 years with increased risks of cardiovascular disease, such as diabetics (e.g., Ramos et al.[28]), with cardiovascular disease risk factors (e.g., the Statins on Clinical Outcomes for Primary prevention in individuals aged > 75 years (SCOPE-75) trial[29]), or in men (e.g., Orkaby et al.[30]).

In the present study, statin use for primary prevention in patients aged over 75 years increased the risk of MACE for the first 3 years. Physicians may have been more likely to prescribe statins to patients with veiled cardiovascular risk factors that were not registered on claim diagnostic codes, which could have increased the healthy user selection bias.[31]

However, our sub-analyses of use duration showed that the risk of MACE, hospitalization, and NODM decreased after 5 years of starting statin prescription. This result is consistent with Mansi's finding that statin users had significantly higher odds of developing diabetes (odds ratio [OR] = 1.93; 95% CI, 1.55–2.41), which persisted throughout follow-up and that short-term statin use was not associated with decreased odds of major acute cardiovascular events (OR = 1.17; 95% CI, 0.72–1.92).[32] These results indicate that statins may be effective for primary prevention when used long-term (e.g., 5 years or more).

Meanwhile, concern about statin use in older adults is related to fear of myalgia, increased fall risk, liver enzyme elevation, cognitive impairment, stroke, fatigue, and drug interactions in polypharmacy patients.[33,34] However, in this study, we observed no differences in the risks of myopathy and hepatitis between statin users and non-users. Moreover, statin therapy was not associated with elevated risks of cancer or hospitalization. Our results are similar to the those of the 2015 the Patient and provider Assessment of Lipid Management (PALM) registry, in which statins appeared to be similarly tolerated in older (> 75 years) and younger adults.[35]

Our study has several limitations. First, there was the possibility of coding errors, missing data, lack of clinically relevant data because of unmeasured variables, or missing relevant drug use that was not typically collected in nationally-based datasets. Second, this was an observational study; hence, it suffers from potential selection bias despite robust exact block matching. One possible selection bias was that frail people might have been less likely to be prescribed statins. However, we observed no difference in physical activity between statin users and non-users and the prevalence of diabetes and HTN, which are potential risk factors for frailty, was higher in the statin group. These findings indicate that it was unlikely that the statin non-user group included more frail population. Moreover, patients with severe frailty were not likely to be included in this study because they could not have visited health examination centers and were excluded. Third, our study may be influenced by an immortal time bias. Statin users with MPR > 20% during the observation period must survive to receive consecutive prescriptions and were, thus, less likely to die, which may have biased the increased mortality in the statin user group. However, our analysis of mortality as of the median time of survival duration showed no difference between statin users and non-users. Thus, we postulate the risk of immortal time bias might be less substantial. Fourth, we did not compare LDL-C, HDL cholesterol, and triglyceride levels between statin users and non-users, which could have affected the results, partly because LDL-C measurement was not included in the national health exam and triglyceride and HDL measurements were introduced in 2009. Fifth, we could not accurately confirm the cumulative or dose effects of statins because we could not determine the daily dose of statins from the available data. Sixth, while alcohol and smoking are risk factors for mortality, they did not differ significantly between statin users and non-users. Therefore, they were not confounding factors and were excluded from the adjustment. Seventh, there was a possibility of unknown confounding regarding adverse outcomes in the statistical analysis, despite the exact block matching method in consideration of this concern.

Despite these limitations, this nationwide study included a large sample of the older Korean adult population (> 75 years) and demonstrated the benefit of statins for primary prevention if used for more than 5 years in terms of reducing all-cause mortality. In conclusion, the results of our study suggested that the use of statins for primary prevention by adults aged over 75 years was associated with a significant lower mortality risk.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

This study was supported grants by the Korea Geriatrics Society. The National Health Information Database was provided by the National Health Insurance Service of Korea.

AUTHOR CONTRIBUTIONS

Conceptualization, WCW, KSY; Data curation, CHS; Funding acquisition, KSY; Investigation, WCW, KSY; Methodology, WCW, KSY, CHS; Project administration, KSY, CHS; Supervision, WCW, KSY; Writing original draft, KSY; Writing-review & editing, KSY, WCW.

Supplementary Materials

Supplement materials can be found via https://doi.org/10.4235/agmr.20.0028.

REFERENCES

1. Jang IY, Lee HY, Lee E. Geriatrics fact sheet in Korea 2018 from national statistics. Ann Geriatr Med Res 2019;23:50-3.
2. Korean Statistical Information Service. Causes of death in 2018 [Internet]. Daejeon, Korea: Korean Statistical Information Service; c2020 [cited 2020 Jun 22]. Available from: http://kosis.kr/statHtml/statHtml.do?orgId=101&tblId=DT_1B34E01&conn_path=I2.
3. Veniant MM, Sullivan MA, Kim SK, Ambroziak P, Chu A, Wilson MD, et al. Defining the atherogenicity of large and small lipoproteins containing apolipoprotein B100. J Clin Invest 2000;106:1501-10.
4. Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. Lancet 2010;376:1670-81.
5. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63(25 Pt B):2889-934.
6. US Preventive Services Task Force. Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force Recommendation Statement. JAMA 2016;316:1997-2007.
7. Mortensen MB, Falk E. Primary prevention with statins in the elderly. J Am Coll Cardiol 2018;71:85-94.
8. Rabar S, Harker M, O'Flynn N, Wierzbicki AS; Guideline Development Group. Lipid modification and cardiovascular risk assessment for the primary and secondary prevention of cardiovascular disease: summary of updated NICE guidance. BMJ 2014;349:g4356.
9. Anderson TJ, Gregoire J, Pearson GJ, Barry AR, Couture P, Dawes M, et al. 2016 Canadian Cardiovascular Society Guidelines for the management of dyslipidemia for the prevention of cardiovascular disease in the adult. Can J Cardiol 2016;32:1263-82.
10. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J 2016;37:2315-81.
11. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;73:3168-209.
12. Korean Academy of Medicine Science. Evidence-based guideline for dyslipidemia in primary care. Cheongju, Korea: Korean Academy of Medicine Science, Korea Centers for Disease Control and Prevention; 2018.
13. Gillmann K, El Ameen A, Massy R, Fabro F, Gasc A, Herbort CP Jr. Assessment of measurement methods of posterior inflammation in stromal choroiditis: the value of quantitative outcome measures versus the presently qualitatively based paradigm. Int Ophthalmol 2019;39:1567-74.
14. Ott BR, Daiello LA, Dahabreh IJ, Springate BA, Bixby K, Murali M, et al. Do statins impair cognition? A systematic review and meta-analysis of randomized controlled trials. J Gen Intern Med 2015;30:348-58.
15. Kwon S. Thirty years of national health insurance in South Korea: lessons for achieving universal health care coverage. Health Policy Plan 2009;24:63-71.
16. Lee J, Lee JS, Park SH, Shin SA, Kim K. Cohort Profile: The National Health Insurance Service-National Sample Cohort (NHIS-NSC), South Korea. Int J Epidemiol 2017;46:e15.
17. Hwang D, Kim S, Choi H, Oh IH, Kim BS, Choi HR, et al. Calcium-channel blockers and dementia risk in older adults - National Health Insurance Service-Senior Cohort (2002-2013). Circ J

2016;80:2336-42.
18. Garcia-Perez LE, Alvarez M, Dilla T, Gil-Guillen V, Orozco-Beltran D. Adherence to therapies in patients with type 2 diabetes. Diabetes Ther 2013;4:175-94.
19. Deedwania P, Stone PH, Bairey Merz CN, Cosin-Aguilar J, Koylan N, Luo D, et al. Effects of intensive versus moderate lipid-lowering therapy on myocardial ischemia in older patients with coronary heart disease: results of the Study Assessing Goals in the Elderly (SAGE). Circulation 2007;115:700-7.
20. Ko SH, Kim DJ, Park JH, Park CY, Jung CH, Kwon HS, et al. Trends of antidiabetic drug use in adult type 2 diabetes in Korea in 2002-2013: Nationwide population-based cohort study. Medicine (Baltimore) 2016;95:e4018.
21. Cziraky MJ, Willey VJ, McKenney JM, Kamat SA, Fisher MD, Guyton JR, et al. Statin safety: an assessment using an administrative claims database. Am J Cardiol 2006;97:61C-68C.
22. Prospective Studies Collaboration. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. Lancet 2007;370:1829-39.
23. Strandberg TE, Kolehmainen L, Vuorio A. Evaluation and treatment of older patients with hypercholesterolemia: a clinical review. JAMA 2014;312:1136-44.
24. Cholesterol Treatment Trialists' Collaboration. Efficacy and safety of statin therapy in older people: a meta-analysis of individual participant data from 28 randomised controlled trials. Lancet 2019;393:407-15.
25. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. J Am Coll Cardiol 2017;70:1-25.
26. Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet 2002;360:1623-30.
27. Glynn RJ, Koenig W, Nordestgaard BG, Shepherd J, Ridker PM. Rosuvastatin for primary prevention in older persons with elevated C-reactive protein and low to average low-density lipoprotein cholesterol levels: exploratory analysis of a randomized trial. Ann Intern Med 2010;152:488-96.
28. Ramos R, Comas-Cufi M, Marti-Lluch R, Ballo E, Ponjoan A, Alves-Cabratosa L, et al. Statins for primary prevention of cardiovascular events and mortality in old and very old adults with and without type 2 diabetes: retrospective cohort study. BMJ 2018;362:k3359.
29. Kim K, Lee CJ, Shim CY, Kim JS, Kim BK, Park S, et al. Statin and clinical outcomes of primary prevention in individuals aged > 75 years: The SCOPE-75 study. Atherosclerosis 2019;284:31-6.
30. Orkaby AR, Gaziano JM, Djousse L, Driver JA. Statins for primary prevention of cardiovascular events and mortality in older men. J Am Geriatr Soc 2017;65:2362-8.
31. Emilsson L, Garcia-Albeniz X, Logan RW, Caniglia EC, Kalager M, Hernan MA. Examining bias in studies of statin treatment and survival in patients with cancer. Version 2. JAMA Oncol 2018;4:63-70.
32. Mansi IA, English J, Zhang S, Mortensen EM, Halm EA. Long-term outcomes of short-term statin use in healthy adults: a retrospective cohort study. Drug Saf 2016;39:543-59.
33. Strandberg TE. Role of statin therapy in primary prevention of cardiovascular disease in elderly patients. Curr Atheroscler Rep 2019;21:28.
34. Odden MC, Pletcher MJ, Coxson PG, Thekkethala D, Guzman D, Heller D, et al. Cost-effectiveness and population impact of statins for primary prevention in adults aged 75 years or older in the United States. Ann Intern Med 2015;162:533-41.
35. Nanna MG, Navar AM, Wang TY, Mi X, Virani SS, Louie MJ, et al. Statin use and adverse effects among adults > 75 years of age: insights from the patient and provider assessment of lipid management (PALM) registry. J Am Heart Assoc 2018;7:e008546.

AGMR
Annals of Geriatric Medicine and Research

Original Article
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):99-106
https://doi.org/10.4235/agmr.20.0018

Physical Performance Correlates with Self-Reported Physical Function and Quality of Life in Patients at 3 Months after Total Knee Arthroplasty

Jun Hwan Choi[1], Bo Ryun Kim[2], Sang Rim Kim[3], Kwang Woo Nam[3], So Young Lee[1], Won Bin Kim[1], Youn Ji Kim[1]

[1]Department of Rehabilitation Medicine, Regional Rheumatoid and Degenerative Arthritis Center, Jeju National University Hospital, Jeju National University College of Medicine, Jeju, Korea
[2]Department of Physical Medicine and Rehabilitation, Korea University Anam Hospital, Seoul, Korea
[3]Department of Orthopedic Surgery, Regional Rheumatoid and Degenerative Arthritis Center, Jeju National University Hospital, Jeju National University College of Medicine, Jeju, Korea

Corresponding Author:
Bo Ryun Kim, MD, PhD
Department of Physical Medicine and Rehabilitation, Korea University Anam Hospital, 73 Goryeodae-ro, Seongbuk-gu, Seoul 02841, Korea
E-mail: brkim08@gmail.com
ORCID:
https://orcid.org/0000-0001-7788-7904

Received: March 31, 2020
Revised: May 21, 2020
Accepted: May 21, 2020

Background: Although total knee arthroplasty (TKA) is an effective treatment for knee osteoarthritis, assessment of postoperative outcomes remains unclear. This study aimed to identify postoperative physical performance factors that are correlated with self-reported physical function and quality of life (QoL) at 3 months after unilateral TKA. **Methods:** In total, 158 patients who underwent unilateral primary TKA completed performance-based physical function tests at 3 months after surgery, including Stair Climbing Tests (SCT), 6-Minute Walk Tests (6MWT), Timed Up and Go tests (TUG), and instrumental gait analysis. We also measured the isometric knee flexor and extensor strengths of the operated and non-operated knees. Self-reported physical function and QoL were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Euro-QoL Five Dimensions (EQ-5D) questionnaire, respectively. **Results:** Bivariate analyses showed that WOMAC function and EQ-5D were correlated with age, other self-reported measures, and performance-based measures. The WOMAC pain ($r=0.71$, $p<0.001$) showed a high positive correlation. While the EQ-5D ($r=-0.7$, $p<0.001$) showed a highly negative correlation with WOMAC function, WOMAC pain ($r=-0.67$, $p<0.001$) showed a moderately negative correlation with EQ-5D. In multivariate linear regression analyses, WOMAC pain, peak torque of the flexor of the non-operated knee, and reductions in extensor and stride length were associated with self-reported physical function, whereas WOMAC pain, SCT ascent, and cadence were associated with postoperative QoL. **Conclusions:** Physical performance factors were significantly associated with self-reported physical function and QoL in patients at 3 months after unilateral TKA. These findings suggest that performance-based physical function could be used to assess outcomes after TKA.

Key Words: Osteoarthritis, Knee, Arthroplasty, Rehabilitation, Quality of life

INTRODUCTION

Knee osteoarthritis (OA) is the single most common joint disease and a major cause of disability in older adults. Pain and swelling of the affected joints can reduce mobility and impair activities of daily living and quality of life (QoL).[1,2]

Total knee arthroplasty (TKA) is an effective and cost-efficient treatment for patients with end-stage knee arthritis.[3] The most prevalent preoperative expectations of TKA are relief of pain.[4,5] However, despite pain relief after successful TKA, patient expectations of physical function and QoL are often unfulfilled.[6,7]

Physical function changes over time after TKA. Our previous

study showed correlations between preoperative performance-based physical function and self-reported physical function and QoL.[8] Dynamic balance and exercise capacity were powerful predictors of self-reported physical function and QoL. During the first month after TKA, physical performance and the results of self-reported questionnaires worsen substantially from preoperative conditions.[9,10] Performance-based measures showed greater responsiveness compared to self-reported questionnaires early after surgery and patients tend to overestimate actual short- and long-term changes in physical function after TKA.[11] In addition, several studies using both questionnaires and physical performance functions have shown that the self-reported physical function of individuals often differs substantially from their actual functional capability.[12,13] Due to the discrepancies between self-reported and performance-based physical function, correlation analysis of both outcomes is necessary in patients who undergo unilateral TKA. By the third postoperative month, self-reported physical function and QoL scores usually surpass preoperative values.[14] Moreover, the greatest improvements in gait and lower extremity function occur during the first 3 months after TKA.[15] By this time, most patients have resumed their daily activities in the community and at home.

We previously reported improvement in functional outcomes during the first 3 months after the application of a critical pathway for patients who underwent TKA.[16] This study included patients who underwent unilateral and bilateral TKA; however, we did not assess the relationship between physical performance and self-reported physical function.

Identifying performance-based measures that affect self-reported measures will likely be meaningful; moreover, it is important to identify factors that prevent patients from fulling their expectations after TKA. Therefore, this study aimed to identify postoperative physical performance factors related with self-reported physical function and QoL at 3 months after unilateral TKA. The results of this study may guide postoperative rehabilitation strategies to improve physical performance and self-reported physical function and QoL.

MATERIALS AND METHODS

Study Design and Participants

This retrospective cross-sectional study enrolled 158 patients who were diagnosed with knee OA and underwent unilateral primary TKA between October 2013 and May 2019. The inclusion criterion for this study was patients who walk independently with or without an ambulatory aid after surgery. Patients with previous neurological, cardiorespiratory, or orthopedic disease that caused ambulatory deficits were excluded.

All patients completed performance-based physical function tests, including Stair Climbing Tests (SCTs), 6-Minute Walk Tests (6MWTs), Timed Up and Go tests (TUGs), and instrumental gait analyses. We also measured the isometric knee flexor and extensor strengths of the operated and non-operated knees. Self-reported physical function and pain were measured using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and self-reported QoL was measured using the Euro-QoL Five Dimensions (EQ-5D) questionnaire.

We informed the patients about the nature of the study and its risks and benefits and all participants provided written consent. The study protocol was approved by the Institutional Review Board at Jeju National University Hospital (No. JEJUNUH 2019-12-013).

Rehabilitation Protocol

Beginning on the first day after TKA, patients underwent a standard rehabilitation program including passive knee range of motion (ROM) and physical modalities such as cryotherapy and transcutaneous electrical nerve stimulation for relief of knee pain and swelling. The patients started progressive resistance strengthening exercises 7 days after surgery and an intensive rehabilitation program including gait training, aerobic exercises using an ergometer, functional training for transfer, and stair climbing beginning on postoperative day 14. The patients participated in the rehabilitation programs twice daily, five times per week for 2 weeks in the rehabilitation department under the supervision of physical therapists.

Outcome Measures

All patients underwent assessments 3 months after surgery, with physical performance and self-reported physical function and QoL tests performed on the same day.

Assessments of performance-based physical function

6MWT: The 6MWT is a performance-based measure of functional exercise capacity, such as walking capacity and gait endurance, in adults. In this test, the participants walk as far as possible for 6 minutes along a 50-m hallway marked with lines.[17]

TUG: The TUG test is used to evaluate a dynamic balance. In this test, the participants sit with their backs against a chair (seat height, 44 cm; width, 49 cm; armrest height, 64 cm) placed at the end of a marked 3-m distance and stand up upon hearing the word "go", walk at a comfortable speed past the 3-m mark, turn around, walk back, and sit down again in the chair without physical assistance, all while being timed.[18]

SCT: The SCT is a measurement of the time required to ascend

and descend a flight of 12 steps, each 17 cm high and 25 cm wide. In this test, the participants ascend or descend the stairs as fast as possible upon hearing the word "go". Each patient completed three trials, with a 5-minute rest interval between each pair of trials. The fastest time was recorded for each patient.[19]

Measurement of knee ROM: The ROM of the affected knee was measured using a standard long-arm goniometer. The axis, movement arm, and stationary arm of the goniometer were aligned with the center of the lateral epicondyle of the femur, the lateral malleolus, and the greater trochanter of the femur, respectively. The knee flexion ROM was measured as the maximal active bending of the knee with the patient in the supine position. Knee extension ROM was measured as the angle of maximal active straightening with the patient's heel propped on a 10-cm wooden block. The degree of extension beyond zero for hyperextension during this assessment was recorded as a negative value.[20,21]

Gait analysis: A wireless inertial sensing device (G-WALK; BTS Bioengineering S.p.A., Milan, Italy) was used to measure the spatiotemporal variables of gait. The patients wore a semi-elastic back-belt device on the waist to measure the acceleration of the anteroposterior, mediolateral, and vertical axes and were instructed to walk barefoot along an 8-m pathway at a comfortable speed. Gait data were transmitted via Bluetooth to a personal computer and were processed using the BTS G-WALK system, a dedicated software program that measures length, duration, and single supports to calculate a typical gait curve. The second positive peak on the curve was the instant at which the patient's foot contacted the ground. Therefore, the step length was defined as the distance between two successive foot contacts with the ground, while stride length was defined as the distance between three successive foot contacts. The first and last steps were removed from all calculations because of abnormal patterns and psychological responses at the start and end of walking, respectively.[22]

Measurements of isometric strengths of knee extensors and flexors: A physical therapist used an isokinetic dynamometer (HUMAC NORM; Computer Sports Medicine Inc., Stoughton, MA, USA) to measure the maximal isometric strengths of the bilateral knee extensors and flexors. All patients were instructed to start a structured warm-up with the knee joint fixed at 60° of flexion to generate maximal isometric force, followed by maximal voluntary contractions until the torque did not increase by more than 5% during three successive attempts. The patients then performed knee flexion and extension as discrete movements in a single direction. Each contraction lasted 4–5 seconds, with 2-minute rest intervals between contractions. After a 5-minute rest, the patients repeated the procedure on the other lower limb. The variables measured included the peak torques (PTs) of the extensor and flexor, the ratio of hamstring to quadriceps strength (H/Q ratio), and the difference in the strengths of the extensors and flexors between the operated and non-operated knees, expressed as percentages of the strengths of the non-operated knee.[21,23]

Assessment of self-reported physical function and QoL

WOMAC: The multidimensional WOMAC index is a questionnaire used to assess pain, stiffness, and physical functional disability[24] and has previously been applied to measure self-reported disability in patients with knee OA. The WOMAC index comprises 24 variables: 5 addressing pain, 2 addressing stiffness, and 17 addressing physical function. Each of these variables is scored using a 5-point Likert scale (0 = none, 1 = slight, 2 = moderate, 3 = very, 4 = extremely). The WOMAC index measures the degree of pain, stiffness, and difficulty in performing 17 activities during the preceding 48 hours. Higher scores indicate greater levels of pain, stiffness, and difficulty.

EQ-5D questionnaires: The EQ-5D questionnaire is widely used to evaluate self-reported QoL by measuring five dimensions of QoL: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.[25] Each dimension has three levels of severity (no problems, some or moderate problems, and extreme problems). The scores were converted using utility weights derived from the general Korean population and ranged from -1 to 1. Lower scores indicated worse overall health status.

Statistical Analysis

All variables were subjected to descriptive statistics. We used Pearson correlation analysis to assess the relationships between postoperative self-reported physical function and QoL, and physical performance. Multivariate linear regression analysis using a backward selection linear regression model was used to determine the postoperative physical performance factors independently associated with self-reported physical function and QoL 3 months after TKA. We used SPSS for Windows version 20.0 (IBM SPSS, Armonk, NY, USA) to perform all analyses, with $p < 0.05$ considered statistically significant.

RESULTS

This study enrolled 158 patients (134 women and 24 men) with a mean age of 72.6 ± 5.8 years and mean body mass index (BMI) of 25.6 ± 3.0 kg/m^2. Their baseline demographic and disease-related characteristics are presented in Table 1. Of these 158 patients, 131 (82.9%) had Kellgren–Lawrence grade IV knee OA.

Table 1. Demographic and disease-related characteristics of the subjects (n=158)

Characteristic	Value
Age (y)	72.6 ± 5.8
Sex	
Male	24 (15.2)
Female	134 (84.8)
BMI (kg/m^2)	25.6 ± 3.0
K–L grade	
3	27 (17.1)
4	131 (82.9)
Comorbidities	
Osteoporosis	81 (51.3)
Pre-sarcopenia	7 (4.4)
Degenerative spine disease	26 (16.5)
Diabetes mellitus	29 (18.4)
Hypertension	106 (67.1)

Values are presented as mean±standard deviation or number (%).
BMI, body mass index; K–L grade, Kellgren–Lawrence grade.

Postoperative Evaluation of Performance-based Physical function, Self-reported Physical Function, and QoL and Their Correlations

Table 2 presents the average postoperative performance-based physical function, self-reported physical function, and QoL scores of these patients.

In bivariate analyses, WOMAC function showed significant positive correlations with age (r = 0.29, p < 0.001), WOMAC pain score (r = 0.71, p < 0.001), WOMAC stiffness score (r = 0.24, p = 0.003), TUG (r = 0.22, p = 0.005), SCT ascent (r = 0.24, p = 0.003), SCT descent (r = 0.22, p = 0.007), and knee extensor deficit (r = 0.16, p = 0.047). WOMAC function also showed significant negative correlations with EQ-5D score (r = -0.70, p < 0.001), stride length (r = -0.19, r = 0.022), and PT of the flexor of the operated (r = -0.38, p < 0.001) and non-operated (r = -0.47, p < 0.001) knees.

EQ-5D scores showed significant negative correlations with age (r = -0.30, p < 0.001), WOMAC pain score (r = -0.67, p < 0.001), WOMAC stiffness score (r = -0.16, p = 0.043), WOMAC function score (r = -0.70, p < 0.001), TUG (r = 0.22, p = 0.005), SCT ascent (r = 0.24, p = 0.003), and SCT descent (r = 0.22, p = 0.007). EQ-5D scores also showed significant positive correlations with 6MWT (r = 0.31, p < 0.001), cadence (r = 0.22, p = 0.007), and the PT of the flexors of the operated (r = 0.24, p = 0.002) and non-operated (r = 0.27, p = 0.001) knees (Table 3).

Table 2. Postoperative evaluation of performance-based physical function, self-reported physical function, and quality of life in patients 3 months after unilateral TKA

Variable	Value
6MWT (m)	443.41 ± 101.76
TUG (sec)	9.24 ± 1.78
SCT (sec)	
Ascent	10.74 ± 3.94
Descent	12.01 ± 3.96
ROM (°)	
Affected ROM flexion	124.66 ± 11.59
Affected ROM extension	-7.69 ± 5.43
Gait linear parameters	
Gait speed (m/s)	1.20 ± 0.82
Cadence (steps/min)	120.09 ± 12.97
Stride length (cm)	111.75 ± 20.71
Gait cycle duration (sec)	1.66 ± 8.07
Stance phase duration (% of gait cycle)	64.67 ± 3.39
Swing phase duration (% of gait cycle)	35.57 ± 1.81
Double support duration (% of gait cycle)	27.91 ± 4.82
Single support duration (% of gait cycle)	35.57 ± 3.21
Isometric strength test	
PT of the extensor of the operated knee (Nm)	80.47 ± 26.00
PT of the extensor of the non-operated knee (Nm)	102.92 ± 63.65
PT of the flexor of the operated knee (Nm)	51.95 ± 14.05
PT of the flexor of the non-operated knee (Nm)	52.56 ± 15.26
Extensor deficit (%)	21.56 ± 21.02
Flexor deficit (%)	10.09 ± 14.86
Self-reported physical function	
WOMAC-Pain	4.13 ± 2.17
WOMAC-Stiffness	1.97 ± 1.04
WOMAC-Function	17.61 ± 8.79
Self-reported quality of life	
EQ-5D	0.82 ± 0.09

Values are presented as mean±standard deviation or number (%).
TKA, total knee arthroplasty; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; 6MWT, 6-Minute Walk Test; TUG, Timed Up and Go test; SCT, Stair Climbing Test; EQ-5D, Euro-QOL Five Dimensions; ROM, range of motion; PT, peak torque.

Factors related with Self-reported Physical Function and QOL by Multivariate Linear Regression Analysis

Postoperative WOMAC-Function score was significantly and independently associated with age (β = 0.15, p = 0.011), WOMAC pain score (β = 0.59, p < 0.001), stride length (β = -0.15, p = 0.009), PT of the flexor of the non-operated knee (β = -0.31, p < 0.001), and extensor deficit (β = 0.16, p = 0.006). The postoperative EQ-5D score was significantly and independently associated with the

Table 3. Correlations between postoperative self-reported physical function and quality of life and physical performance in patients 3 months after unilateral TKA

Variable	Correlation coefficients (r)	
	WOMAC function	EQ-5D
Age (y)	0.29*	-0.30*
BMI (kg/m^2)	-0.08	-0.01
Self-reported physical function		
WOMAC-Pain	0.71*	-0.67*
WOMAC-Stiffness	0.24*	-0.16*
WOMAC-Function	1	-0.70*
Self-reported quality of life		
EQ-5D	-0.70*	1
6MWT (m)	0.01	0.31*
TUG (sec)	0.22*	-0.42*
SCT (sec)		
Ascent	0.24*	-0.41*
Descent	0.22*	-0.43*
ROM (°)		
Affected ROM flexion	0.10	-0.07
Affected ROM extension	-0.14	0.14
Gait linear parameters		
Gait speed (m/s)	-0.02	-0.03
Cadence (steps/min)	-0.03	0.22*
Stride length (cm)	-0.19*	0.10
Gait cycle duration (sec)	-0.04	0.04
Stance phase duration (% of gait cycle)	0.00	-0.10
Swing phase duration (% of gait cycle)	0.12	-0.06
Double support duration (% of gait cycle)	0.11	-0.02
Single support duration (% of gait cycle)	0.02	-0.09
Isometric strength test		
PT of the extensor of the operated knee (Nm)	-0.15	0.14
PT of the extensor of the non-operated knee (Nm)	-0.13	0.11
PT of the flexor of the operated knee (Nm)	-0.38*	0.24*
PT of the flexor of the non-operated knee (Nm)	-0.47*	0.27*
Extensor deficit (%)	0.16*	-0.08
Flexor deficit (%)	0.02	0.13

TKA, total knee arthroplasty; BMI, body mass index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; 6MWT, 6-Minute Walk Test; TUG, Timed Up and Go test; SCT, Stair Climbing Test; EQ-5D, Euro-QOL Five Dimensions; ROM, range of motion; PT, peak torque.
*p<0.05.

WOMAC pain score ($\beta = -0.62$, $p < 0.001$), SCT ascent ($\beta = -0.18$, $p = 0.013$), and cadence ($\beta = 0.13$, $p = 0.031$) (Table 4).

DISCUSSION

The results of the present study showed that objective performance-based physical function was correlated with self-reported physical function and QoL at 3 months after unilateral TKA. WOMAC function and EQ-5D scores were correlated with age, other self-reported measures, and performance-based measures. Based on the classification of correlations as very high, high, moderate, low, or negligible,[26] the WOMAC pain score showed a highly positive correlation with the WOMAC function score ($r = 0.71$, $p < 0.001$), whereas the EQ-5D showed a highly negative correlation with WOMAC function score ($r = -0.70$, $p < 0.001$). Pain after TKA was inversely correlated with time to recovery[27] and preoperative pain is correlated with self-reported physical function.[8] Patients experience pain for up to 3 months after surgery; however, even reduced pain can negatively affect physical function. Our results suggested that preoperative and postoperative pain control in patients could improve their physical function.

Among the performance-based physical function parameters tested in the present study, strengthening of non-operated knee flexor and extensor had significant correlations with WOMAC function. Quadriceps strength is frequently reduced after TKA and may affect physical functions.[10,29,30] Reduced quadriceps strength after TKA was related to lower gait speed,[31] and mobility limitations have been reported to be associated with large deficits of strength in surgical knee.[19] Moreover, the ratio of quadriceps to hamstring muscle strength was a strong predictor of weight-bearing asymmetry.[32] Hamstring muscles on both the operated and non-operated sides were found to be weaker after unilateral TKA. Many rehabilitation programs, however, target quadriceps strengthening of operated side alone, resulting in less information regarding hamstring muscle strength. These results may explain our finding that PT flexor of the non-operated knee and a deficit of the extensor correlated negatively with WOMAC function, and may be useful predictors of postoperative self-reported physical function.

WOMAC-Function score is inversely correlated with gait speed and stride length.[33] Older adults with gait speed < 1 m/s are at high risk of poor health-related outcomes.[34] Comfortable gait speeds for healthy women and men aged 70–79 years are 1.13 and 1.26 m/s, respectively.[35] The mean gait speed in our patients was > 1 m/s, which was comparable to that of healthy adults, suggesting that gait speed had little effect on their physical functions. Normal adults have a mean stride length of 1.39 m,[36] about 20% higher than that in our patient population, suggesting that stride length rather than gait speed might have affected their physical function. Together, these results may explain the negative correlation between stride length and WOMAC function. Rehabilitation strategies after TKA should emphasize pain relief, strengthening the knee extensor and flexor, and gait training to increase stride length to improve functional outcome.

We also found that EQ-5D scores at 3 months after unilateral

Table 4. Factors associated with self-reported physical function and quality of life by multivariate linear regression analysis

Outcome/independent factors	Standardized (β)	p-value	Adjusted R^2
Postoperative WOMAC-Function			0.64
Age	0.15	0.011	
WOMAC-Pain	0.59	< 0.001	
Stride length (cm)	-0.15	0.009	
PT of the flexor of the non-operated knee (Nm)	-0.31	< 0.001	
Extensor deficit (%)	0.16	0.006	
Postoperative EQ-5D			0.58
Age	-0.18	0.004	
WOMAC-Pain	-0.62	< 0.001	
SCT ascent	-0.18	0.013	
Cadence (steps/min)	0.13	0.031	

The logistic regression analyses were adjusted for age, sex, and body mass index (BMI).
WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; PT, peak torque; EQ-5D, Euro-QOL Five Dimensions; SCT, Stair Climbing Test.

TKA were correlated with age, WOMAC pain, WOMAC stiffness, WOMAC function, 6MWT, TUG, SCT ascent, SCT descent, affected ROM extension, cadence, and PT flexor of the operated and non-operated knees. Among these performance-based physical function parameters. Lower pain scores and higher satisfaction scores have been reported in patients after TKA.[27] Our results suggested that postoperative pain control and improved physical performance could increase postoperative QoL.

WOMAC pain was strongly and significantly associated with postoperative EQ-5D. The goals of TKA are to reduce pain, restore knee mobility and function, and improve QoL in cases of severe knee OA. Our previous study also showed a correlation between preoperative pain and self-reported QoL.[8] Moreover, the most significant predictor of patient dissatisfaction is persistent pain after surgery.[37] The results of these and the current study showed that patients continued to experience pain, albeit reduced, for up to 3 months after TKA, which possibly affected their QoL. The patients in our study had relatively lower WOMAC pain scores than those in other studies.[38] These lower scores may have been due to the cross-sectional nature of this study, with all patients receiving adequate rehabilitation for 3 weeks. Nevertheless, our findings suggested that pain relief, even if the surgery was successful, is required to improve patient QoL.

We also found that SCT ascent and cadence were useful factors of postoperative EQ-5D scores. Stair activity is one of three recommended performance-based measures in patients with knee OA.[39] Stair activity is frequently limited in these patients and, as well as being a goal of postoperative rehabilitation, necessary for patient safety and independence. The SCT test is the most responsive performance-based measurement of recovery early after TKA.[11]

Reduced cadence leads to reduced gait speed after TKA.[40,41] Limited gait speed is a significant issue; thus, increasing gait speed is a rehabilitation goal in patients with knee OA.[32] However, because the gait speed of our patients was similar to the comfortable gait speed of healthy individuals, gait speed was unlikely to have a major effect on QoL 3 months after surgery. Thus, rehabilitation strategies should emphasize pain relief, stair activity, and gait training with increased cadence to improve QoL.

Although both gait function (including spatiotemporal parameters) and physical function (including lower limb strengthening) improve greatly during the first 3 months after TKA, patients' subjective expectations of physical function remain unfulfilled until 1 year after TKA.[6] These parameters, as well as isometric strengthening of the knee 1 month after TKA, showed greater improvement in our previous study than in the present study.[42] Accordingly, the self-reported physical function and QoL 3 months after TKA may have been lower than the actually measured values.

Knee flexion and extension ROM at 3 months after TKA were not significantly correlated with physical function or QoL. Moreover, knee ROM at 1 month after TKA did not significantly affect physical function. These findings indicate that for at least 1 month after TKA, knee ROM is unrelated to physical function and QoL.

This study has some limitations. First, the results may not be generalizable to all TKA surgeries since the participants underwent only unilateral primary TKA. Accordingly, studies of patients who underwent bilateral TKA or revision are warranted. Second, the cross-sectional design of this study prevented analyses of the causal relationships among variables. Finally, we did not compare participants to those who did not receive postoperative rehabilitation after unilateral TKA.

In conclusion, the results of this study identified physical performance factors correlated with self-reported physical function and

QoL in patients at 3 months after unilateral TKA. These findings suggest that these performance-based physical function could be used to assess outcomes after TKA.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

AUTHOR CONTRIBUTION

Conceptualization, BRK, JHC; Data curation, BRK, JHC, SYL, WBK, YJK; Investigation, BRK, JHC; Methodology: BRK, JHC; Project administration, BRK, JHC, SRK, KWN, SYL, WBK, YJK; Writing original draft, BRK, JHC; Review & editing: BRK, JHC.

REFERENCES

1. Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: a review of community burden and current use of primary health care. Ann Rheum Dis 2001;60:91-7.
2. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2163-96.
3. Cross WW 3rd, Saleh KJ, Wilt TJ, Kane RL. Agreement about indications for total knee arthroplasty. Clin Orthop Relat Res 2006;446:34-9.
4. Yoo JH, Chang CB, Kang YG, Kim SJ, Seong SC, Kim TK. Patient expectations of total knee replacement and their association with sociodemographic factors and functional status. J Bone Joint Surg Br 2011;93:337-44.
5. Mancuso CA, Sculco TP, Wickiewicz TL, Jones EC, Robbins L, Warren RF, et al. Patients' expectations of knee surgery. J Bone Joint Surg Am 2001;83:1005-12.
6. Nilsdotter AK, Toksvig-Larsen S, Roos EM. Knee arthroplasty: are patients' expectations fulfilled?: a prospective study of pain and function in 102 patients with 5-year follow-up. Acta Orthop 2009;80:55-61.
7. Jones CA, Voaklander DC, Johnston DW, Suarez-Almazor ME. Health related quality of life outcomes after total hip and knee arthroplasties in a community based population. J Rheumatol 2000;27:1745-52.
8. Hyun CW, Kim BR, Han EY, Kim SR. Preoperative physical performance predictors of self-reported physical function and quality of life in patients scheduled for total knee arthroplasty. J Phys Ther Sci 2016;28:3220-6.
9. Fitzgerald JD, Orav EJ, Lee TH, Marcantonio ER, Poss R, Goldman L, et al. Patient quality of life during the 12 months following joint replacement surgery. Arthritis Rheum 2004;51:100-9.
10. Mizner RL, Petterson SC, Snyder-Mackler L. Quadriceps strength and the time course of functional recovery after total knee arthroplasty. J Orthop Sports Phys Ther 2005;35:424-36.
11. Mizner RL, Petterson SC, Clements KE, Zeni JA Jr, Irrgang JJ, Snyder-Mackler L. Measuring functional improvement after total knee arthroplasty requires both performance-based and patient-report assessments: a longitudinal analysis of outcomes. J Arthroplasty 2011;26:728-37.
12. Wittink H, Rogers W, Sukiennik A, Carr DB. Physical functioning: self-report and performance measures are related but distinct. Spine (Phila Pa 1976) 2003;28:2407-13.
13. Hidding A, van Santen M, De Klerk E, Gielen X, Boers M, Geenen R, et al. Comparison between self-report measures and clinical observations of functional disability in ankylosing spondylitis, rheumatoid arthritis and fibromyalgia. J Rheumatol 1994;21:818-23.
14. Ethgen O, Bruyere O, Richy F, Dardennes C, Reginster JY. Health-related quality of life in total hip and total knee arthroplasty: a qualitative and systematic review of the literature. J Bone Joint Surg Am 2004;86:963-74.
15. Kennedy DM, Stratford PW, Riddle DL, Hanna SE, Gollish JD. Assessing recovery and establishing prognosis following total knee arthroplasty. Phys Ther 2008;88:22-32.
16. Kim JH, Kim BR, Kim SR, Han EY, Nam KW, Lee SY, et al. Functional outcomes after critical pathway for inpatient rehabilitation of total knee arthroplasty. Ann Rehabil Med 2019;43:650-61.
17. Enright PL, McBurnie MA, Bittner V, Tracy RP, McNamara R, Arnold A, et al. The 6-min walk test: a quick measure of functional status in elderly adults. Chest 2003;123:387-98.
18. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991;39:142-8.
19. Almeida GJ, Schroeder CA, Gil AB, Fitzgerald GK, Piva SR. Interrater reliability and validity of the stair ascend/descend test in subjects with total knee arthroplasty. Arch Phys Med Rehabil 2010;91:932-8.
20. Cibere J, Bellamy N, Thorne A, Esdaile JM, McGorm KJ, Chalmers A, et al. Reliability of the knee examination in osteoarthritis: effect of standardization. Arthritis Rheum 2004;50:458-68.
21. Lee SY, Kim BR, Kim SR, Han EY, Nam KW, Park YG. Influence of preoperative physical function on gait 1 month after total knee arthroplasty. Ann Geriatr Med Res 2017;21:188-96.

22. Bugane F, Benedetti MG, Casadio G, Attala S, Biagi F, Manca M, et al. Estimation of spatial-temporal gait parameters in level walking based on a single accelerometer: validation on normal subjects by standard gait analysis. Comput Methods Programs Biomed 2012;108:129-37.
23. Krishnan C, Williams GN. Variability in antagonist muscle activity and peak torque during isometric knee strength testing. Iowa Orthop J 2009;29:149-58.
24. Stucki G, Meier D, Stucki S, Michel BA, Tyndall AG, Dick W, et al. Evaluation of a German version of WOMAC (Western Ontario and McMaster Universities) Arthrosis Index. Z Rheumatol 1996;55:40-9.
25. Kim MH, Cho YS, Uhm WS, Kim S, Bae SC. Cross-cultural adaptation and validation of the Korean version of the EQ-5D in patients with rheumatic diseases. Qual Life Res 2005;14:1401-6.
26. Mukaka MM. A guide to appropriate use of correlation coefficient in medical research. Malawi Med J 2012;24:69-71.
27. Lamplot JD, Wagner ER, Manning DW. Multimodal pain management in total knee arthroplasty: a prospective randomized controlled trial. J Arthroplasty 2014;29:329-34.
28. Wailoo A, Hernandez Alava M, Escobar Martinez A. Modelling the relationship between the WOMAC Osteoarthritis Index and EQ-5D. Health Qual Life Outcomes 2014;12:37.
29. Berth A, Urbach D, Awiszus F. Improvement of voluntary quadriceps muscle activation after total knee arthroplasty. Arch Phys Med Rehabil 2002;83:1432-6.
30. Stevens JE, Mizner RL, Snyder-Mackler L. Quadriceps strength and volitional activation before and after total knee arthroplasty for osteoarthritis. J Orthop Res 2003;21:775-9.
31. Christiansen CL, Bade MJ, Weitzenkamp DA, Stevens-Lapsley JE. Factors predicting weight-bearing asymmetry 1month after unilateral total knee arthroplasty: a cross-sectional study. Gait Posture 2013;37:363-7.
32. Pua YH, Seah FJ, Clark RA, Lian-Li Poon C, Tan JW, Chong HC. Factors associated with gait speed recovery after total knee arthroplasty: a longitudinal study. Semin Arthritis Rheum 2017;46:544-51.
33. Nebel MB, Sims EL, Keefe FJ, Kraus VB, Guilak F, Caldwell DS, et al. The relationship of self-reported pain and functional impairment to gait mechanics in overweight and obese persons with knee osteoarthritis. Arch Phys Med Rehabil 2009;90:1874-9.
34. Cesari M, Kritchevsky SB, Penninx BW, Nicklas BJ, Simonsick EM, Newman AB, et al. Prognostic value of usual gait speed in well-functioning older people: results from the Health, Aging and Body Composition Study. J Am Geriatr Soc 2005;53:1675-80.
35. Bohannon RW, Williams Andrews A. Normal walking speed: a descriptive meta-analysis. Physiotherapy 2011;97:182-9.
36. Burnfield J. Normal and pathologic gait. In: Placzek JD, Boyce DA, editors. Orthopaedic physical therapy secrets. 3rd ed. St Louis, MO: Elsevier; 2016. p. 105-11.
37. Baker PN, Rushton S, Jameson SS, Reed M, Gregg P, Deehan DJ. Patient satisfaction with total knee replacement cannot be predicted from pre-operative variables alone: a cohort study from the National Joint Registry for England and Wales. Bone Joint J 2013;95-B:1359-65.
38. Giesinger JM, Hamilton DF, Jost B, Behrend H, Giesinger K. WOMAC, EQ-5D and Knee Society Score Thresholds for Treatment Success After Total Knee Arthroplasty. J Arthroplasty 2015;30:2154-8.
39. Dobson F, Hinman RS, Roos EM, Abbott JH, Stratford P, Davis AM, et al. OARSI recommended performance-based tests to assess physical function in people diagnosed with hip or knee osteoarthritis. Osteoarthritis Cartilage 2013;21:1042-52.
40. Webster KE, Wittwer JE, Feller JA. Quantitative gait analysis after medial unicompartmental knee arthroplasty for osteoarthritis. J Arthroplasty 2003;18:751-9.
41. McClelland JA, Webster KE, Feller JA, Menz HB. Knee kinematics during walking at different speeds in people who have undergone total knee replacement. Knee 2011;18:151-5.
42. Suh MJ, Kim BR, Kim SR, Han EY, Nam KW, Lee SY, et al. Bilateral quadriceps muscle strength and pain correlate with gait speed and gait endurance early after unilateral total knee arthroplasty: a cross-sectional study. Am J Phys Med Rehabil 2019;98:897-905.

AGMR
Annals of Geriatric Medicine and Research

Original Article
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):107-114
https://doi.org/10.4235/agmr.20.0008

Effects of Sleep Patterns on the Subjective Health Status in Older Men from the 7th Korea National Health and Nutrition Examination Survey, 2016

Hye Rim Hwang, Yun-Jin Kim

Department of Family Medicine, Pusan National University Hospital, Pusan National University School of Medicine, Pusan, Korea

Corresponding Author:
Yun-Jin Kim, MD
Department of Family Medicine, Pusan National University Hospital, Pusan National University School of Medicine, 179 Gudeok-ro, Seo-gu, Busan 49241, Korea
E-mail: yujkim@pusan.ac.kr
ORCID:
https://orcid.org/0000-0002-0204-3253

Received: March 2, 2020
Revised: April 30, 2020
Accepted: May 23, 2020

Background: Sleeping is a major component of health. The prevalence of sleep disorders is expected to be high in older adults, and sleep habits generally differ on weekdays and weekends. This study aimed to clarify the associations between sleep habits and the subjective health status of older adults. **Methods:** This study analyzed data of 1,678 older adults (695 men and 883 women) aged 65 years or older who had participated in the 2016 Korea National Health and Nutrition Examination Survey (KNHANES VII-1) conducted by the Korea Centers for Disease Control and Prevention. The participants' subjective health perceptions were analyzed according to their sleep habits. **Results:** Weekday and weekend sleep durations were related to subjective health in older men ($p<0.05$) but not in women. The subjective health perception was significantly better for a 9-hour sleep duration than for a 7-hour sleep duration in older men. Sleeping and waking times on weekdays and weekends were not related to the subjective health of either men or women. **Conclusion:** Weekday and weekend sleep durations were related to subjective health perception in older men.

Key Words: Sleep, Health status, Elderly

Introduction

Sleeping is a major component of health, and sleep disorders increase the risk of major diseases, including cardiovascular disease.[1] A previous study reported associations between sleep disorder and heart failure, coronary heart disease, and irritable bowel syndrome.[2] Sleep problems are well known to affect the quality of life,[3] including poor response to health that indicates a decrease in subjective health perception. Furthermore, sleep disorders, including insomnia, daytime sleepiness,[4] short sleep duration, and long sleep duration,[5] are associated with decreases in subjective health perception. Sleep quality is also associated with decreased quality of life, including subjective health perception.[6]

Subjective health perception involves recognizing one's health status; this information can then be used to assess an individual's general health status.[7] In addition, regardless of the actual state of health, if the subjective health perception is poor, the level of daily activity is low, which could negatively affect the state of wellbeing.[8]

In contrast, it is well-known that sleep patterns change with age,[1] that aging is a major cause of sleep disorders, and that various factors are related to sleep disorders in older adults.[9] They have decreased deep sleep, difficulty falling asleep, increased arousal while sleeping, and decreased total sleeping duration.[10] These observations suggest a high prevalence of sleep disorders in older adults.[11] Thus, these individuals with a high prevalence of sleep problems may also have a high possibility of reduced subjective health perception, which may ultimately affect the actual health status.

This study assessed the relationship between sleep habits and subjective health perception rather than the quality of sleep and sleep disorders, which have been evaluated in previous studies. Sleep habits generally differ between weekdays and weekends. In most cases, weekend sleep duration is relatively longer, as reported by the Korean National Health and Nutrition Examination Survey

(KNHANES),[12] and may do so even after retirement. Moreover, as older adults are more likely to live according to traditional gender roles, sleep habits may also differ according to sex. Thus, the purpose of this study was to clarify the association between sleep habits and subjective health status in older adults.

Materials and Methods

Participants

This study analyzed data of 1,678 older people (695 men and 883 women) aged 65 years or older who participated in the 2016 Korea National Health and Nutrition Examination Survey (KNHANES VII-1) conducted by the Korea Centers for Disease Control and Prevention.[13]

From the KNHANES, the extraction frame was stratified based on cities, provinces, municipalities, and housing types (general houses, apartments, newly built apartments). This study was conducted from January to December 2016 for all households with person over one year old or older from among 4,416 households nationwide. Because the KNHANES datasets do not include identifiable personal information, all studies using these data are excluded from the requirement for institutional review board approval.

Data Collection and Variables

We analyzed data on the participants' age, spouse cohabitation, household income, weekday and weekend sleeping times, weekday and weekend waking times, number of days walked per week, number of strength exercise days per week, and the presence of chronic diseases (hypertension, type 2 diabetes, hypercholesterolemia, and hypertriglyceridemia).

Spouse cohabitation was defined as living with a spouse. The weekly walking days were classified into four groups: no walking at all, 1–3 days walking, 4–6 days walking, and daily walking. The weekly strength exercise days were divided into three groups: no exercise at all, 1–3 days, and 4 or more days.

Sleep Habits and Subjective Health Perception

We defined sleep duration in this study as the difference between sleeping time and waking time and classified into five groups: under 6 hours, 6–7 hours, 7–8 hours, 8–9 hours, and more than 9 hours. Sleeping time was classified into six groups: before 9 pm, 9–10 pm, 10–11 pm, 11–12 pm, 12–1 am, and after 1 am. Waking up time was classified into six stages: before 4 am, 4–5 am, 5–6 am, 6–7 am, 7–8 am, and after 8 am. Subjective health perception was classified into three stages: good, normal, and bad. Health perception data were acquired from responses to a simple question ("how do you normally think of your health?").

Statistical Analysis

We performed statistical analysis using complex sample analysis in IBM SPSS Statistics for Windows, version 23.0 (IBM, Armonk, NY, USA). We used t-tests to compare the mean age and weekday and weekend sleeping times among the participants. We used chi-square tests to compare the age groups, spouse living status, household income, hypertension, diabetes mellitus, hypercholesterolemia, hypertriglyceridemia, weekly walking days, weekly strength exercise days, and subjective health status between older men and women.

We also used chi-square tests to compare the differences in weekday and weekend sleep duration, sleeping time, and waking up time between older men and women. We applied a generalized linear model to compare differences in sleep duration according to sleeping and waking times on weekdays and weekends between older men and women. Ordinal regression was used to examine the relationship between subjective health and stages of sleep duration, sleeping time, and waking time.

Results

Baseline Participants Characteristics

The mean ages of the men and women in this study were 72.26 ± 0.239 and 74.41 ± 0.203 years, respectively. The age composition differed significantly by sex ($p < 0.01$). We also observed a difference in the spouse cohabitation status between men and women ($p < 0.01$). The sleep duration was longer in men compared to that in women on both weekdays and weekends. The prevalence of hypertension, diabetes mellitus, and hypertriglyceridemia did not differ significantly between men and women; however, the prevalence of hypercholesterolemia differed significantly ($p < 0.01$). The walking days in a week did not differ significantly between the sex; however, muscular exercise duration and walking practice were significantly higher in men than in women (Table 1).

Comparisons of Sleep Duration, Sleeping Time, and Waking Time between Men and Women

Weekday and weekend sleep durations differed significantly between men and women ($p < 0.012$). Sleep durations between 7 and 8 hours were highest on weekdays. The weekend sleep duration differed significantly between men and women ($p = 0.006$). On weekdays, the most common sleep time was between 10 pm and 11 pm. The weekend sleeping times were similar to those on weekdays. There was no difference in sleeping time between the sexes with regard to weekend sleeping time. On weekdays, the

Table 1. Baseline participant characteristics

Characteristic	Men (n = 695)	Women (n = 883)	p-value[a)]
Age (y)	72.26 ± 0.239	74.41 ± 0.203	< 0.01
65–74	430 (64.5)	519 (53.8)	
≥ 75	265 (35.5)	364 (46.2)	
Living status with spouse			< 0.01
Living with spouse	603 (87.9)	439 (45.8)	
Living without spouse	88 (12.1)	439 (54.2)	
Household income			< 0.01
Low	297 (42.8)	479 (54.3)	
Middle	203 (27.4)	227 (24.7)	
High	187 (29.8)	173 (21.0)	
Total weekday sleep duration	442.16 ± 4.48	422.46 ± 4.00	< 0.01
Total weekend sleep duration	454.32 ± 4.62	430.54 ± 4.06	< 0.01
Chronic disease			
Hypertension	413 (61.7)	593 (67.7)	0.131
Diabetes	187 (27.2)	208 (27.4)	0.452
Hypercholesterolemia	132 (20.8)	282 (34.7)	< 0.01
Hypertriglyceridemia	89 (15.9)	106 (14.9)	0.662
Weekly walking days			0.075
No walking	167 (24.5)	262 (30.1)	
1–3	144 (23.2)	223 (25.6)	
4–6 days	128 (19.4)	134 (16.2)	
Daily	211 (32.9)	209 (28.2)	
Weekly days of muscular exercise			< 0.01
No muscle exercise	488 (70.4)	754 (90.9)	
1–3	56 (9.2)	38 (4.0)	
> 4	112 (16.8)	39 (5.1)	
Walking practice rate	301 (46.6)	287 (37.7)	0.040

Values are presented as mean±standard error or number (%).
[a)]t-test or chi-square test.

waking times for both were predominantly between 5 am and 6 am (Table 2).

Sleep Duration according to Sleeping and Waking Times on Weekdays and Weekends

The weekday sleep durations in men and women who went to sleep between 10 and 11 pm were 447.56 ± 5.13 and 435.04 ± 6.02 minutes, respectively, and 454.22 ± 5.78 and 441.21 ± 6.18 minutes, respectively, on the weekends. The weekend sleep duration was higher than the weekday sleep duration. The sleep duration of men who woke between 6 and 7 am on weekdays did not differ from those who woke between 7 and 8 am and after 8 am (Table 3).

Relationships between Sleep Habits and Subjective Health

The weekday and weekend sleeping durations were associated with subjective health in men ($p < 0.05$) but not in women. Compared to a sleep duration of 7 hours, a duration of 9 hours was significantly associated with improved health perception in men. Sleeping and waking times on weekdays and weekends were not related to subjective health in either sex (Table 4).

Discussion

This study investigated the associations between sleep habits and subjective health perception. A previous study reported that sleep duration affected the quality of life at all ages, as assessed by the European Quality of Life-5 Dimensions (EQ-5D) index.[14] Inconsistent with the results of our study, previous studies reported an association between the quality of life and sleep patterns. However, previous studies also reported that responses to the EQ-5D were related to subjective health status.[15,16] This trend was expected to be prominent in older adults who often have an overall lower quality of sleep.[11] We observed different associations between sleep habits and health perceptions between sexes in the present study.

Table 2. Comparisons of sleep duration, sleeping time, and waking time between men and women

Sleep habit	Male (n = 695)	Female (n = 883)	p-value[a)]
Weekday sleep duration (hr)			0.012
< 6	73 (13.0)	148 (18.3)	
6–7	111 (18.0)	160 (21.1)	
7–8	186 (26.0)	223 (26.6)	
8–9	162 (24.5)	165 (18.7)	
> 9	122 (18.5)	132 (15.4)	
Weekend sleep duration (hr)			0.006
< 6	69 (12.1)	140 (17.0)	
6–7	93 (15.7)	157 (19.4)	
7–8	179 (24.6)	210 (25.9)	
8–9	164 (24.7)	176 (19.9)	
> 9	148 (22.9)	145 (17.8)	
Weekday sleeping time			0.263
Before 9 pm	78 (11.1)	62 (7.4)	
9 pm–10 pm	156 (21.5)	192 (21.4)	
10 pm–11 pm	202 (30.6)	243 (30.1)	
11 pm-12 am	115 (17.6)	171 (21.0)	
12 am–1 am	72 (13.0)	107 (13.8)	
After 1 am	32 (6.2)	55 (6.5)	
Weekend sleeping time			0.066
Before 9 pm	79 (11.4)	59 (7.2)	
9 pm–10 pm	150 (21.6)	171 (18.8)	
10 pm–11 pm	199 (29.3)	241 (29.7)	
11 pm–12 am	119 (18.2)	176 (21.8)	
12 am–1 am	78 (13.8)	123 (15.1)	
After 1 am	29 (5.6)	59 (7.3)	
Weekday waking time			0.250
Before 4 am	33 (5.5)	61 (7.7)	
4 am–5 am	100 (13.8)	140 (16.7)	
5 am–6 am	205 (30.3)	244 (30.5)	
6 am–7 am	186 (28.5)	227 (25.9)	
7 am–8 am	94 (14.8)	113 (13.7)	
After 8 am	37 (7.4)	47 (5.5)	
Weekend waking time			0.395
Before 4 am	32 (5.4)	55 (6.9)	
4 am–5 am	78 (10.7)	122 (14.3)	
5 am–6 am	200 (29.8)	221 (27.4)	
6 am–7 am	178 (26.6)	231 (26.2)	
7 am–8 am	109 (16.8)	128 (15.2)	
After 8 am	57 (10.8)	75 (10.1)	

Values are presented as number (%).
[a)]Chi-square tests.

In this study, weekday and weekend sleep durations were associated with subjective health perception in men but not in women. Subjective health perception is how an individual perceives his or her health, which may differ from their actual health. However, negative subjective health perceptions are associated with an increased prevalence of depression or stress-related symptoms;[17,18] thus, subjective health perception is considered an objective indicator of health.[19] In this study, men with sleep durations of 9 hours perceived their subjective health to be significantly compared that in men with 7 hours of sleep duration on both weekdays and week-

Table 3. Sleep duration according to sleeping and waking time of weekdays and weekends

Sleep pattern	Male (n=695)			Female (n=883)		
	Estimate	SE	p-value[a]	Estimate	SE	p-value[a]
Weekday sleep duration by sleeping time						
(Intercept)	447.563	5.129	<0.001	435.041	6.024	<0.001
Before 9 pm	101.796	12.086	<0.001	101.713	18.356	<0.001
9 pm–10 pm	37.608	9.168	<0.001	34.373	10.278	0.001
11 pm–12 am	-36.835	9.375	<0.001	-35.172	9.758	<0.001
12 am–1 am	-74.05	11.888	<0.001	-79.515	9.543	<0.001
After 1 am	-140.895	18.051	<0.001	-141.493	17.881	<0.001
10 pm–11 pm	0.000[b]	-	-	0.000[b]	-	-
Weekend sleep duration by sleeping time						
(Intercept)	454.215	5.763	<0.001	441.421	6.132	<0.001
Before 9 pm	102.563	12.114	<0.001	98.29	21.28	<0.001
9 pm–10 pm	47.493	11.645	<0.001	43.685	9.496	<0.001
11 pm–12 am	-28.158	9.95	0.005	-24.546	8.972	<0.001
12 am–1 am	-67.624	10.681	<0.001	-70.313	10.314	<0.001
After 1 am	-131.391	19.439	<0.001	-139.416	17.031	<0.001
10 pm–11 pm	0.000[b]	-	-	0.000[b]	-	-
Weekday sleep duration by wake time						
(Intercept)	471.848	7.352	<0.001	447.212	6.454	<0.001
Before 4 am	-130.92	17.645	<0.001	-138.742	13.421	<0.001
4 am–5 am	-92.516	11.759	<0.001	-75.769	10.7	<0.001
5 am–6 am	-47.398	9.588	<0.001	-39.449	8.521	<0.001
7 am–8 am	19.492	10.114	0.054	46.299	11.558	<0.001
After 8 am	23.22	21.718	0.285	78.164	21.072	<0.001
6 am–7 am	0.000[b]	-	-	0.000[b]	-	-
Weekend sleep duration by wake time						
(Intercept)	474.45	7.28	<0.001	442.249	5.562	<0.001
Before 4 am	-123.436	17.311	<0.001	-128.5	14.004	<0.001
4 am–5 am	-87.397	12.844	<0.001	-71.917	10.068	<0.001
5 am–6 am	-49.029	9.544	<0.001	-36.231	7.982	<0.001
7 am–8 am	21.684	9.699	0.026	49.862	10.466	<0.001
After 8 am	62.479	19.179	0.001	98.845	15.104	<0.001
6 am–7 am	0.000[b]	-	-	0.000[b]	-	-

SE, standard error.
[a]Analysis of variance.
[b]Reference (standard time).

ends. However, compared to 7 hours of sleep duration, we observed no significant difference in subjective health perception for other sleep durations. Older adults have a higher prevalence of sleep disorders;[10,11] thus, the impact of insufficient sleep duration on subjective health perception could be greater in this population than in younger populations. In other words, if older adults perceive that they are lacking sleep, their subjective health perception is likely to be worse compared to those in younger populations.

Many factors affect positive subjective health perception; among these, a sleep duration that is not too long and not too short is important,[5] which is consistent with our results. However, subjective health perception was not related to sleeping or waking times in men in our study. Lifestyle determines sleeping or waking time, and these are considered insignificant if the sleep duration is sufficient.

In women, sleep duration, sleeping time, and waking time were not related to subjective health perception. The prevalence of sleep disorders is higher in older women than in older men.[20,21] Thus, sleep disorders may negatively affect the relationship between sleep habits and subjective health perception compared to that in individuals without sleep disorders. Therefore, sleep habits are unlikely to be a significant factor for subjective health perception in older women with sleep disorders. Also, sleep patterns of older women might be affected by both social and familial roles, meanwhile these in older men are more likely to be affected by only social roles, in Korean cultural perspective. Additionally, alterations

Table 4. Relationships between sleep habits and subjective health

	Male						Female					
	Weekday			Weekend			Weekday			Weekend		
	OR	95% CI	p-value[a)]	OR	95% CI	p-value[a)]	OR	95% CI	p-value[a)]	OR	95% CI	p-value[a)]
Sleep duration (hr)			0.043			0.025			0.480			0.398
5	1.053	0.496–1.819		1.076	0.572–2.024		1.559	0.912–2.668		1.371	0.811–2.319	
6	1.016	0.583–1.661		0.891	0.514–1.547		1.053	0.682–1.626		1.138	0.725–1.786	
8	0.966	0.664–1.613		0.983	0.622–1.553		1.186	0.807–1.743		1.076	0.727–1.593	
9	0.570	0.359–0.904		0.513	0.321–0.822		1.273	0.895–1.812		1.426	0.958–2.123	
7	1	-		1	-		1	-		1	-	
Sleeping time			0.058			0.148			0.815			0.801
< 9 pm	0.495	0.250–0.982		0.621	0.313–1.231		1.015	0.547–1.883		0.947	0.543–1.651	
9 pm–10 pm	0.787	0.531–1.164		0.876	0.580–1.325		0.897	0.608–1.325		0.835	0.575–1.212	
11 pm–12 am	0.949	0.606–1.486		1.185	0.769–1.827		1.081	0.703–1.662		1.003	0.692–1.454	
12 am–1 am	0.843	0.487–1.457		1.125	0.641–1.973		0.864	0.575–1.297		0.787	0.520–1.190	
> 1 am	1.539	0.545–4.346		1.597	0.594–4.293		0.664	0.268–1.643		0.770	0.313–1.897	
10 pm–11 pm	1	-		1	-		1	-		1	-	
Waking time			0.999			0.561			0.132			0.206
< 4 am	1.059	0.522–2.148		0.880	0.431–1.799		0.939	0.462–1.907		0.886	0.473–1.589	
4 am–5 am	0.981	0.608–1.584		0.856	0.515–1.423		1.296	0.767–2.192		1.237	0.772–1.982	
5 am–6 am	1.027	0.668–1.580		1.283	0.823–2.000		1.492	0.998–2.229		1.303	0.906–1.873	
7 am–8 am	0.960	0.581–1.588		1.208	0.700–2.086		0.874	0.545–1.403		0.829	0.515–1.334	
> 8 am	0.906	0.495–1.660		0.847	0.405–1.770		1.084	0.614–1.913		0.750	0.378–1.488	
6 am–7 am	1	-		1	-		1	-		1	-	

OR, odds ratio; CI, confidence interval.
[a)]Ordinal regression.

in sleeping patterns may differ between older men and women. In older men, a lack of deep sleep is a major problem, while sleep latency was a predominant sleeping problem in older women.[22] Consequently, insufficient sleep duration was related to poor subjective health perception in older men lacking deep sleep.

We observed associations between weekday and weekend sleep duration and subjective health perception in men. These results may inform the regulation of health policy in this population. Generally, 8 hours is considered a sufficient sleep duration in adults, although one study reported 7 hours to be sufficient.[23] Older men with a lack of deep sleep may not perceive their subjective health to be high despite having a sufficient sleep duration (7–8 hours); in this study, those with 9 hours of sleep duration perceived their health to be good. Subjective health perception is not a substitute for actual health status but is helpful as an objective indicator to predict the actual health status.[24,25] Additionally, one study reported that poor perception of subjective health increased the risk of suicide and decreased daily life activities.[8,26] Thus, older men may not sleep enough due to sleep disorders, or if they did sleep, their sleep duration was less than 8 hours. Their subjective perception could also be deteriorating, leading to an increased risk of disease. Therefore, sleep duration should be assessed in the initial medical examinations of older men. If the sleep duration is insufficient, sleep hygiene should be managed or pharmacologic intervention should be considered. Further study is needed regarding the effects on older adult women.

This study has a few limitations. First, due to the cross-sectional design, the observed relationships established did not establish causality. Prospective studies are needed to clarify the causality of subjective health perception and sleep habits. Second, data on medical history and sleep patterns were obtained through a questionnaire; thus, missing variables or overstatement are possible. The question used to estimate sleep duration, "when do you usually go to bed and when do you wake up?" was very simple and might not reflect the average duration of sleep. Third, we analyzed only sleep habits as represented by sleep duration, sleeping time, and waking time, but not sleep quality, which was not considered is as important as sleep pattern. Despite these limitations, the strength of this study was that the study population may represent the Korean older population. Moreover, to our knowledge, this is the first study to assess the relationship between sleep habits and subjective health perception in this population.

In conclusion, weekday and weekend sleep durations were related to subjective health perception in older men. Additional studies are needed to determine how sleep habits, including sleep quality, affect the subjective health perception of older adults.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

This work was supported by a 2-year research grant from Pusan National University.

AUTHOR CONTRIBUTIONS

Conceptualization, YJK; Data curation, YJK; Funding acquisition, YJK; Methodology, YJK; Supervision, YJK; Investigation, HRH; Writing original draft, HRH; Reviewing & editing, HRH.

REFERENCES

1. Foley D, Ancoli-Israel S, Britz P, Walsh J. Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey. J Psychosom Res 2004;56:497-502.
2. Wallander MA, Johansson S, Ruigomez A, Garcia Rodriguez LA, Jones R. Morbidity associated with sleep disorders in primary care: a longitudinal cohort study. Prim Care Companion J Clin Psychiatry 2007;9:338-45.
3. Lee M, Choh AC, Demerath EW, Knutson KL, Duren DL, Sherwood RJ, et al. Sleep disturbance in relation to health-related quality of life in adults: the Fels Longitudinal Study. J Nutr Health Aging 2009;13:576-83.
4. Silva GE, An MW, Goodwin JL, Shahar E, Redline S, Resnick H, et al. Longitudinal evaluation of sleep-disordered breathing and sleep symptoms with change in quality of life: the Sleep Heart Health Study (SHHS). Sleep 2009;32:1049-57.
5. Magee CA, Caputi P, Iverson DC. Relationships between self-rated health, quality of life and sleep duration in middle aged and elderly Australians. Sleep Med 2011;12:346-50.
6. Tel H. Sleep quality and quality of life among the elderly people. Neurol Psychiatry Brain Res 2013;19:48-52.
7. Lewis LM, Riegel BJ. Determinants of perceived health in older adults with hypertension. Heart Lung 2010;39:41-9.
8. Menec VH. The relation between everyday activities and successful aging: a 6-year longitudinal study. J Gerontol B Psychol Sci Soc Sci 2003;58:S74-82.
9. Li J, Vitiello MV, Gooneratne NS. Sleep in normal aging. Sleep Med Clin 2018;13:1-11.
10. Rodriguez JC, Dzierzewski JM, Alessi CA. Sleep problems in the elderly. Med Clin North Am 2015;99:431-9.
11. Amer MS, Hamza SA, El Akkad RM, Abdel Galeel YI. Does self-reported sleep quality predict poor cognitive performance among elderly living in elderly homes? Aging Ment Health 2013;17:788-92.
12. Korea Institute of Health and Social Affairs. Korea National Health and Nutrition Examination Survey 2017 [Internet]. Sejong, Korea: Ministry of Health and Welfare; c2019 [cited 2020 Jun 1]. Available from: https://knhanes.cdc.go.kr/knhanes/sub04/sub04_03.do?classType=7.
13. Korean Ministry of Health and Welfare. The 7th Korea National Health and Nutrition Examination Survey (KNHANES VII-1). Sejong, Korea: Ministry of Health and Welfare; 2016.
14. Cho J, Kwak N, Choi SM, Lee J, Park YS, Lee CH, et al. Sleep duration and health-related quality of life in Korean adults: 2007-2015 Korea National Health and Nutrition Examination Survey. Sleep Breath 2019;Dec 2;[Epub]. http://doi.org/10.1007/s11325-019-01972-7.
15. Golicki D, Niewada M, Jakubczyk M, Wrona W, Hermanowski T. Self-assessed health status in Poland: EQ-5D findings from the Polish valuation study. Pol Arch Med Wewn 2010;120:276-81.
16. Konig HH, Bernert S, Angermeyer MC, Matschinger H, Martinez M, Vilagut G, et al. Comparison of population health status in six European countries: results of a representative survey using the EQ-5D questionnaire. Med Care 2009;47:255-61.
17. Park JI, Park TW, Yang JC, Chung SK. Factors associated with depression among elderly Koreans: the role of chronic illness, subjective health status, and cognitive impairment. Psychogeriatrics 2016;16:62-9.
18. Bailis DS, Segall A, Mahon MJ, Chipperfield JG, Dunn EM. Perceived control in relation to socioeconomic and behavioral resources for health. Soc Sci Med 2001;52:1661-76.
19. Gold M, Franks P, Erickson P. Assessing the health of the nation: the predictive validity of a preference-based measure and self-rated health. Med Care 1996;34:163-77.
20. Brabbins CJ, Dewey ME, Copeland JR, Davidson IA, McWilliam C, Saunders P, et al. Insomnia in the elderly: prevalence, gender differences and relationships with morbidity and mortality. Int J Geriatr Psychiatry 1993;8:473-80.
21. Arber S. Gender, marital status and sleep problems in Britain. Przegl Lek 2012;69:54-60.
22. Luca G, Haba Rubio J, Andries D, Tobback N, Vollenweider P, Waeber G, et al. Age and gender variations of sleep in subjects

without sleep disorders. Ann Med 2015;47:482-91.
23. Taheri S, Lin L, Austin D, Young T, Mignot E. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. PLoS Med 2004;1:e62.
24. Cockerham WC, Sharp K, Wilcox JA. Aging and perceived health status. J Gerontol 1983;38:349-55.
25. Luchi CA, Peres KG, Bastos JL, Peres MA. Inequalities in self-rated oral health in adults. Rev Saude Publica 2013;47:740-51.
26. Fujino Y, Mizoue T, Tokui N, Yoshimura T. Prospective cohort study of stress, life satisfaction, self-rated health, insomnia, and suicide death in Japan. Suicide Life Threat Behav 2005;35:227-37.

AGMR
Annals of Geriatric Medicine and Research

Original Article
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):115-124
https://doi.org/10.4235/agmr.20.0005

Translation and Validation of the Malay Version of Comprehensive Geriatric Assessment Questionnaire for Older Adults in Malaysia

Sakinah Harith[1], Sze Lin Tan[2]

[1]Faculty of Health Sciences, Universiti Sultan Zainal Abidin, Terengganu, Malaysia
[2]School of Health Sciences, Universiti Sains Malaysia, Kelantan, Malaysia

Corresponding Author:
Sakinah Harith, PhD
Faculty of Health Sciences, Universiti Sultan Zainal Abidin, Terengganu, Malaysia
Email: sakinahharith72@gmail.com
ORCID:
https://orcid.org/0000-0002-4687-2651

Received: February 9, 2020
Revised: May 7, 2020
Accepted: May 18, 2020

Background: This study aimed to translate and validate the comprehensive geriatric assessment (CGA) questionnaire among older adult patients in Malaysia in the Malay language. **Methods:** The questionnaire contained items on the socio-demographic characteristics, medical condition, quality of life (QOL), nutritional status, functional capacity, and depression status. The forward and backward translation processes of the original English language version of the questionnaire were undertaken by three independent linguistic translators, while its content was validated by an expert team consisting of seven geriatricians, physicians, dietitian, and lecturers. The Malay version of the questionnaire was tested for face validity in 10 older adult patients over 65 years of age. The internal consistency reliability and construct validity were evaluated among 166 older adult patients (mean age, 71.0 years; 73.5% male). The questionnaire was administered through face-to-face interviews with the patients. Minor amendments were made after the content and face validity tests. **Results:** The internal consistency reliability was good, as the Cronbach's alpha for most of the scales surpassed 0.70, ranging from 0.70 to 0.98, with only one exception (Mini Nutritional Assessment Short-Form, Cronbach's alpha=0.62). The factor loadings for all scales were satisfactory (>0.40), ranging from 0.45 to 0.90. **Conclusion:** The Malay-version CGA showed evidence of satisfactory internal consistency reliability and construct validity in Malaysian geriatric patients.

Key Words: Translation, Validation, Geriatic assessment, Older adult, Malaysia

INTRODUCTION

Aging is a global phenomenon. Worldwide, the proportion of older adult population consisting of people aged ≥ 60 years is growing faster than any other age group.[1)] According to the World Health Organization, the 703 million older adult individuals in the world today is expected to increase to 1.5 billion by 2050.[2)] In Malaysia, the older adult population (age ≥ 65 years) is also the fastest-growing age group. In 2017, 6.2% of 32.3 million people in Malaysia were aged over 65 years. In terms of ethnicity, 7% of Malaysian older adults are from the Malay population. The Malaysian Healthy Ageing Society reported that the proportion of Malaysians aged 60 years and older had increased from 6.2% in 2000 and is predicted to reach 13.6% by 2030.[3)] This increasing trend of aging population implies that Malaysia is moving towards an aging population. Based on data reported by the National Population and Family Development Board (LPPKN), Malaysia is predicted to reach aging population status by 2035, in which citizens aged 60 years and older will comprise 15% of the total population (5.6 million).[4)]

The occurrence of a variety of conditions and disorders unique to this age group has increased notably in recent years, in line with the rapidly aging society. Older adults experience progressive declines in their biological and psychological functions. A compre-

hensive assessment is thus required to ensure a holistic approach in their care plans. Comprehensive Geriatric Assessment (CGA) is a multidimensional and interdisciplinary diagnostic process to determine the medical, psychological, and functional capabilities of older adults. CGA has been applied widely in many medical contexts including orthopedic[5], coronary artery disease[6], and multimorbidity.[7] Its purpose is tailored towards developing a coordinated and integrated plan for treatment and long-term follow-up. The basic components of the CGA include functional status, co-morbidity, cognition, depression, polypharmacy, nutrition, presence of geriatric syndromes, and socioeconomic factors. While integrating standard medical diagnostic evaluation, CGA emphasizes the quality of life (QOL) and functional status, prognosis, and outcome that entail a workup with more depth and breadth.[8-10]

Most of the standardized questionnaires in CGA that are developed in English-speaking countries are not applicable in Malaysia, which is a country with a multi-ethnic population and more than one spoken language. Thus, the questionnaires must be translated into the local Malay language, adapted to the local culture, and validated against the original version while also considering important cultural differences. The Malay language is the language of knowledge and union and it is the national language in Malaysia.[11] This language is related to the Austronesian family of Malay, which has spread across nearly half of the world, with more than 300 million speakers, making it the fourth-largest language globally in terms of the number speakers.[12] Thus, the objectives of this study were to translate the original English version of CGA questionnaires into the Malay language and determine the reliability and validity of this Malay version among the Malaysian older adult population.

MATERIALS AND METHODS

Instrument Translation

The CGA questionnaire consists of five sections (A to E): Section A enquires about participant socio-demographic data, medical conditions, and health and nutritional risk factors, while Sections B–E comprise the screening tools to assess nutritional status (Mini Nutritional Assessment-Short Form [MNA-SF]), QOL (36-items Short Form Health Survey version 2.0 [SF-36 Health Survey v2]), functional capability (activities of daily living [ADLs] and instrumental activities of daily living [IADLs]), and depression status (Geriatric Depression Scale-Short Form [GDS-SF]). All five sections were translated together according to the international guidelines after obtaining permission from the respective original authors of the questionnaires.

The first step of the translation involved the forward translation of the original English questionnaire into the Malay language by two qualified and independent linguistic translators fluent in both languages. The translators were requested to produce a forward translation that was conceptually equivalent to the original English-version questionnaire. Each translator produced a forward translation version without mutual consultation. The translations were then reviewed and reconciled by the researchers to create a preliminary version of the forward translation. This version was subsequently given to a third translator, who translated the questionnaire back into English. The backward translation version was compared to the original English questionnaire by the researchers, with consideration regarding whether the items were rewritten using the same words (literal assessment) or if the original meaning had been retained (semantic equivalence). When discrepancies between backward translation and original versions arose, the word choices were discussed among the researchers and translators until a final forward translation version was reconciled. The comprehensibility and appropriateness of the language in the Malaysian cultural context were emphasized during the translation procedure.

Ethical Clearance

This study was approved by the Malaysia Research Ethics Committee (MREC) of the Ministry of Health Malaysia (Registration No. (2)dlm.KKM/NIHSEC/08/0804/P10-337) and the Human Research Ethics Committee (HREC) of USM (No. USMKK/PPP/JEPeM (228.4[1.6])).

Content and Face Validity

An expert team comprising seven geriatricians, physicians, dietitian, and lecturers assessed the final forward translation questionnaire for its content. They made their judgments about the relevance of the questionnaire and suggested the use of better terms and format.

For face validity, we tested the questionnaire in 10 geriatric patients aged ≥ 65 years who were admitted to the medical wards in Hospital Universiti Sains Malaysia (HUSM) after obtaining informed consent from all participants. The researcher went through each item and allowed the patients to clarify their doubts and comment on the questions and response choices. The researchers discussed these comments and developed the final Malay version of the CGA questionnaire, which was then evaluated for its reliability and validity among Malaysian geriatric patients.

Internal Consistency Reliability and Construct Validity

Study design and participants

A cross-sectional study was conducted using convenience sam-

pling at the Medical Outpatients Department (MOPD) and medical wards of Hospital Sultanah Nur Zahirah (HSNZ), Kuala Terengganu, Malaysia. This study was approved by the MREC of Ministry of Health, Malaysia in November 2010.

The inclusion criteria were geriatric patients aged ≥ 65 years and admitted to the medical wards or who visited the MOPD. We identified eligible participants from the patient admission list at the admission counter of the medical wards and the patient appointment list located at the registration counter of daily MOPD. A trained interviewer collected data collection via face-to-face interviews.

Measures

This study integrated a revised MNA-SF[13] in the CGA tool to screen the patients' nutritional status. The revised MNA-SF consisted of six items and included the calf circumference (CC) parameter as a substitute for body mass index (BMI). This change enabled its application to immobile individuals or in circumstances where the weight and height could not be measured. A total score ranging from 0–14 distinguishes patients into those with normal nutritional status (12–14 points), risk of malnutrition (8–11 points), and who are malnourished (0–7 points).

The CGA applies the SF-36 Health Survey v2[14] with standard 4-week recall periods to assess the health-related QOL among the participants. It contained 36 items across eight different scales of health; namely: physical functioning (PF), role limitations due to physical problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (MH). These eight scales were further aggregated into two summary measures; namely, physical (21 items: PF, RP, BP, GH) and mental (14 items: VT, SF, RE, MH) components. The survey additionally included a single-item scale on health translation (HT) to describe the comparison between current health status and health status 1 year prior. The response choices of these 36 items based on 3-, 5-, or 6-point scales, with item scores of 1–3, 5, or 6 points. We recoded the scores for 11 items so that all 36 items would score in the same direction, with higher values indicating better health status.

The functional capacity of patients was measured as the ability to perform both the ADL and IADL. This entailed the use of the 10-item Barthel Index[15,16] for the ADL; and 7-item IADL subscale of the Older Americans Resources and Services (OARS)[17] for the IADL assessment.

The Barthel Index[15,16] measures patients' level of independence using 10 basic activities rated with scores ranging between 0 and 3 and a maximum total score of 20 points. Scores of 15–19 and < 14 points indicated mild and moderate to severe functional disabilities, respectively.

The IADL subscale of the OARS[17] assesses patients' level of independence on seven instrumental activities. The questionnaire used three levels of scoring (0 = fully dependent; 1 = requiring some help; 2 = fully independent) for a total score ranging from 0–14 points. Scores < 10 points indicated functional disability.

The GDS-SF[18] is modified from the original GDS and used to screen patient depression levels. As a 15-item scale with a "yes/no" format, 10 items suggest probable depression for negative responses (negative items); the remaining 5 items suggest probable depression when answered positively (positive items). The scores ranged from 0–15, whereby 1 point was given for each response suggestive of probable depression. Points ≥ 5 were indicative of the risk of depression.

Along with MNA-SF, SF-36, GDS-SF, ADL, and IADL assessment, the questionnaire also integrated variables on socio-demographic characteristics, medical conditions, and health and nutritional risk factors. Patients' medical records were reviewed for other related information besides the interview.

Statistical analysis

Data entry and analysis were performed using SPSS Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). This study assessed the reliability of the CGA questionnaire based on the internal consistency from the item-total correlation (ITC) and Cronbach's alpha coefficient for each of the screening tools (MNA-SF, SF-36, ADL, IADL, and GDS-15).

The corrected ITC consisted of the Pearson correlation coefficient between the score for the individual item and the sum of the scores on the remaining items, which was computed to assess the extent to which an individual item was related to the remainder of its scale. Values > 0.30 indicated item appropriateness.

We performed Principal Component Analysis (PCA; exploratory factor analysis) followed by a varimax rotation to identify whether the items in the questionnaire were structured comparably to the original questionnaires. We first used Bartlett's test of sphericity ($p < 0.05$) and Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy (with values > 0.60 considered acceptable) to measure the appropriateness of the factor analysis. The number of factors was determined by examining the eigenvalues (recommended value ≥ 1.0) and via a scree plot (recommended to determine the cutoff point at which the slope appeared to change into minor decrement). The ability of the factors to represent the data was expressed by the percentage of explained variance (recommended range, at least 50%–60%). We also examined the factor loading of the items (recommended value > 0.4).

RESULTS

General Participant Characteristics

A total of 166 older adult patients (110 and 56 patients from MOPD and the wards, respectively) met the inclusion criteria and agreed to participate in this study with written consent. Table 1 shows the general characteristics of the participants. Their mean age was 70.92 ± 4.64 years (range, 65–92 years). Most respondents were male (73.5%), Malay (98.2%), married (77.1%), literate (had formal education, 74.7%), living with family (93.4%), retired (73.5%), non-smoker/ex-smoker (90.4%), and did not depend on others economically (61.4%).

Table 1. General participant characteristics (n=166)

Characteristic	Value
Type of patient	
Outpatient (MOPD)	110 (66.3)
Inpatient (ward)	56 (33.7)
Age (y)	70.92 ± 4.64
65–74	138 (83.1)
≥ 75	28 (16.9)
Sex	
Male	122 (73.5)
Female	44 (26.5)
Ethnicity	
Malay	163 (98.2)
Chinese	3 (1.8)
Marital status	
Married	128 (77.1)
Widowed	38 (22.9)
Education level	
Literate	124 (74.7)
Illiterate	42 (25.3)
Living arrangement	
With family	155 (93.4)
Alone	11 (6.6)
Occupation	
Retired	122 (73.5)
Housewife	17 (10.2)
Working	27 (16.3)
Smoking status	
Non-smoker/ex-smoker	150 (90.4)
Current smoker	16 (9.6)
Economic dependency	
No	102 (61.4)
Yes	64 (38.6)

Values are presented as frequency (%) or mean±standard deviation.
MOPD, Medical Outpatients Department.

Validity and Reliability

MNA-SF

The Cronbach's alpha coefficient was 0.62. Regarding item internal consistency, the corrected ITC of the 6 items in the scale ranged from 0.18 to 0.60, with 2 items not achieving the accepted value. Their corrected ITC values were 0.21 and 0.18 (Table 2).

A PCA of MNA-SF was feasible in this study, as indicated by the significant Bartlett's test of sphericity ($p < 0.001$) and the KMO measure of 0.63. Factor analysis with no structural restrictions revealed a two-factor solution, which explained 62.0% of the total variance. Four items were grouped under the first factor, the item contents of which were more related to the modifiable nutritional and functional risk factors. Two items were grouped under the second factor, the item contents of which were more related to patient diseases and comorbidities. All factor loadings were above 0.40 and ranged from 0.58 to 0.87 (Table 3).

SF-36 Health Survey v2

All correlation coefficients between the items and the remainders of their own scales were > 0.30, except for one item within the GH ("I expect my health to get worse", corrected ITC = 0.23). For all eight subscales of the SF-36 health survey, the Cronbach's alpha coefficients achieved the minimum criterion of 0.70, ranging from 0.70 to 0.98 (Table 2).

PCA with varimax rotation was performed with 35 items of the SF-36 Health Survey. An item on HT ("Compared to one year ago, how would you rate your health in general now?") was excluded from the factor analysis as it was not included in the eight scales scores. The Bartlett's test of sphericity was highly significant ($p < 0.001$), while the KMO measure was high (0.92). An 8-factor solution explaining 76.5% of the observed variance was generated. Table 4 shows the rotated component matrix and total variance explained by factors 1–8 in the whole group. The 10 items of the subscale PF were shared between factors 1 and 6. Factor 2 included all 3 items of the RE subscale and 4 items the MH subscale that explored aspects such as sadness/happiness. Items exploring RP loaded on factor 3, while those exploring BP and SF loaded on factor 5. All 4 items of the VT subscale were distributed between factors 4 and 7, with those positive items being differentiated from the negative items. Besides the items of the VT subscale, factor 2 also loaded with 4 items of the GH subscale and one item of the MH subscale. Factor loading of all items within the eight subscales was satisfactory (above 0.40), ranging from 0.49 to 0.86 (Table 4).

ADL-Barthel Index and IADL-OARS

Both showed good internal consistency reliability, as indicated by

Table 2. Internal consistency reliability of the questionnaires used for CGA

Questionnaire	Number of items	Corrected ITC	Cronbach's alpha
MNA-SF	6	0.18–0.60	0.62
SF-36 Health Survey			
Subscale – Physical functioning	10	0.46–0.89	0.94
Subscale – Role limitations – physical	4	0.93–0.97	0.98
Subscale – Bodily pain	2	0.86	0.92
Subscale – General health[a)]	5	0.23–0.64	0.70
Subscale – Vitality[a)]	4	0.63–0.74	0.85
Subscale – Role limitations – emotional	3	0.92–0.94	0.97
Subscale – Social functioning[a)]	2	0.86	0.93
Subscale – Mental health[a)]	5	0.59–0.76	0.85
ADL-Barthel Index	10	0.52–0.88	0.89
IADL-OARS	7	0.31–0.69	0.78
GDS-SF	15	0.12–0.56	0.75

CGA, comprehensive geriatric assessment; ITC, item total correlation; MNA-SF, Mini Nutritional Assessment-Short Form; ADL, activities of daily living; IADL, instrumental activities of daily living; OARS, Older Americans Resources and Services; GDS-SF, Geriatric Depression Scale-Short Form.
[a)]For SF-36 Health Survey, the subscale included items scored with reverse coding.

Table 3. Factor analysis of MNA-SF in the study population

	MNA-SF item#	Factor 1	Factor 2
A	Has your food intake declined over the past 3 months due to a loss of appetite, digestive problems, or chewing or swallowing difficulties?	**0.858**	-
B	Weight loss during the last 3 months	**0.780**	-
C	Mobility	**0.717**	**0.849**
D	Have you suffered psychological stress or acute disease in the past 3 months?	0.105	-
E	Neuropsychological problems	-	**0.865**
F2	Calf circumference (cm)	**0.575**	-
Eigenvalues before rotation		2.334	1.384
Percentage of variance (%)		38.9	23.1

Extraction method: Principal Component Analysis. Rotation method: varimax with Kaiser normalization. The greatest loading is reported in boldface to show the relationship with the principal components.
MNA-SF, Mini Nutritional Assessment-Short Form.

their corrected ITC (> 0.3) and Cronbach's alpha coefficient (> 0.70) (Table 2).

Table 5 shows the results of the factor analysis. For ADL-Barthel Index, the result of Bartlett's test of sphericity was significant ($p < 0.001$) and the KMO measure was acceptable (0.85). A two-factor solution explaining 74.0% of the observed variance was generated. Eight items grouped under the first factor, the item contents of which were more related to patient's self-care functioning. Next, two items grouped under the second factor, the item contents of which were more related to patient physiological needs. All factor loadings were above 0.40, ranging from 0.64 to 0.90 (Table 5).

For IADL-OARS, the result of Bartlett's test of sphericity was significant ($p < 0.001$) and the KMO measure was acceptable (0.76). A two-factor solution explaining 67.7% of the observed variance was generated. Five items grouped under the first factor, while two items related to domestic chores grouped under the second factor. All factor loadings were above 0.40, ranging from 0.52 to 0.87 (Table 5).

GDS-SF

The Cronbach's alpha coefficient was 0.75. Regarding item internal consistency, the corrected ITC ranged between 0.12 and 0.56 and three items did not achieve an acceptable value (> 0.30) (Table 2).

We performed PCA with varimax rotation. The result of Bartlett's test of sphericity was significant ($p < 0.001$) and the KMO measure was acceptable (0.72). A five-factor solution explaining 60.9% of the total variance was generated. The loadings of factors on the items did not reflect an easily interpretable pattern of psy-

Table 4. Factor analysis of the SF-36 Health Survey in the study population

Subscales of SF-36	Factor							
	1	2	3	4	5	6	7	8
Physical functioning (PF)								
PF 1 – Vigorous activities	**0.709**	0.127	0.272	0.134	0.150	-0.168	-	0.202
PF 2 – Moderate activities	**0.807**	0.149	0.271	0.181	-	-	-	
PF 3 – Lifting or carrying groceries	**0.755**	0.148	0.279	-	0.129	0.274	-	0.128
PF 4 – Climbing several flights of stairs	**0.831**	0.211	-	0.141	0.103	-	0.100	-
PF 5 – Climbing one flight of stair	**0.816**	0.120	0.188	0.109	-	0.282	-	-
PF 6 – Bending, kneeling, stooping	0.374	0.228	0.265	-	0.235	**0.584**	-	-
PF 7 – Walking more than 2 miles	**0.771**	0.133	-	0.258	0.126		0.139	-
PF 8 – Walking several hundred yards	**0.818**	0.150	0.180	0.160	0.138	0.263	-	-
PF 9 – Walking 100 yards	0.517	0.220	0.244	0.196	0.258	**0.519**	-	-
PF 10 – Bathing or dressing	0.228	-	0.130	0.108	-	**0.814**	-	-
Role limitation – physical (RP)								
RP 1 – Reduced time spent on work/activities	0.333	0.228	**0.816**	0.240	0.190	0.139	0.124	-
RP 2 – Accomplished less than would like	0.340	0.228	**0.822**	0.203	0.160	0.154	0.117	-
RP 3 – Limited in kinds of work/activities	0.251	0.246	**0.823**	0.209	0.165	0.145	0.126	-
RP 4 – Difficulty performing work/activities	0.312	0.237	**0.824**	0.201	0.172	0.161	0.118	-
Bodily pain (BP)								
BP 1 – Intensity of bodily pain[a)]	0.225	0.177	0.131	0.264	**0.781**	-	0.154	0.105
BP 2 – Extent pain interferes with work[a)]	0.254	0.200	0.217	0.194	**0.772**	-	0.125	0.169
General health (GH)								
GH 1 – Rating of general health[a)]	0.271	0.259	-	**0.54**	0.149	0.118	-	-0.306
GH 2 – Seem to get sick easier than others	0.151	0.123	-	**0.641**	0.109	-	0.189	0.213
GH 3 – As healthy as anybody know[a)]	0.108	-	0.175	**0.693**	-	0.161	0.179	0.326
GH 4 – Expect health to get worse	-	-	-	0.152	-	-	-	**0.806**
GH 5 – Health is excellent[a)]	0.302	0.270	0.208	**0.681**	-	-	0.163	-
Vitality (VT)								
VT 1 – Feel full of life[a)]	0.245	0.191	0.285	**0.659**	0.248	-	0.238	-
VT 2 – Have a lot of energy[a)]	0.195	0.203	0.323	**0.509**	0.348	0.213	0.144	-
VT 3 – Feel worn out	0.202	0.205	0.143	0.237	0.180	-	**0.836**	-
VT 4 – Feel tired	0.195	0.245	0.203	0.238	0.114	-	**0.814**	-
Role limitations – emotional (RE)								
RE 1 – Reduced time spent on work/activities	0.154	**0.845**	0.156	0.222	-	0.126	-	-
RE 2 – Accomplished less than would like	0.189	**0.864**	0.148	0.184	-	-	-	-
RE 3 – Performed work/activities less carefully	0.195	**0.829**	0.196	0.196	0.105	-	0.103	0.112
Social functioning (SF)								
SF 1 – Extent to which health problems interfered[a)]	0.166	0.344	0.255	0.172	**0.520**	0.343	0.156	-0.135
SF 2 – Frequency with which health problems interfered	0.148	0.453	0.258	0.200	**0.494**	0.322	-	-
Mental health (MH)								
MH 1 – Felt very nervous	0.211	**0.629**	0.169	0.332	0.131	0.135	0.105	0.177
MH 2 – Felt discouraged	-	**0.776**	-	0.120	0.200	-	-	-
MH 3 – Felt calm and peaceful[a)]	-	0.342	0.176	**0.606**	0.361	-	-0.109	0.200
MH 4 – Felt downhearted and depressed	0.155	**0.793**	0.123	-	0.184	-	0.211	-
MH 5 – Felt happy[a)]	0.106	**0.489**	0.192	0.431	0.356	-	-	-0.106
Eigenvalues before rotation	15.538	3.095	1.943	1.617	1.343	1.203	1.021	1.001
Percentage of variance (%)	44.4	8.8	5.6	4.6	3.8	3.4	2.9	2.9

Extraction method: Principal Component Analysis. Rotation method: varimax with Kaiser normalization. The greatest loading is reported in boldface to show the relationship with the principal components. Item #2 of the SF-36 Health Survey was not considered in the analysis because it is a summary item and is not included in the eight scale scores.

a)Item scores were reverse-coded.

Table 5. Factor analysis of ADL-Barthel Index and IADL-OARS in the study population

	Item#	Factor 1	Factor 2
ADL-Barthel Index	1. Bowels	0.202	**0.901**
	2. Bladder	0.229	**0.899**
	3. Grooming	**0.639**	0.512
	4. Toilet use	**0.751**	0.490
	5. Feeding	**0.533**	0.388
	6. Transfer	**0.855**	0.352
	7. Mobility	**0.824**	0.328
	8. Dressing	**0.745**	0.496
	9. Stairs	**0.760**	-
	10. Bathing	**0.746**	0.435
	Eigenvalues before rotation	6.300	1.097
	Percentage of variance (%)	63.0	11.0
IADL-OARS	1. Can you use the telephone?	**0.724**	-0.151
	2. Can you get to places out of walking distance?	**0.868**	0.166
	3. Can you go shopping for groceries or clothes?	**0.727**	0.421
	4. Can you prepare your own meals?	-	**0.872**
	5. Can you do your housework?	0.178	**0.856**
	6. Can you take your own medicine?	**0.519**	0.421
	7. Can you handle your own money?	**0.850**	0.105
	Eigenvalues before rotation	3.272	1.467
	Percentage of variance (%)	46.7	21.0

Extraction method: Principal Component Analysis. Rotation method: varimax with Kaiser normalization. The greatest loading is reported in boldface to show the relationship with the principal components.
ADL, activities of daily living; IADL, instrumental activities of daily living; OARS, Older Americans Resources and Services.

chological dimensions. All factor loadings were above 0.40, ranging from 0.45 to 0.89 (Table 6).

DISCUSSION

The translation, cultural adaptation, and validation of questionnaires are time-consuming and demanding tasks. However, these tasks are necessary to be able to compare results from studies performed in different countries and cultures. The results of this study provide preliminary evidence of the psychometric properties behind the Malay translation version of the CGA questionnaire in Malaysia. Due to the good reliability and validity of their original English versions, the current version selected and implemented the MNA-SF, SF-36 Health Survey, Barthel Index, IADL subscales of OARS, and GDS-SF for the comprehensive screening and assessment among geriatric patients. Most of our results suggested that the CGA questionnaire attained good psychometric characteristics in the study population of 166 Malay medical geriatric patients.

The MNA-SF showed moderate reliability, as measured by internal consistency, with a Cronbach's alpha coefficient of 0.62. Two items of MNA-SF had low corrected ITC, which indicated their poor correlation with the overall scale. This finding is probably due to the item variability of the MNA-SF, which consists of a number of items associated with malnutrition (i.e., food intake, weight loss, mobility, comorbidities, etc.). Omitting these two items from the analysis increased the Cronbach's alpha coefficient to 0.66 from 0.62. However, the MNA-SF was developed as a comprehensive instrument reflecting a number of factors associated with malnutrition; thus, no items could be omitted from the instrument. The two latent factors solution of the MNA-SF revealed in our factor analysis further supported the results of the reliability test, as the two items mentioned above were separated into a new factor with adequate factor loadings around 0.90.

The Malay version of the SF-36 Health Survey showed satisfactory results in the study population. The reliability, as measured by the Cronbach's alpha coefficient, ranged from 0.70 for GH and 0.98 for RP. All items passed the tests for item internal consistency, except for one item in GH ("I expect my health to get worse", corrected ITC = 0.23). This finding is supported by the results of a study by Tseng et al.[19] that also reported a slightly lower corrected ITC for this item in GH, along with another three items in the PF,

Table 6. Factor analysis of GDS-SF in the study population

GDS-SF item#	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
1. Are you basically satisfied with your life?	-0.080	0.134	**0.717**	0.125	0.308
2. Have you stopped many of your activities and interests?	0.104	-0.094	-0.201	0.293	**0.663**
3. Do you feel that your life is empty?	0.232	0.100	0.358	**0.734**	0.110
4. Do you often get bored?	0.169	0.268	0.109	**0.672**	0.152
5. Are you in good spirits most of the time?	**0.555**	0.509	0.172	-0.088	0.174
6. Are you afraid that something bad is going to happen to you?	0.300	0.102	0.288	**0.509**	-0.215
7. Do you feel happy most of the time?	**0.701**	0.119	0.120	0.144	0.075
8. Do you often feel helpless?	**0.763**	-0.041	0.164	0.239	0.014
9. Do you prefer to stay at home, rather than going out and doing new things?	**0.450**	0.074	0.121	-0.426	-0.044
10. Do you feel that you have more problems with memory than most?	0.145	0.168	0.309	-0.142	**0.668**
11. Do you think it is wonderful to be alive now?	0.085	**0.887**	0.097	0.191	0.111
12. Do you feel pretty worthless the way you are now?	0.230	0.065	**0.694**	0.278	-0.140
13. Do you feel full of energy?	**0.590**	0.059	-0.116	0.131	0.104
14. Do you feel that your situation is hopeless?	0.061	**0.886**	0.155	0.121	-0.096
15. Do you think that most people are better off than you are?	0.074	0.120	**0.686**	0.053	-0.036
Eigenvalues before rotation	4.039	1.492	1.402	1.141	1.057
Percentage of variance (%)	26.9	10.0	9.4	7.6	7.0

Extraction method: Principal Component Analysis. Rotation method: varimax with Kaiser normalization. The greatest loading is reported in boldface to show the relationship with the principal components.
GDS-SF, Geriatric Depression Scale-Short Form.

RE, and MH. Similarly, another study also reported a lower corrected ITC for that particular item in GH.[20] Factor analysis of the SF-36 generally supported the eight-subscale structure of the original SF-36.

In this study, we observed good reliability for both the ADL-Barthel Index and IADL-OARS, indicating that the Malay versions maintained the original scale reliability. For the Barthel Index, the two latent factors revealed by the factor analysis were consistent with those reported previously.[21,22] As impairments to the bowels and bladder were not common in the study population, the between-individual variation of participants' ratings on these two items were small. The relatively high scores and small variances of these two items may explain the two-factor structure of the Malay version of the Barthel Index. For the IADL-OARS, two items related to domestic chores were separated into a new factor with adequate factor loadings (around 0.90). This finding is probably due to the predominance of men (73.5%) in this study, who were not involved in domestic chores.

Three GDS-SF items did not pass the tests for item internal reliability, indicated a lack of discriminatory power in differentiating cases and non-cases of depression in the study population. While the Cronbach's alpha coefficient increased to 0.78 from 0.75 if these three items were omitted from the analysis, they were not omitted from the tool as the result of this study were inconsistent with those reported in another local study conducted by Teh and Hasanah.[23] The prior work reported that only one item ("Do you prefer to stay at home, rather than going out and doing new things?", corrected ITC = 0.09) had no discriminatory power in the local context. The five-factor solution that explained 60.9% of the variance was difficult to interpret; thus, a dimensional structure similar to that in the original English version was not confirmed in the study population.

The CGA questionnaire can be used as a screening tool to identify geriatric syndrome such as medical, psychosocial, and functional issues to allow the subsequent appropriate provision of interventions to older adult patients. The CGA may be used to reduce the length of stay, morbidity, and mortality, maximize overall well-being, and improve QOL.[24] However, the present study has some limitations. First, we assessed no parameters related to cognitive and physical performance. Thus, this tool might not be able to be applied to thoroughly assess the nutritional status of older adults. Next, this study has possible issues with selection bias and generalizability as the respondents were sampled only from HSNZ, Terengganu, Malaysia. Therefore, we recommend that future studies include older adult patients from different states (north, south, and west regions) to fully assess the CGA questionnaire applicability in Malaysia.

In conclusion, the Malay version of the CGA questionnaire showed evidence of satisfactory internal consistency reliability and construct validity in the context of the study population compris-

ing 166 medically geriatric patients. Further studies should explore the structural validity and stability of this questionnaire across different diagnostic groups and populations in Malaysia.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

This study was financially supported by the Short-Term Research Grant (No. 304/PPSK/61310061) and Postgraduate Research Grant Scheme (No. 1001/PPSL/8145004) of Universiti Sains Malaysia (USM), Malaysia.

AUTHOR CONTRIBUTIONS

Conceptualization, SH, SLT; Data curation, SLT; Funding acquisition, SH, SLT; Investigation, SLT; Methodology, SH; Project administration, SLT; Supervision, SH; Writing original draft, SH; Review & editing, SH.

ADDITIONAL CONTRIBUTION

We express our gratitude and appreciation to all participating patients and health care providers for their cooperation, support, and contributions to this study. Furthermore, our special thanks to Miss Ying Qian Ong for her help in editing and reviewing the manuscript.

REFERENCES

1. United Nations. World Population Ageing highlight [Internet]. New York, NY: United Nations; 2017 [cited 2020 May 23]. Available from: https://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2017_Highlights.pdf.
2. United Nations. World Population Ageing 2019 Highlight [Internet]. New York, NY: United Nations; 2019 [cited 2020 May 23]. Available from: https://www.un.org/en/development/desa/population/publications/pdf/ageing/WorldPopulationAgeing2019-Highlights.pdf.
3. Malaysia Healthy Ageing Society. Silent 'epidemic' of ageing [Internet]. NKuala Lumpur, Malaysia: Malaysia Healthy Ageing Society; 2015 [cited 2020 May 23]. Available from: http://healthyageing.org/index.php/silent-epidemic-of-ageing/.
4. Ministry of Women, Family and Community Development. Fact Sheet Malaysia Demographic Trends [Internet]. Kuala Lumpur, Malaysia: Ministry of Women, Family and Community Development; c2019 [cited 2020 May 23]. Available from: https://www.lppkn.gov.my/index.php/en/population-services/194-factsheet-malaysia-demographic-trends.
5. Kim GE, Kim S, Won CW, Choi HR, Kim BS, Cho YJ. Comprehensive geriatric assessment for elderly orthopedic inpatients consulted by geriatric medicine in a hospital. J Korean Geriatr Soc 2014;18:213-20.
6. Park MS, Cheon KS, Yoo KJ, Suh YW, Jung SH, Kim EY, et al. Role of comprehensive geriatric assessment in evaluating the efficacy of treatment in elderly patients with coronary artery disease. J Korean Geriatr Soc 2008;12:129-37.
7. Jung HW, Kim KI. Multimorbidity in Older Adults. J Korean Geriatr Soc 2014;18:65-71.
8. Lee H, Lee E, Jang IY. Frailty and comprehensive geriatric assessment. J Korean Med Sci 2020;35:e16.
9. Spirgiene L, Brent L. Comprehensive geriatric assessment from a nursing perspective. In: Hertz K, Santy-Tomlinson J, editors. Fragility fracture nursing. Springer, Cham: Springer; 2018. p. 41-52.
10. Comprehensive Geriatric Assessment [Internet]. [place unknown]: CGA Toolkit; 2019 [cited 2020 May 23]. Available from: https://www.cgakit.com/cga.
11. Mansor NR, Azmy SN, Yusoff SZ. Malay as the language of advanced knowledge: scientific review in national academia scholarship. Int J Asian Soc Sci 2018;8:694-705.
12. Mansor NR. Language, culture and community modules. Kuala Terengganu: Universiti Malaysia Terengganu Publisher; 2013.
13. Kaiser MJ, Bauer JM, Ramsch C, Uter W, Guigoz Y, Anthony P, et al. The short-form Mini Nutritional Assessment (MNA-SF): can it be improved to facilitate clinical use. J Nutr Health Aging 2009;13(Suppl 2):S16.
14. Ware JE, Kosinski M. The SF-36 Health Survey (Version 2.0): technical note. Boston, MA: Health Assessment Lab; 1996.
15. Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. Md State Med J 1965;14:61-5.
16. Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. Int Disabil Stud 1988;10:61-3.
17. Fillenbaum GG. Multidimensional functional assessment of older adults: the Duke Older Americans Resources and Services procedures. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
18. Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent findings and development of a shorter version. In: Brink TL, editors. Clinical gerontology: a guide to assessment and intervention. New York, NY: The Haworth Press; 1986. p. 165-173.
19. Tseng HM, Lu JF, Gandek B. Cultural issues in using the SF-36 Health Survey in Asia: results from Taiwan. Health Qual Life Outcomes 2003;1:72.

20. Garratt AM, Stavem K. Measurement properties and normative data for the Norwegian SF-36: results from a general population survey. Health Qual Life Outcomes 2017;15:51.
21. Kucukdeveci AA, Yavuzer G, Tennant A, Suldur N, Sonel B, Arasil T. Adaptation of the modified Barthel Index for use in physical medicine and rehabilitation in Turkey. Scand J Rehabil Med 2000;32:87-92.
22. Leung SO, Chan CC, Shah S. Development of a Chinese version of the Modified Barthel Index: validity and reliability. Clin Rehabil 2007;21:912-22.
23. Teh EE, Hasanah CI. Validation of Malay version of geriatric depression scale among older adult inpatients [Internet]. Penang: Universiti Sains Malaysia; 2004 [cited 2020 May 23]. Available from: http://priory.com/psych/MalayGDS.htm.
24. Ellis G, Gardner M, Tsiachristas A, Langhorne P, Burke O, Harwood RH, et al. Comprehensive geriatric assessment for older adults admitted to hospital. Cochrane Database Syst Rev 2017;9:CD006211.

AGMR
Annals of Geriatric Medicine and Research

Original Article
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):125-138
https://doi.org/10.4235/agmr.20.0021

Development of Korean Frailty Index for Primary Care (KFI- PC) and Its Criterion Validity

Chang Won Won[1,2], Yunhwan Lee[3], Seoyoon Lee[1,4], Miji Kim[1,5]

[1]Elderly Frailty Research Center, Department of Family Medicine, College of Medicine, Kyung Hee University, Seoul, Korea
[2]Department of Family Medicine, Kyung Hee University Medical Center, Seoul, Korea
[3]Department of Preventive Medicine and Public Health, Ajou University School of Medicine, Suwon, Korea
[4]Graduate School of Social Welfare, Yonsei University, Seoul, Korea
[5]Department of Biomedical Science and Technology, East-West Medical Research Institute, College of Medicine, Kyung Hee University, Seoul, Korea

Corresponding Author:
Miji Kim, PhD
Department of Biomedical Science and Technology, East-West Medical Research Institute, College of Medicine, Kyung Hee University, 23 Kyungheedae-ro, Dongdaemun-gu, Seoul 02447, Korea
E-mail: mijiak@khu.ac.kr
ORCID:
https://orcid.org/0000-0002-0852-8825

Received: April 8, 2020
Revised: May 19, 2020
Accepted: May 31, 2020

Background: The objective of this study was to develop and validate the Korean Frailty Index for Primary Care (KFI-PC) based on a comprehensive geriatric assessment. **Methods:** We developed a 54-item KFI-PC comprising 10 standard domains: cognitive status including delirium or dementia; mood; communication including vision, hearing, and speech; mobility; balance; bowel function; bladder function; ability to carry out activities of daily living; nutrition; and social resources. To test its validity, we applied KFI-PC to participants of the Korean Frailty Aging and Cohort Study (KFACS). We analyzed 1,242 participants (mean age, 77.9±3.9 years; 47.2% men) from the KFACS who visited 10 study centers in 2018, after excluding 32 participants with missing data required to assess Fried's physical frailty phenotype. **Results:** The mean KFI-PC score was 0.17±0.08, ranging from 0.02 to 0.52. The median KFI-PC score was higher in women than in men, and there was a trend toward higher values in older age groups. The prevalence of frailty when applying a generally used frailty index cutoff point of >0.25 was 17.5% in the whole study sample. As a construct validation of KFI-PC, the area under the receiver operating characteristic curve for Fried's physical frailty was 0.921, and the optimal cutoff value to predict frailty phenotype was 0.23. The KFI-PC score also correlated well with physical, cognitive, and psychological functions; nutritional status; disability in activities of daily living; and instrumental activities of daily living. The Cronbach's alpha coefficient of the 54 total items was 0.737. **Conclusion:** We developed KFI-PC with 53 deficits, including comprehensive geriatric assessment components, and demonstrated the acceptable construct validity and internal consistency of KFI-PC.

Key Words: Frailty, Validity, Comprehensive geriatric assessment

INTRODUCTION

Number of frail older people has been ever growing with the increase of global population aging. Frailty is defined as a status of vulnerability to identified stressors that exposes individuals to higher risks of negative health-related outcomes. The condition is usually caused by the interaction between progressive aging-related declines in multiple organ function and chronic diseases that often lead to a decreased level of functional reserve capacities.[1)]

Both phenotypic and deficit accumulation approaches are commonly used to define frailty. Representing the phenotypic approach, Fried's frailty phenotype defines frailty as the presence of three or more of five frailty items; namely, slow walking speed, impaired grip strength, declining physical activity levels, exhaustion,

and unintended weight loss.[2] The other approach to defining frailty is through the use of a frailty index that sums health deficits. In this context, health deficits can be any physical or mental disability, symptom and sign, disease, laboratory finding, etc.[3] Healthcare professionals have used comprehensive geriatric assessment (CGA) to develop a holistic overview of patients with complex needs, which is the essential step for the development of individualized, patient-centered care plans. CGA evaluates multiple aspects of older adults' health, including cognition, emotion, motivation, health attitude, vision, hearing, speech, sleep, pain, strength, balance, mobility, activities of daily living, social engagement, medication, control of life, etc. In primary care settings, frailty indices can be developed based on CGA.

A CGA-based frailty index (FI-CGA) was first developed using clinical examination data from the Canadian Study of Health and Aging.[4,5] The standardized CGA used to constitute the frailty index comprises assessments in 10 standard domains: (1) cognitive status including delirium or dementia; (2) mood and motivation; (3) communication including vision, hearing, and speech; (4) mobility; (5) balance; (6) bowel function; (7) bladder function; (8) instrumental activities of daily livings (IADLs) and activities of daily living (ADLs); (9) nutrition; and (10) social resources.[4] Based on this principle, Theou et al.[3] constructed FI-CGA containing 56 variables chosen from among a CGA adapted for use within the primary care setting.

The authors demonstrated that FI-CGA was feasible to assess frailty in primary care for a multidisciplinary primary care program for frailty. Additionally, FI-CGA was useful for the care of frail older persons in primary care as any specific problems out of 10 domains can be identified and managed effectively. Following these principles and the example of FI-CGA in Canada, we developed a Korean Frailty Index for Primary Care (KFI-PC) and investigated its validity and reliability.

MATERIALS AND METHODS

Development of KFI-PC

The deficits included in KFI-PC, along with their cutoff values, scoring measures, and related references, are described in Table 1.[2,6-18] The Korean version of the KFI-PC is provided in Supplementary Table S1. We adopted questionnaires or assessments validated in Korea for items of KFI-PC while referring to FI-CGA and the validated Korean frailty indices. We replaced or excluded items that were not appropriate for use in busy primary care settings in Korea; for example, "low mood" in FI-CGA was excluded because it is duplicated with the evaluation of "depression". We also excluded "motivation", "health attitude", and "control of life events" because they were not appropriate for Korean older adults. We excluded the timed up and go test because it requires a 3-m length of space to perform; it was replaced by a chair stand test (rising from a chair five times).[19] We also excluded IADLs of cooking and cleaning as those activities are not appropriate to assess older Korean men. We replaced these IADLs with "walking to distant destinations". FI-CGA also includes the Montreal Cognitive Assessment; however, as it takes more than 20 minutes to complete, we replaced it with the Mini-Cog test. The Mini-Cog test combines two simple cognitive tasks (a three-item word memory and clock drawing) with a scoring algorithm.[20] It can be completed in 2–4 minutes and has shown high diagnostic accuracy for dementia (sensitivity 76%, specificity 99%). We included factors related to hospital admission within 1 year and self-assessment of health as they are included in the Korean frailty index.[8] Contact frequency with friends,[17] living with family (a spouse), and frequency of going out of the home[7] were included as known social risk factors for frailty. Finally, we included data regarding appetite and number of full meals eaten per day from the Short Nutritional Assessment Questionnaire (SNAQ) as nutritional assessment.[18] Regarding comorbidities, FI-CGA allowed a maximum of 18 current conditions. The comorbidities included hypertension, diabetes, cancer, chronic obstructive pulmonary disease, myocardial infarction, heart failure, angina, asthma, arthritis, stroke, and kidney disease as they are embedded in the Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight (FRAIL) questionnaire.[21] Spinal stenosis was included as the 12th disease to be questioned.[22] If the subjects had other diseases, each additional condition was recorded up to 18 diseases. We selected these items through article review and the consensus of three experts and authors (CWW, MK, and YL).

KFI-PC Scoring

In this study, similar to the FI-CGA scoring strategy, each deficit item was scored up to 1 point except for strength (item# 12-1) and climbing stairs (item# 12-2), which represented muscle strength of the upper and lower extremities, respectively. As suggested by Rockwood and Searle, each deficit variable was dichotomized or polychotomized and mapped to the interval 0–1 (e.g., for self-rating of health, "Excellent" was coded as 0, "very good" as 0.25, "good" as 0.5, "fair" as 0.75 and "poor" as 1) to represent the deficit frequency or severity.[23] Although KFI-PC includes a total of 54 items, the maximum deficit score is 53 as the questions on strength (item# 12-1) and climbing stairs (item# 12-2) had maximum scores of 0.5. The final scoring method was decided based on the consensus of the three experts. In general, missing variables can be imputed or removed from the denominator.[24] This study followed the latter approach of scoring KFI-PC. The KFI-PC score of each

Table 1. Overview of deficits included in the KFI-PC

No.	Deficit	Additional information	Cutoff values and KFI-PC score	References
1	Construct recall (drawing two interlocking pentagons)	CERAD-K, drawing two interlocking pentagons, assessed by trained clinical research coordinators	Abnormal = 1 Normal = 0	Lee et al. (2002) [6]
2	Three-item recall memory	CERAD-K, three-word recall, assessed by trained clinical research coordinators	Recall none = 1 Recall one or two words = 0.5 Recall all three words = 0	Lee et al. (2002) [6]
3	Recognition	Kihon Checklist for frailty, knowing current date (month and date), assessed by trained clinical research coordinators	Both wrong = 1 One correct = 0.5 Both correct = 0	Satake et al. (2016) [7]
4	Depressive mood	KFI, depressive mood over the past month, completed by trained clinical research coordinators	Yes = 1 No = 0	Hwang et al. (2010) [8]
5	Exhaustion	Fried's frailty phenotype, frequency of exhaustion per week, completed by trained clinical research coordinators	≥ 3 days = 1 0–2 days = 0	Fried et al (2001) [2]
6	Delirium or hallucination	Evaluated by professional medical practitioners	Yes = 1 No = 0	
7	Visual or auditory problem	KFI, completed by trained clinical research coordinators	Yes = 1 No = 0	Hwang et al. (2010) [8]
8	Sleeping pattern	Sleep latency (≥ 1 hour) or long sleep duration (≥ 8 hours), completed by trained clinical research coordinators	Yes to either one = 1 No = 0	Kang et al. (2019) [9]
9	Napping	Frequency of napping in the past week, information gathered by trained clinical research coordinators	More than once = 1 None = 0	
10	Inactivity	FPQ for use in screening community-dwelling older adults, moderate to vigorous physical activities of International Physical Activity Questionnaire (IPAQ) in the past week, completed by trained clinical research coordinators	Never = 1 More than once = 0	Oh et al. (2007) [10] & Kim et al. (2020) [11]
11	Chair rise test (chair stand test)	European Working Group on Sarcopenia in Older People (EWGSOP) definition, time (seconds) to rise five times from a chair, assessed by trained clinical research coordinators	≥ 12 sec = 1 10–12 sec = 0.5 < 10 sec = 0	Cruz-Jentoft et al. (2019) [12]
12-1	Strength	SARC-F, difficulty in lifting and moving 4.5 kg (a box of nine Korean pears), completed by trained clinical research coordinators	Yes = 0.5 No = 0	Kim et al. (2018) [13]
12-2	Climbing stairs	SARC-F, difficulty in climbing 10 stairs without pause, completed by trained clinical research coordinators	Yes = 0.5 No = 0	Kim et al. (2018) [13]
13	Balance confidence	Activities-specific Balance Confidence (ABC) scale, average total score, assessed by trained clinical research coordinators	≤ 58.13 = 1 > 58.13 = 0	Moiz et al. (2017) [14]
14	Fall	SARC-F, frequency of falls in the past year, completed by trained clinical research coordinators	≥ 2 = 1 1 = 0.5 None = 0	Kim et al. (2018) [13]
15	Assistance in walking	SARC-F, difficulty in walking from the room, completed by trained clinical research coordinators	A lot/have to use aids (A walking stick)/unable = 1 A little = 0.5 Not at all = 0	Kim et al. (2018) [13]
16	Ambulation	FPQ for use in screening community-dwelling older adults, able to walk one lap of a 400-m track, completed by trained clinical research coordinators	Little or very difficult = 1 Not difficult at all = 0	Kim et al. (2020) [11]
17	Transferring from a bed to a chair	SARC-F, difficulty in transferring from a chair (wheelchair) to a bed (mattress) or from a bed (mattress) to a chair (wheelchair), completed by trained clinical research coordinators	A lot/unable without help = 1 A little = 0.5 Not at all = 0	Kim et al. (2018) [13]

(Continued to next page)

Table 1. Continued

No.	Deficit	Additional information	Cutoff values and KFI-PC score	References
18	Mobility	Information gathered by trained clinical research coordinators	Wheelchair = 1 Use cane or walker = 0.5 Walks independently = 0	-
18	Fecal incontinence	KFI, fecal incontinent experience over the past month, completed by trained clinical research coordinators	Yes = 1 No = 0	Hwang et al. (2010) [8]
20	Bladder control	KFI, urinary incontinence experience in the past month, completed by trained clinical research coordinators	Yes = 1 No = 0	Hwang et al. (2010) [8]
21	Shopping	IADLs, difficulty in buying or shopping, completed by trained clinical research coordinators	Unable/require complete assistance = 1 Capable with partial assistance = 0.5 Capable by oneself = 0	Won et al. (2002) [15]
22	Managing medications	IADLs, difficulty in managing medication with correct dosages at the correct time, completed by trained clinical research coordinators	Unable/require complete assistance = 1 Capable with partial assistance = 0.5 Capable by oneself = 0	Won et al. (2002) [15]
23	Driving or using public transportation	IADLs, difficulty in driving or using public transportation, completed by trained clinical research coordinators	Unable/require complete assistance = 1 Capable with partial assistance = 0.5 Capable by oneself = 0	Won et al. (2002) [15]
24	Managing finances	IADLs, difficulty in managing own money or financial matters, completed by trained clinical research coordinators	Unable/require complete assistance = 1 Capable with partial assistance = 0.5 Capable by oneself = 0	Won et al. (2002) [15]
25	Polypharmacy	The number of prescribed medications taken regularly, assessed by trained clinical research coordinators	≥ 8 = 1 5–7 = 0.5 ≤ 4 = 0	Park et al. (2018) [16]
26	Hypertension	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-
27	Diabetes	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-
28	Cancer	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-
29	Chronic obstructive pulmonary disease (COPD)	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-
30	Myocardial infarction (MI)	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-
31	Heart failure	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-
32	Angina	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-
33	Asthma	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-
34	Arthritis	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-
35	Stroke	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-

(Continued to next page)

Table 1. Continued

No.	Deficit	Additional information	Cutoff values and KFI-PC score	References
36	Kidney disease	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-
37	Spinal stenosis	Current condition, information gathered by trained clinical research coordinators	Yes = 1 No = 0	-
38–43	Additional health conditions	Current condition: number of additional diseases other than 12 diseases above, information gathered by trained clinical research coordinators	1 = 1 2 = 2 3 = 3 4 = 4 5 = 5 6 = 6	-
44	Hospitalization	KFI, hospitalization experience over the past year, completed by trained clinical research coordinators	≥ 1 = 1 None = 0	Hwang et al. (2010) [8]
45	Self-assessment of health status	KFI, completed by trained clinical research coordinators	Bad = 1 Good = 0	Hwang et al. (2010) [8]
46	Social contact	Contact frequency with friends in the past week, completed by trained clinical research coordinators	Rarely = 1 Weekly/monthly = 0	Chon et al. (2018) [17]
47	Spouse	Currently living with spouse or someone else, information gathered by trained clinical research coordinators	Live alone = 1 With someone else, not spouse = 0.5 Spouse = 0	-
48	Meals	SNAQ, number of full meals per day, completed by trained clinical research coordinators	< 1 meal = 1 1 meal = 0.33 2 meals = 0.66 ≥ 3 meals = 0	Oh et al. (2019) [18]
49	Appetite	SNAQ, self-rated appetite, completed by trained clinical research coordinators	Very poor = 1 Poor = 0.66 Average = 0.33 Good/very good = 0	Oh et al. (2019) [18]
50	Walking to distant destinations	IADLs, difficulty in going out to a shop, neighborhood, hospital, or government offices within walking distance, completed by trained clinical research coordinators	Unable/require complete assistance = 1 Capable with partial assistance = 0.5 Capable by oneself = 0	Won et al. (2002) [15]
51	Frequency of going out	Kihon Checklist for frailty, going out frequency over the past week, completed by trained clinical research coordinators	None = 1 1 day = 0.75 2–3 days = 0.5 4–6 days = 0.25 Every day = 0	Satake et al. (2016) [7]
52	Weight loss	FPQ for use in screening community-dwelling older adults, unintended weight loss of 4.5 kg over the past year, completed by trained clinical research coordinators	Yes = 1 No = 0	Kim et al. (2020) [11]
53	Underweight	Medical examination, information gathered by trained clinical research coordinators	BMI < 18.5 kg/m^2 = 1 BMI ≥ 18.5 kg/m^2 = 0	

KFI-PC, Korean Frailty Index for Primary Care; CERAD-K, Korean version of the Consortium to Establish a Registry for Alzheimer's Disease; KFI, Korean Frailty Index; FPQ, Frailty Phenotype Questionnaire; SARC-F, Simple Sarcopenia Screening Tool, IADL, Instrumental Activities of Daily Living; SNAQ, Simplified Nutritional Appetite Questionnaire.

participant was calculated by dividing the number of deficits by the number of total variables that were recorded for that patient. For example, we divided the total score of deficits by 53 for patients with recorded data for all variables. If a patient was missing data on two variables, then the number of deficits for this patient was divided by 51. If data on one of the strength or climbing question was missing, the total KFI-PC score was calculated by dividing by 52.5. In this way, the KFI-PC score is continuous (0 to 1), with higher scores indicating an increased likelihood of frailty.

Study Sample and Study Design

To establish the feasibility and preliminary validity analysis of KFI-PC, we used cross-sectional data from the Korean Frailty Aging and Cohort Study (KFACS). KFACS is a multicenter longitudinal study whose participants were recruited from among community-dwelling residents in urban and rural areas nationwide in 10 study centers across different regions.[25] Each center recruited participants using quota sampling stratified by age and sex at local senior welfare centers, community health centers, apartments, housing complexes, and outpatient clinics. We used quota sampling based on age (70–74, 75– 79, and 80–84 years with a ratio of 6:5:4, respectively) and sex (male, female) with an aim of recruiting 1,500 men and 1,500 women. The inclusion criteria were age 70–84 years, living independently at home, having no plans to move out in the next 2 years, and no problems with communication due to serious cognitive impairment. The first wave of baseline data collection started in 2016–2017; of 3,014 participants who underwent baseline survey, 1,559 (51.7%) and 1,455 (48.3%) were enrolled in the study in 2016 and 2017, respectively. The follow-up rate in 2018 (baseline survey in 2016) was 92.5%, with 88.4% visiting the clinical sites, 11% completing telephone interviews, and approximately 0.5% involving home visits. This study included its sample from the second wave of a 2016 baseline survey, from among the 1,274 participants who visited the 10 study centers in 2018 as SNAQ was first included in the second wave in 2018. KFI-PC was assessed in on-site clinical examinations. The final analysis included 1,242 participants, after excluding 32 participants who did not have the data required to assess the Fried's physical frailty phenotype.

Ethics

The KFACS protocol was approved by the Institutional Review Board (IRB) of the Clinical Research Ethics Committee of Kyung Hee University Hospital, Seoul, Korea, and all subjects provided written informed consent (No. 2015-12-103). The present study was exempt from the requirement for IRB approval by the Clinical Research Ethics Committee of Kyung Hee University Hospital (No. 2020-04-033).

Assessment of Fried's Physical Frailty Phenotypes

This study defined physical frailty using a modified operational definition of Fried's physical frailty phenotypes from the Cardiovascular Health Study (CHS).[2] The five different components of frailty indicators were (1) weight loss: answering "yes" to "In the last year, have you lost more than 4.5 kg unintentionally?"; (2) weakness: maximal grip strength in the lowest 20% of the weighted KFACS population distribution, adjusted for sex and body mass index; (3) slowness: 4-m usual gait speed in the lowest 20% of the weighted KFACS population distribution, adjusted for sex and height; (4) exhaustion: answering "yes" to either one of the following statements from the Center for Epidemiological Studies-Depression scale "I felt that everything I did was an effort" or "I could not get going" for three or more days per week; and (5) low physical activity: kilocalorie per week (kcal/week) expenditures were calculated for each activity using its metabolic equivalent score using the International Physical Activity Questionnaire, with low physical activity defined as <494.65 kcal for men and <283.50 kcal for women, which was the lowest value for 20% of the sex-specific total energy consumed from a general Korea population-based survey of older adults.[26] Although the Physical Activity Scale for the Elderly (PASE) is one of the most commonly used methods, the Korean version takes up to 10 minutes to administer. A Korean study found moderate to high agreement between the CHS frailty phenotype definitions based on the K-PASE or International Physical Activity Questionnaire short form.[27] In this context, subjects with three or more components were considered to have physical frailty.

Statistical Analysis

Data are presented as mean ± standard deviation or as numbers (percentages). Continuous variables were compared using independent t-tests, and categorical variables were compared using chi-square or Fisher exact tests. We used Shapiro–Wilks tests to assess normality and Mann–Whitney U tests and Kruskal–Wallis tests to assess KFI-PC scores with respect to sex and age groups. Significant differences in KFI-PC scores between age groups were assessed using non-parametric post-hoc tests with Mann–Whitney U tests ($p<0.016$). The internal consistency of the 54 items was assessed based on Cronbach's alpha coefficients. For construct validation of KFI-PC-index, we used Spearman rank correlation coefficients (r_s) to explore the relationships between KFI-PC score and outcomes. Receiver operating characteristic (ROC) analysis was performed to explore the cutoff values of the KFI-PC score and to verify the criterion validity for frailty according to Fried's physical

frailty phenotype. The optimal cutoff values with the greatest sum of sensitivity and specificity for correctly identifying frail individuals were determined using Youden's index. The statistical analyses were performed using Stata (version 14.0; Stata Corp., College Station, TX, USA) and IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA). Two-tailed $p < 0.05$ indicated statistical significance in this study.

RESULTS

Table 2 shows the characteristics of the study participants. Overall, the mean age was 77.9 and 28.9% of participants were living in rural areas. As the KFACS cohort study included participants who could visit 10 centers, ADL disability in any of five basic activities of daily living (i.e., dressing, bathing, toileting, transferring, and feeding) was rare (1.5%). Furthermore, the average overall KFI-PC score was 0.17. The KFI-PC score was higher in women and older groups in both sexes. The median and quartile KFI-PC scores for men and women and for age groups are shown in Supplementary Table S2. The KFI-PC scores showed a right-skewed distribution ranging from 0.02 to 0.52 (Fig. 1). Participants with KFI-PC score over 0.25, usually recognized the cutoff of frailty, represented 17.5% of the total population; however, the frailty prevalence by Fried's phenotype criteria was 9.2%. The KFI-PC score increased with age levels and the pattern was more exaggerated in women (Fig. 2). The deficit scores and missing data for each item of KFI-PC are presented in Table 3. The highest saturated deficit score was 60.2% with the current condition of hypertension. The highest rate of missing was 1.4% for the sleeping pattern item. The Cronbach's alpha coefficient of the 54 items total was 0.737, within the acceptable range (0.7 or above) for internal consistency (reliability).

Construct Validity of KFI-PC

To assess the construct validity (convergent validity) of KFI-PC, we compared it to Fried's physical frailty (Fig. 3, Table 4). ROC analysis performed to confirm the criterion-related validity of KFI-PC for Fried's physical frailty showed an area under the curve of

Table 2. Characteristics of the study sample

Variable	Overall (n = 1,242)	Men (n = 586)	Women (n = 656)	p-value
Age (y)	77.9 ± 3.9	78.2 ± 3.9	77.6 ± 3.9	0.014
Marriage status (n = 1,241)				
Married	800 (64.5)	523 (89.2)	277 (42.3)	<0.001
Widowed/divorced	440 (35.5)	62 (10.6)	378 (57.7)	<0.001
Single	1 (0.1)	1 (0.2)	0 (0)	<0.001
Living in rural area	358 (28.9)	18 (31.0)	177 (27.0)	0.068
Education (n = 1,240)				
< Middle school	646 (52.1)	205 (35.0)	441 (67.3)	<0.001
Middle and high school	402 (32.4)	232 (39.7)	170 (26.0)	<0.001
College	192 (15.5)	148 (25.3)	44 (6.7)	<0.001
ADL disability	19 (1.5)	7 (1.2)	12 (1.8)	0.250
KFI-PC score	0.17 ± 0.08	0.15 ± 0.07	0.20 ± 0.08	<0.001
KFI-PC score by age group				
70–74 years	0.16 ± 0.07	0.13 ± 0.07	0.17 ± 0.07	<0.001
75–79 years	0.17 ± 0.08	0.14 ± 0.07	0.20 ± 0.08	<0.001
≥ 80 years	0.20 ± 0.09	0.16 ± 0.07	0.24 ± 0.09	<0.001
KFI-PC score > 0.25 cutoff point	217 (17.5)	57 (9.7)	160 (24.4)	<0.001
Fried's phenotype criteria				
Frail	114 (9.2)	44 (7.5)	70 (10.7)	0.001
Pre-frail	601 (48.4)	263 (44.9)	338 (51.5)	0.001
Robust	527 (42.4)	279 (47.6)	248 (37.8)	0.001

Values are presented as mean±standard deviation or number (%).
ADL, activities of daily living; KFI-PC, Korean Frailty Index for Primary Care.
ADL disability, dependent in any of five basic activities of daily living (i.e., dressing, bathing, toileting, transferring, and feeding).
p-values based on chi-square, Fisher exact, or independent t-test.

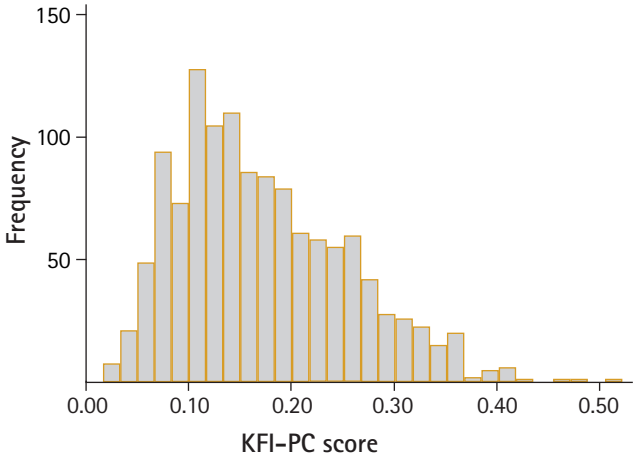

Fig. 1. The Korean Frailty Index for Primary Care (KFI-PC) score distribution in the study sample.

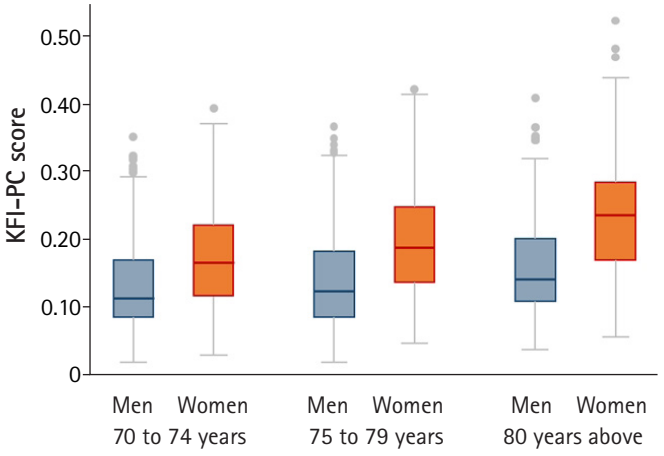

Fig. 2. Boxplot of the Korean Frailty Index for Primary Care (KFI-PC) scores for men and women and for three age groups. The median (horizontal line) is shown within each box. The KFI-PC score differed significantly between men and women in all age groups ($p<0.001$) and between the three age groups in men and women ($p<0.01$) except for 70–74 years vs. 75–79 years in men ($p=0.144$).

Table 3. The KFI-PC characteristics of the study sample

No	Deficit variable	Deficit score	Frequency (%)	Missing data
1	Construct recall (drawing two interlocking pentagons)	0	938 (75.5)	1 (0.1)
		1	303 (24.4)	
2	Three-item recall memory	0	514 (41.4)	1 (0.1)
		0.5	604 (48.6)	
		1	123 (9.9)	
3	Recognition	0	1,129 (90.9)	1 (0.1)
		0.5	95 (7.6)	
		1	17 (1.4)	
4	Depressive mood	0	821 (66.1)	0 (0)
		1	421 (33.9)	
5	Exhaustion	0	855 (68.8)	0 (0)
		1	421 (33.9)	
6	Delirium or hallucination	0	1,242 (100)	0 (0)
		1	0 (0)	
7	Visual or auditory problem	0	101 (81.6)	1 (0.1)
		1	227 (18.3)	
8	Sleeping pattern	0	908 (73.21)	18 (1.4)
		1	316 (25.4)	
9	Napping	0	683 (55.0)	0 (0)
		1	559 (45.0)	
10	Inactivity	0	761 (61.3)	0 (0)
		1	481 (38.7)	
11	Chair rise test	0	474 (38.2)	
		0.5	295 (23.8)	0 (0)
		1	473 (38.1)	
12-1	Strength	0	978 (78.7)	1 (0.1)
		0.5	263 (21.2)	
12-2	Climbing stairs	0	724 (58.3)	0 (0)
		0.5	518 (41.7)	

(Continued to next page)

Table 3. Continued

No	Deficit variable	Deficit score	Frequency (%)	Missing data
13	Balance confidence	0	988 (79.5)	1 (0.1)
		1	253 (20.4)	
14	Fall	0	972 (78.3)	6 (0.5)
		0.5	166 (13.4)	
		1	98 (7.9)	
15	Assistance in walking	0	1,192 (96.0)	0 (0)
		0.5	42 (3.4)	
		1	8 (0.6)	
16	Ambulation	0	886 (71.3)	1 (0.1)
		1	355 (28.6)	
17	Transferring from a bed to a chair	0	1,100 (88.6)	0 (0)
		0.5	128 (10.3)	
		1	14 (1.1)	
18	Mobility	0	1,198 (96.5)	0 (0)
		0.5	44 (3.5)	
		1	1 (0.1)	
19	Fecal incontinence	0	1,172 (94.4)	2 (0.2)
		1	68 (5.5)	
20	Bladder control	0	1,196 (96.3)	2 (0.2)
		1	4 (3.5)	
21	Shopping	0	1,211 (97.5)	0 (0)
		0.5	25 (2.0)	
		1	6 (0.5)	
22	Managing medications	0	1,233 (99.3)	0 (0)
		0.5	4 (0.3)	
		1	4 (0.3)	
23	Driving or using public transportation	0	1,218 (98.1)	0 (0)
		0.5	24 (1.9)	
		1	0 (0)	
24	Managing finances	0	1,118 (90.0)	0 (0)
		0.5	102 (8.2)	
		1	22 (1.8)	
25	Polypharmacy	0	770 (62.0)	3 (0.2)
		0.5	302 (24.3)	
		1	167 (13.4)	
26	Hypertension	0	494 (39.8)	0 (0)
		1	748 (60.2)	
27	Diabetes	0	959 (77.2)	0 (0)
		1	283 (22.8)	
28	Cancer	0	1,206 (97.1)	0 (0)
		1	36 (2.9)	
29	Chronic obstructive pulmonary disease	0	1,232 (99.2)	0 (0)
		1	10 (0.8)	
30	Myocardial infarction	0	1,214 (97.7)	0 (0)
		1	28 (2.3)	
31	Heart failure	0	1,228 (98.9)	0 (0)
		1	14 (1.1)	
32	Angina	0	1,141 (91.9)	0 (0)
		1	101 (8.1)	

(Continued to next page)

Table 3. Continued

No	Deficit variable	Deficit score	Frequency (%)	Missing data
33	Asthma	0	1,195 (96.2)	0 (0)
		1	47 (3.8)	
34	Arthritis	0	881 (70.9)	0 (0)
		1	361 (29.1)	
35	Stroke	0	1,239 (99.8)	0 (0)
		1	3 (0.2)	
36	Kidney disease	0	1,128 (98.9)	0 (0)
		1	3 (0.2)	
37	Spinal stenosis	0	1,196 (96.3)	0 (0)
		1	46 (3.7)	
38-43	Additional health conditions	0	525 (42.3)	0 (0)
		1	482 (38.8)	
		2	192 (15.5)	
		3	42 (3.4)	
		4	1(0.1)	
		5	0 (0)	
		6	0 (0)	
44	Hospitalization	0	1,055 (84.9)	0 (0)
		1	187 (15.1)	
45	Self-assessment of health status	0	853 (68.7)	1 (0.1)
		1	388 (31.2)	
46	Social contact	0	944 (76.0)	0 (0)
		1	298 (24.0)	
47	Spouse	0	779 (62.7)	0 (0)
		0.5	152 (12.2)	
		1	311 (25.0)	
48	Meals	0	1,135 (91.4)	0 (0)
		0.33	105 (8.5)	
		0.66	2 (0.2)	
		1	0 (0)	
49	Appetite	0	586 (47.2)	0 (0)
		0.33	476 (38.3)	
		0.66	155 (12.5)	
		1	25 (2.0)	
50	Walking to distant destinations	0	1,234 (99.4)	0 (0)
		0.5	8 (0.6)	
		1	0 (0)	
51	Going out	0	707 (56.9)	0 (0)
		0.25	238 (19.2)	
		0.5	158 (12.7)	
		0.75	28 (2.3)	
		1	111 (8.9)	
52	Weight loss	0	1,148 (92.4)	0 (0)
		1	94 (7.6)	
53	Underweight	0	1,215 (97.8)	0 (0)
		1	27 (2.2)	
Total score			9.2 ± 4.4	
Cronbach's alpha coefficient[a)]			0.737	

KFI-PC, Korean Frailty Index for Primary Care.
[a)]The internal consistency of the instrument items, assessed by Cronbach's alpha. The acceptable range of Cronbach's alpha is a value of 0.70 or above.

0.921 (95% confidence interval, 0.910–0.940). The ROC analysis revealed an optimal cutoff value, statistically defined as the best compromise between sensitivity and specificity, of 0.23 (sensitivity=89%, specificity=81%). The KFI-PC score showed correlations with physical, cognitive, and psychological functions, as well as nutritional status, disability in ADLs, and IADLs irrespective of age and sex (Table 4).

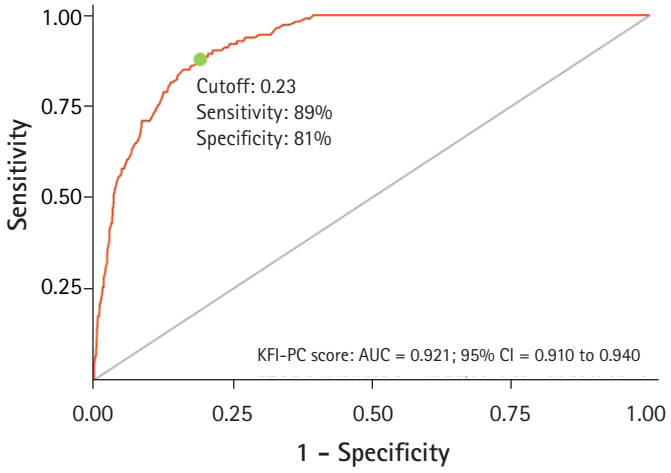

Fig. 3. Receiver operating characteristic (ROC) curve of the Korean Frailty Index for Primary Care (KFI-PC) score according to Fried's phenotype criteria. AUC, area under the ROC curve; CI, confidence interval.

DISCUSSION

We developed a KFI-PC containing 54 items with a maximum deficit score of 53 and demonstrated its acceptable internal consistency and construct validity. Broadly speaking, KFI-PC is a comprehensive assessment that covers health-related areas related to cognitive, mental, physical, social, and nutritional factors, as well as ADLs and medical illness.

Generally, frailty indices should contain at least 30 items and cover a range of health indicators including chronic conditions, physical/cognitive limitations, and general health. Another characteristic of frailty index is that each deficit should be health-related and increase with age.[24] Previous studies used 30–70 deficits to construct frailty indices. However, Searle et al.[23] recommended that frailty indices should include at least 30–40 total deficits. Another criterion is that the deficit should not saturate too early, i.e., it should not be present in all or most people. A reasonable criterion

Table 4. Construct validation of the KFI-PC

Variable	KFI-PC score		Age- and sex-adjusted KFI-PC score[a]	
	r_s	p-value	r_s	p-value
Fried's phenotype (score)	0.612	0.000	0.633	<0.001
Physical function				
Handgrip strength (kg)	-0.478	0.000	-0.284	<0.001
Usual gait speed (m/s)	-0.570	0.000	-0.512	<0.001
Timed Up and Go test (s)	0.570	0.000	0.530	<0.001
Short Physical Performance Battery (score)	-0.565	0.000	-0.532	<0.001
SARC-F (score)	0.434	0.000	0.463	<0.001
Cognitive function				
Mini-Mental State Examination (score)	-0.380	0.000	-0.335	<0.001
Frontal Assessment Battery (score)	-0.413		0.330	<0.001
Psychological status				
Geriatric Depression Scale (score)	0.534	0.000	0.510	<0.001
Nutritional status				
Mini Nutritional Assessment Screening (score)	-0.473	0.000	-0.448	<0.001
Total MNA (score)	-0.529	0.000	-0.513	<0.001
Disability				
K-ADL (score)[b]	0.251	0.000	0.287	<0.001
K-IADL (score)[c]	0.202	0.000	0.322	<0.001

KFI-PC, Korean Frailty Index for Primary Care; SARC-F, simple 5-item questionnaire for sarcopenia screening; K-ADL, Korean activities of daily living; K-IADL, Korean instrumental activities of daily living.
p-values calculated using Spearman rank correlation coefficients (r_s).
[a]Age-and sex-adjusted Spearman partial correlation coefficients between KFI-PC score and outcomes.
[b]n=1,238.
[c]n=1,129.

for saturation appears to be about 80% or less as any deficits present in more than 80% of people do not make a significant difference in grading frailty.[28] KFI-PC satisfied all these requirements. Moreover, it covers a range of not only chronic conditions, physical/cognitive limitations, and general health but also the factors related to social and psychological health.

In this study, the ROC analysis demonstrated an optimal KFI-PC cutoff value of 0.23, consistent with the consensus cutoff point for frailty of 0.25 for the frailty index used to define frailty in other studies.[29] The original paper suggested a frailty cutoff of 0.25 based on a physical frailty index containing 70 deficits and data from participants aged 70 years and older in the Canadian Study of Health and Aging. However, another paper proposed a frailty cutoff of 0.21.[30] A study analyzing Canadian Health Survey data from participants aged 65 years and over reported that the risk of hospital-related events increased at a value of 0.21. The cutoff is the lowest point for predicting outcomes; it may be sensitive but not specific and, therefore, not the optimal threshold.

Regarding participants with missing variables, studies commonly exclude any item with more than 5% of missing data[31] and any participant with at least one missing item from more than 20% of the items.[30] In this study, 40 of 53 (75.5%) items had complete data. Of the 13 items with missing data, 10 items were missing only 1 or 2 value; the other three items had 3, 6, and 18 missing values. Thus, missing variables were not an issue in this study. KFI-PC is easily evaluated in primary care, as it is mainly made of self-responding questionnaires, with only the Mini-Cog and chair rise tests requiring healthcare provider evaluations. The Mini-Cog test can be completed in 2–4 minutes. The chair rise test takes approximately 1–2 minutes to administer after a simple demonstration. The chair rise test can be used as an alternative for gait speed or handgrip strength. It is particularly valuable and applicable to studies that do not or cannot include gait testing due to a lack of space or instrument to measure handgrip strength.

The KFI-PC score increased with age levels, a pattern that was more pronounced in women. Previous studies reported that deficits consistently accumulate exponentially with age at an average relative rate of approximately 3% per year on a log scale and that in general, at any given age, women on an average have more deficits than do men.[32] The reason for the sex difference may be mainly because of a higher incidence of comorbidities in women than in men, in addition to social, behavioral, and biological differences between men and women.[33]

We observed a frailty prevalence of 9.2% based on Fried's phenotype criteria and 17.5% based on KFI-PC, with a cutoff of 0.25. This result is compatible with that of previous reports of a 10% higher frailty prevalence using the frailty index compared with that using the phenotype criteria.[34] The frailty index is associated with adverse health outcomes even among people categorized as non-frail by frailty phenotype.[34] This finding suggests that the frailty index is a more sensitive measure for determining frailty owing to its ability to detect this condition at even the early stage of a frailty trajectory.[34] Furthermore, the continuous nature of the frailty index allows it to trace slight changes in frailty to intervene before an individual reaches a definite frail phenotype.[33] The prevalence of ADL disability in this study was only 1.5%. As the participants of the KFACS are comparatively healthy older adults who can visit the centers, the percentage of ADL disability may be lower than other home visit surveys. However, KFI-PC was developed for use in outpatient primary care and those patients must be ambulatory to visit clinics. In comparison, the reported prevalence of ADL disability was 2.6% in four outpatient clinics and two welfare centers.[35]

In conclusion, we developed KFI-PC containing 53 deficits including comprehensive geriatric assessment components. KFI-PC comprises mainly self-administered questionnaires; only the Mini-Cog and chair rise tests are assessed by medical personnel and require limited time to perform. We demonstrated the construct validity and internal consistency (reliability) of KFI-PC. KFI-PC is easily assessed, was not considered a burden on the medical personnel who practice in primary care, and was well validated. Further studies are needed to determine whether KFI-PC is a good indicator for the prevention of adverse health outcomes and if it is feasible in real-world primary care settings.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

This research was supported by a grant from the Korea Health Technology R&D Project through the Korean Health Industry Development Institute, funded by the Ministry of Health and Welfare, Republic of Korea (No. HI15C3153).

AUTHOR CONTRIBUTIONS

Conceptualization, CWW; Data curation, CWW, SL, MK; Funding acquisition, CWW; Investigation, CWW, SL, YL, MK; Methodology, CWW, SL, YL, MK; Project administration, CWW; Supervision, CWW; Writing-original draft, CWW, MK; Writing-review & editing, CWW, SL, YL, MK.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.20.0021

Table S1. KFI-PC in Korean version

Table S2. Median and quartiles (Q1, Q3) of the Korean Frailty Index for Primary Care scores for men and women and for three age groups

REFERENCES

1. Won CW. Frailty: its scope and implications for geriatricians. Ann Geriatr Med Res 2019;23:95-7.
2. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-56.
3. Theou O, Park GH, Garm A, Song X, Clarke B, Rockwood K. Reversing frailty levels in primary care using the CARES Model. Can Geriatr J 2017;20:105-11.
4. Sepehri K, Braley MS, Chinda B, Zou M, Tang B, Park G, et al. A computerized frailty assessment tool at points-of-care: development of a standalone electronic comprehensive geriatric assessment/frailty index (eFI-CGA). Front Public Health 2020;8:89.
5. Jones DM, Song X, Rockwood K. Operationalizing a frailty index from a standardized comprehensive geriatric assessment. J Am Geriatr Soc 2004;52:1929-33.
6. Lee JH, Lee KU, Lee DY, Kim KW, Jhoo JH, Kim JH, et al. Development of the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet (CERAD-K): clinical and neuropsychological assessment batteries. J Gerontol B Psychol Sci Soc Sci 2002;57:P47-53.
7. Satake S, Senda K, Hong YJ, Miura H, Endo H, Sakurai T, Kondo I, Toba K. Validity of the Kihon Checklist for assessing frailty status. Geriatr Gerontol Int 2016;16:709-15.
8. Hwang HS, Kwon IS, Park BJ, Cho B, Yoon JL, Won CW. The validity and reliability of Korean frailty index. J Korean Geriatr Soc 2010;14:191-202.
9. Kang I, Kim S, Kim BS, Yoo J, Kim M, Won CW. Sleep latency in men and sleep duration in women can be frailty markers in community-dwelling older adults: the Korean Frailty and Aging Cohort Study (KFACS). J Nutr Health Aging 2019;23:63-7.
10. Oh JY, Yang YJ, Kim BS, Kang JH. Validity and reliability of Korean version of International Physical Activity Questionnaire (IPAQ) Short Form. J Korean Acad Fam Med 2007;28:532-41.
11. Kim S, Kim M, Jung HW, Won CW. Development of a frailty phenotype questionnaire for use in screening community-dwelling older adults. J Am Med Dir Assoc 2020;21:660-4.
12. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16-31.
13. Kim S, Kim M, Won CW. Validation of the Korean version of the SARC-F Questionnaire to assess sarcopenia: Korean Frailty and Aging Cohort Study. J Am Med Dir Assoc 2018;19:40-45. e1.
14. Moiz JA, Bansal V, Noohu MM, Gaur SN, Hussain ME, Anwer S, et al. Activities-specific balance confidence scale for predicting future falls in Indian older adults. Clin Interv Aging 2017;12:645-51.
15. Won CW, Yang KY, Rho YG, Kim SY, Lee EJ, Yoon JL, et al. The development of Korean activities of daily living (K-ADL) and Korean instrumental activities of daily living (K-IADL) scale. J Korean Geriatr Soc 2002;6:107-20.
16. Park HY, Sohn HS, Kwon JW. Reviews on the current status and appropriate management of polypharmacy in South Korea. Korean J Clin Pharm 2018;28:1-9.
17. Chon D, Lee Y, Kim J, Lee KE. The association between frequency of social contact and frailty in older people: Korean Frailty and Aging Cohort Study (KFACS). J Korean Med Sci 2018;33:e332.
18. Oh SY, Koh SJ, Baek JY, Kwon KA, Jeung HC, Lee KH, et al. Validity and reliability of Korean version of Simplified Nutritional Appetite Questionnaire in patients with advanced cancer: a multicenter, longitudinal study. Cancer Res Treat 2019;51:1612-9.
19. Santos KT, Fernandes MH, Carneiro JA, da Silva Coqueiro R. Motor performance tests as screening instruments for frailty in the older adults. Appl Nurs Res 2016;32:80-4.
20. Borson S, Scanlan JM, Chen P, Ganguli M. The Mini-Cog as a screen for dementia: validation in a population-based sample. J Am Geriatr Soc 2003;51:1451-4.
21. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging 2012;16:601-8.
22. Kim HJ, Park S, Park SH, Lee JH, Chang BS, Lee CK, et al. The prevalence and impact of frailty in patients with symptomatic lumbar spinal stenosis. Eur Spine J 2019;28:46-54.
23. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. BMC Geriatr 2008;8:24.
24. McCarthy AL, Peel NM, Gillespie KM, Berry R, Walpole E, Yates P, et al. Validation of a frailty index in older cancer patients with solid tumours. BMC Cancer 2018;18:892.
25. Won CW, Lee Y, Choi J, Kim KW, Park Y, Park H, et al. Starting construction of frailty cohort for elderly and intervention study. Ann Geriatr Med Res 2016;20:114-7.
26. Jeon SY, Won CW, Choi HR, Kim BS, Kim SY, Hur JH. Physical

frailty predicts cognitive decline in elderly people: Prospective findings from the living profiles of older people survey in Korea. Korean J Fam Pract 2015;5:702-7.
27. Jang IY, Jung HW, Lee CK, Lee YS, Lee E, Kim DH. Comparison between Korean version of Physical Activity Scale for the elderly and International Physical Activity Questionnaire-Short Form in evaluation of frailty phenotype. Ann Geriatr Med Res 2017;21:101-7.
28. Lacas A, Rockwood K. Frailty in primary care: a review of its conceptualization and implications for practice. BMC Med 2012;10:4.
29. Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. J Gerontol A Biol Sci Med Sci 2007;62:738-43.
30. Blodgett J, Theou O, Kirkland S, Andreou P, Rockwood K. Frailty in NHANES: comparing the frailty index and phenotype. Arch Gerontol Geriatr 2015;60:464-70.
31. Li G, Ioannidis G, Pickard L, Kennedy C, Papaioannou A, Thabane L, et al. Frailty index of deficit accumulation and falls: data from the Global Longitudinal Study of Osteoporosis in Women (GLOW) Hamilton cohort. BMC Musculoskelet Disord 2014;15:185.
32. Rockwood K, Mitnitski A. Frailty defined by deficit accumulation and geriatric medicine defined by frailty. Clin Geriatr Med 2011;27:17-26.
33. Abbasi M, Khera S, Dabravolskaj J, Vandermeer B, Theou O, Rolfson D, et al. A cross-sectional study examining convergent validity of a frailty index based on electronic medical records in a Canadian primary care program. BMC Geriatr 2019;19:109.
34. Theou O, Brothers TD, Mitnitski A, Rockwood K. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. J Am Geriatr Soc 2013;61:1537-51.
35. Cho EJ, Park SJ, Lee JE, Lee JS, Kim MY, Yoon JL. (2007). Results of'short-form comprehensive geriatric assessment' application to elderly outpatients. J Korean Geriatr Soc 2007;11:1-8.

AGMR
Annals of Geriatric Medicine and Research

Original Article
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):139-147
https://doi.org/10.4235/agmr.20.0020

Cross-sectional Evaluation of the Sarcopenia Quality of Life (SarQoL) Questionnaire: Translation and Validation of its Psychometric Properties

Marta Dzhus[1], Maria Dzhus[1], Marta Masnyi[2], Myroslava Kulyk[1], Halyna Mostbauer[1], Oleksiy Ivashkivsky[3], Yaryna Boyko[4], Kateryna Cherchenko[5], Anton Geerinck[6,7], Jean-Yves Reginster[6,7], Olivier Bruyere[6,7], Charlotte Beaudart[6,7]

[1]Department of Internal Medicine, O. Bogomolets National Medical University, Kyiv, Ukraine
[2]Toronto Catholic District School Board, Toronto, Canada
[3]Oleksandrivsky Clinical Hospital, Kyiv, Ukraine
[4]Department of Pediatric, Lviv Regional Specialized Children's Hospital, Lviv, Ukraine
[5]Kyiv Clinical Hospital, Kyiv, Ukraine
[6]Division of Public Health, Epidemiology and Health Economics, University of Liege, Liege, Belgium
[7]World Health Organization Collaborating Center for Public Health Aspects of Musculoskeletal Health and Aging, University of Liege, Liege, Belgium

Corresponding Author:
Marta Dzhus, PhD, MD
Department of Internal Medicine,
O. Bogomolets National Medical
University, Kyiv, Ukraine
E-mail: dzhusm@yahoo.co.uk
ORCID:
https://orcid.org/0000-0002-7500-8520

Received: April 2, 2020
Revised: April 30, 2020
Accepted: May 13, 2020

Background: The SarQoL, a quality-of-life questionnaire specific to sarcopenia, was developed in 2015 and has since been translated into a number of other languages. The main reason to introduce this new Ukrainian version of the questionnaire was to measure sarcopenic individuals' perceptions regarding their positions in life in the context of their culture and value systems. **Methods:** The questionnaire was translated using a forward-backward approach with a pre-test. A total of 49 participants were recruited for the validation study. Sarcopenia was diagnosed according to the Ishii test. The validation analyses included discriminative power, internal consistency, floor and ceiling effects, construct validity, and test-retest reliability. We compared the SarQoL questionnaire to the Short-Form 36 and the EuroQoL-5 Dimensions. **Results:** A total of 28 participants out of 49 were categorized as probably sarcopenic. They had a significantly lower quality of life (overall score 58.43±17.13 vs. 69.89±13.31; p=0.014). The internal consistency was excellent (α=0.898), with none of the domains showing a disproportionate influence on the homogeneity of the questionnaire. Convergent construct validity was also confirmed. The results indicated a near-perfect degree of test-retest reliability. **Conclusions:** The first Ukrainian version of the questionnaire is equivalent to the available original English version.

Key Words: Sarcopenia, Quality of life, Translations, Validation study

INTRODUCTION

Sarcopenia is a progressive and generalized loss of muscle mass and function with advancing age.[1,2] This geriatric syndrome is now considered an increasing public health issue worldwide.[3] Sarcopenia is associated with adverse health outcomes such as physical impairment, mobility limitations, increased fall risk, hospitalization, and mortality.[4] In the last decade, several sarcopenia definitions and proposals for diagnostic criteria have been published. Among these, the revised consensus criteria of the European Working Group on Sarcopenia in Older People (EWGSOP2) appear to be the most promising. The EWGSOP2 considers sarcopenia to be present when a person presents with both low muscle strength and low muscle mass. Additionally, people with low physical performance are categorized as severely sarcopenic.[3]

This condition can also impact patient quality of life. Since this aspect is not straightforward for clinical evaluation, the issue is less studied so far. The existing quality of life questionnaires, such as the Short Form 36 (SF-36) and EuroQoL 5-dimension (EQ-5D), are designed for use in a broad swath of health conditions and pa-

tient populations and, thus, do not cover all physical dysfunctions associated with sarcopenia. Consequently, it would be useful to have a specific questionnaire to assess the impact of sarcopenia on quality of life.

The SarQoL questionnaire is the first multidimensional disease-specific questionnaire designed for community-dwelling sarcopenic subjects aged 65 years and older. It comprises 22 questions rated on a 3-, 4-, or 5-point Likert scale. Items are categorized into the following sevens domains of dysfunction: physical and mental health, locomotion, body composition, functionality, activities of daily living, leisure activities, and fears. The questionnaire was initially developed and validated in French in 2015[5,6] and was later translated and validated into English, Dutch, Romanian, Polish, Hungarian, Russian, and Greek.[7-13]

To provide the Ukrainian nation with a qualitative and reliable questionnaire to measure the quality of life of sarcopenic patients, we have created the Ukrainian version of the SarQoL questionnaire. The process of translation and validation followed the protocol for translation provided by the authors of the SarQoL questionnaire, which were based on the recommendations of Beaton et al.[14] This protocol included translation, cross-cultural adaptation, and validation of psychometric properties of the questionnaire. This process ensures standardization of the translated versions and makes them valid instruments for clinical purposes.

The objectives of this study were to translate the SarQoL questionnaire from English into Ukrainian and to assess its main psychometric properties.

MATERIALS AND METHODS

Ukrainian Translation

The translation was performed by a group of experts to exclude any cultural divergence and ensure the usefulness of the questionnaire in different populations. The process of translation from English to Ukrainian and cross-cultural adaptation was performed according to specific guidelines[14] and included five phases: (1) independent forward translation by two bilingual translators (one of whom had a medical background; the other was a novice regarding the topic of questionnaire), both native Ukrainian speakers; (2) synthesis of the initial translations providing a single "Version 1"; (3) independent backward translations of "Version 1" from Ukrainian to English by two bilingual translators who were native English speakers, had no medical background, and were blind to the original version of the SarQoL questionnaire; (4) comparison of the Version 1 and backward translations by an expert committee, resulting in a pre-final version of the Ukrainian SarQoL questionnaire and a full written report of the issues encountered at each step; and (5) a test of the pre-final version on 10 sarcopenic subjects to ensure understanding of the purpose and meaning of each question, which led to the final version of the SarQoL-UA.

The translation was performed with the permission of the rights holder of the SarQoL questionnaire (SarQoL sprl, Brussel, Belgium); the original developers also provided assistance and advice during the translation and validation process. The original developers of the questionnaire (OB and CB) were kept informed of the major choices made during the translation process and the results of the pre-test of the questionnaire and confirmed the equivalence between the English and Ukrainian versions.

Validation

Participants and protocol

A total of 49 patients aged 65 years and older were recruited in Oleksandrivska Clinical Hospital in Kyiv, Ukraine, where large proportions of older and geriatric patients are treated.

All patients were informed about the objective and form of subsequent questions and tests before providing their informed consent. Patients with severe exacerbations of chronic illnesses, decompensations of heart failure and diabetes, physical malformations, or traumas associated with decreased mobility, amputations, malignant diseases, and also mental illnesses that prevented understanding and correct response to the questions were not included in the investigation. The study was approved by the Ethics Committee of Oleksandrivska Clinical Hospital (No. 22/2016). We collected clinical and demographic variables such as age, sex, body mass, height, waist, hip and thigh circumference, muscle strength, and gait speed using standard methods by trained examiners. Due to limited access to dual-energy X-ray absorptiometry (DEXA) equipment, the probability of sarcopenia was determined using the Ishii screening test.[15] The objective of this test is to identify older adults at a high risk of sarcopenia; the test relies on a combination of age, grip strength, and calf circumference. The exact formulas are as follows:

Score in men = 0.62 × (age 64 y) – 3.09 × (grip strength 50 kg) – 4.64 × (calf circumference 42 cm)

Score in women = 0.80 × (age 64 y) – 5.09 × (grip strength 34 kg) – 3.28 × (calf circumference 42 cm)

The established cutoff values that maximize the sum of sensitivity and specificity are ≥ 105 for men and ≥ 120 for women,[3] with higher scores indicating an increased probability of sarcopenia.

Muscle strength was evaluated based on handgrip strength measured using a manual spring dynamometer (DRP-90, GOST 22224-76, Russia) with a cutoff value of < 20 kg for women and < 30 kg for men. The measurements were performed on both the

patients' dominant and non-dominant hands, with the highest value recorded. To evaluate physical performance, we used gait speed in the form of the 3-minute timed walk test. The patients were asked to walk at their standard speed and the mean of the meters walked was converted to speed in meters per second (m/s) for analysis. Values < 0.8 m/s indicated poor physical performance.[16]

Procedures

Psychometric validation of the Ukrainian version of the SarQoL

Validation of the psychometric properties of the SarQoL-UA consisted of an assessment of its discriminative power, internal consistency, potential floor and ceiling effects, construct validity, and test-retest reliability, all of which were performed according to the recommendations of Terwee et al.[17]

(1) **Discriminative power,** also called known-groups validity, was evaluated by comparing the QoL scores between participants who were categorized as probably having sarcopenia by the Ishii test and those categorized as probably not having sarcopenia. Additionally, we examined two components of sarcopenia, grip strength and gait speed, by comparing subjects with low and normal values. The sample was dichotomized using the EWGSOP2 cutoffs (< 27 kg for men and < 16 kg for women for grip strength and ≤ 0.8 m/s for gait speed).[3] To assess the discriminative power of the questionnaire, we assumed that the QoL scores should be higher (indicating better QoL) in population categorized as probably non-sarcopenic, or with normal grip strength or gait speed, compared to those categorized as probably sarcopenic or with low grip strength or gait speed.

(2) **Internal consistency.** To measure internal consistency, understood as an estimation of the questionnaire's homogeneity, we calculated the Cronbach's alpha coefficient.[18] A coefficient value between 0.7 and 0.9 indicates a high level of internal consistency. By deleting one domain at a time, we also considered the impact of each domain on internal consistency. The correlation of each domain with the total SarQoL-UA score was also assessed by correlation analysis. We defined excellent correlation as r > 0.81, very good correlation as r between 0.61 and 0.80, and good correlation as r between 0.41 and 0.60.

(3) **Floor and ceiling effects** are present when a high percentage of the population has the lowest or the highest scores, respectively. We considered significant floor and ceiling effects when higher than 15%.

(4) **Construct validity.** The construct validity of the questionnaire indicates whether the questionnaire measures the construct it claims to measures. This was investigated by measuring the convergent and divergent validity; i.e., the level of agreement between the SarQoL questionnaire and domains of other questionnaires that are theorized to be similar or different. Every patient completed, at the same time as the SarQoL-UA questionnaire, the SF-36v2 and the EQ-5D, two generic QoL questionnaires. The generic SF-36 questionnaire (SF-36v2)[19] contains 36 items in eight health domains. Two components of the health survey were calculated: the physical component summary (PCS) and the mental component summary (MCS), providing reliable and valid summaries of a patient's physical and mental status. The total raw score computed for each health domain scale was calculated, in which 0 and 100 points indicated the worst and best QoL, respectively.[20]

For the evaluation of overall self-rated health status, we used the EQ-5D questionnaire,[21] which includes five domains: mobility, usual activities, self-care, pain/discomfort, and anxiety/depression, as well as the EQ Visual Analogue Scale (EQ-VAS).[22] Each of the five dimensions comprising the EQ-5D was divided into five levels of perceived impairment, from level 1 (no problem) to level 5 (extreme problems). A unique health state was defined by combining the reported level from each of the five dimensions and referring the result to a five-digit code that was subsequently converted to a single index value (EQ-5D index value).[23]

For convergent construct validity, we hypothesized strong correlations between the overall QoL SarQoL score and the mobility and usual activities questions of the EQ-5D, as well as with the SF-36 PCS and the EQ-VAS. For divergent construct validity, we expected to find weak or non-existent correlations between the overall QoL SarQoL score and the self-care, pain/discomfort, and anxiety/depression questions of the EQ-5D, as well as the SF-36 MCS.

(5) **Test-retest reliability.** The test-retest reliability of the questionnaire, defined as the degree to which the questionnaire produces the same results in identical circumstances over time, was evaluated by intra-class correlation coefficient (ICC). To analyze the test-retest stability of our Ukrainian version of the SarQoL, participants who did not report any significant health change over a 2-week period were asked to complete the questionnaire again after a 2-week interval. The reliability was considered acceptable for ICC > 0.7.

Statistical Analysis

The distribution of quantitative variables was assessed using Shapiro-Wilk tests. Quantitative variables with a normal distribution are expressed as mean ± standard deviation, and quantitative variables with non-normal distributions are expressed as medians (P25–P75) and categorical variables are reported as absolute (n) and relative frequencies (%). Results were considered statistically significant at the 5% critical level ($p < 0.05$).

Differences in characteristics between groups were tested using the parametric Student t-test or the non-parametric Mann-Whitney U-test for quantitative variables and chi-square tests for nominal variables. For internal consistency, the Cronbach's alpha coefficient was calculated. The correlation of each domain with the total score of the SarQoL-UA was determined using Pearson or Spearman correlations based on the distribution of the variables. The evaluation of the construct validity also used Pearson or Spearman correlations. The test-retest reliability was assessed using ICC (two-way mixed-absolute agreement). All of the analyses were performed using IBM SPPS Statistics version 25.0.0.0 for Windows (IBM, Armonk, NY, USA).

RESULTS

Translation

No major conceptual discrepancies were observed between translations and all differences were resolved by consensus. We reached out to CB and OB for clarification on the content of certain questions, to make sure that the translated questions were conceptually equivalent to the questions in English. The 22 questions of the SarQoL questionnaire were translated without any major difficulties. Certain adaptions were made to optimize the questionnaire for the cultural context of Ukraine, such as discussion regarding the forward translation of the words "light" (in question 3) and "moderate" (in question 4), "frail" (in question 16) and "do it yourself (DIY)" (in question 3), which were solved in the initial translators' meeting. A pretest in the third and prefinal version was performed on 20 participants.

The pre-test did not reveal problems in the comprehensibility of the questions in the questionnaire or the language used therein.

Sample Characteristics

In the study population, median age was 71 years (range, 67.0-75.5 years) (Table 1), including 29 (59.2%) men and 20 (40.8%) women. The study population were overweight, with a median body mass index of 29.06 kg/m^2 (range, 25.28–32.62 kg/m^2).

We observed that both male and female participants had low grip strength, as evidenced by the fact that 70% of the female subjects and 65.5% of male subjects had low maximum grip strengths according to the EWGSOP2 cutoffs. For physical performance, represented by gait speed, we observed a mean value of 0.95 ± 0.37 m/s, well above the ≥ 0.8 m/s threshold used by the EWGSOP2 to indicate low gait speed.

We divided the patients into two groups according to the probable presence or absence of sarcopenia, as indicated by Ishii test results. A total of 28 and 21 people were probably sarcopenic and probably non-sarcopenic, respectively. As expected, age, grip strength, and calf circumference differed between the two groups. Although the median gait speed was considerably higher is the probably non-sarcopenic group (1.2 vs. 0.8 m/s), the difference was not significant (p = 0.056).

Validation Analyses

Discriminative power

The discriminative power was examined by comparing the quality of life scores between the people classified as probably and probably non-sarcopenic according to the Ishii screening test (Table 2).

Additionally, a discriminative power analysis was also performed by dichotomizing the people by grip strength (men < 27 kg; women < 16 kg) and gait speed (≥ 0.8 m/s).

Categorization of the patients into probably and probably non-sarcopenic according to the Ishii test showed significantly

Table 1. Clinical characteristics of the patients

Variable	All (n = 49)	Probably sarcopenic (n = 28)	Probably non-sarcopenic (n = 21)	p-value
Age (y)	71.00 (67.00–77.50)	73.50 (68.50–79.00)	69.00 (67.00–73.50)	0.046[a]
Sex				0.737[b]
Female	20 (40.8)	12 (42.9)	8 (38.1)	
Male	29 (59.2)	16 (57.1)	13 (61.9)	
BMI (kg/m^2)	29.06 (25.28–32.62)	28.00 (25.64–32.28)	30.91 (24.33–34.65)	0.391[a]
Calf circumference (cm)	37.00 (33.75–40.00)	35.75 (33.00–38.38)	39.00 (35.50–41.50)	0.016[a]
Maximum grip strength (kg)	16 (8.00–25.50)	9 (6.25–15.00)	30 (19.50–33.00)	< 0.001[a]
Gait speed (m/s)	0.95 (0.65–1.26)	0.80 (0.59–1.22)	1.20 (0.71–1.36)	0.056[a]

Values are presented as median (25th percentile–75th percentile) or number (%).
BMI, body mass index.
[a]Mann–Whitney U-test.
[b]Chi-square test.

lower quality of life scores for five of the seven of the domain scores, as well as the overall QoL sscore (58.43 ± 17.13 vs. 69.89 ± 13.31 points; p = 0.014).

In contrast, no significant differences were found for the SF-36 PCS and MCS summary scores, as well as for the EQ-VAS. Examination of the individual questions of the EQ-5D showed that participants in the probably sarcopenic group scored higher on the pain/discomfort item, indicating more pain/discomfort and thus worse QoL—3 (2–3) vs. 2 (1–3); p = 0.032. The other EQ-5D items did not differ significantly between the two groups.

We observed that people with low grip strength or low gait speed generally showed lower quality of life scores on the SarQoL questionnaire, except for domains 6 and 7. Crucially, the overall QoL score was significantly lower for people with low grip strength (56.71 ± 16.96 vs. 68.73 ± 15.33 points; p = 0.0169) and people with low gait speed (49.93 ± 12.23 vs. 73.40 ± 11.29; p < 0.001). The results for all domains are reported in Tables 3 and 4.

Internal Consistency

Cronbach's alpha coefficient

The complete questionnaire showed an alpha of 0.898; the value within the 0.7–0.9 threshold indicated adequate internal consistency with a low risk of redundancy in the questionnaire. Deletions

Table 2. Quality of life characteristics

Variable	All (N = 49)	Probably sarcopenic (n = 28)	Probably non-sarcopenic (n = 21)	p-value
SarQoL D1 Physical and mental health	59.97 (47.20–72.75)	56.72 ± 16.63	66.43 ± 16.85	0.050[a]
SarQoL D2 Locomotion	66.67 (47.22–86.11)	56.95 (33.34–87.50)	72.22 (58.33–87.50)	0.069[b]
SarQoL D3 Body composition	58.33 (41.67–75.00)	43.75 (37.50–66.67)	66.67 (56.25–75.00)	0.010[b]
SarQoL D4 Functionality	71.15 (49.04–85.17)	62.85 ± 18.61	77.24 ± 14.18	0.005[a]
SarQoL D5 Activities of daily living	61.67 (43.10–76.67)	55.15 ± 19.84	66.18 ± 16.14	0.043[a]
SarQoL D6 Leisure activities	33.25 (33.25–49.88)	41.57 (33.25–49.88)	33.25 (33.25–49.88)	0.366[b]
SarQoL D7 Fears	87.50 (75.00–100)	87.50 (75.00–87.50)	87.50 (87.50–100)	0.016[b]
SarQoL Overall QoL	63.72 (45.96–79.24)	58.43 ± 17.13	69.89 ± 13.31	0.014[a]
SF-36 PCS	36.00 (27.00–43.50)	34.14 ± 10.85	38.19 ± 8.94	0.171[a]
SF-36 MCS	47.40 (39.93–53.78)	48.17 ± 10.28	44.36 ± 9.67	0.194[a]
EQ-5D Mobility	2 (1–3)	2 (1.25–3)	2 (1–2)	0.092[b]
EQ-5D Self-care	1 (1–2)	1 (1–2)	1 (1–1)	0.211[b]
EQ-5D Usual activities	2 (1–3)	2 (1–3)	1 (1–2)	0.137[b]
EQ-5D Pain/discomfort	2 (2–3)	3 (2–3)	2 (1–3)	0.032[b]
EQ-5D Anxiety/depression	2 (1–2)	2 (1–2)	1 (1–3)	0.870[b]
EQ-VAS	50 (50.00–65.00)	50 (46.25–65.00)	55 (50.00–65.00)	0.592[b]

Values are presented as median (25th percentile–75th percentile) or mean±standard deviation.
EQ-5D, EuroQoL 5-dimension; PCS, physical component summary; MCS, mental component summary; VAS, visual analog scale.
[a]Student t-test.
[b]Mann–Whitney U-test.

Table 3. Discriminative power for grip strength

	Low grip strength (n = 32)	Normal grip strength (n = 17)	p-value
SarQoL D1 Physical and mental health	56.71 ± 16.96	68.73 ± 15.33	0.019[a]
SarQoL D2 Locomotion	58.33 ± 24.00	75.49 ± 18.46	0.014[a]
SarQoL D3 Body composition	43.75 (37.50–65.63)	75.00 (60.42–79.17)	0.001[b]
SarQoL D4 Functionality	63.53 ± 18.07	79.34 ± 13.61	0.003[a]
SarQoL D5 Activities of daily living	54.17 (38.75–72.08)	73.33 (62.98–80.00)	0.008[b]
SarQoL D6 Leisure activities	33.25 (33.25–49.88)	33.25 (33.25–49.88)	0.973[b]
SarQoL D7 Fears	87.50 (75.00–87.50)	87.50 (87.50–100)	0.080[b]
Overall score	58.30 ± 16.31	72.82 ± 12.37	0.002[a]

Values are presented as mean±standard deviation or median (25th percentile–75th percentile).
[a]Student t-test for independent samples.
[b]Mann–Whitney U-test.

Table 4. Discriminative power for gait speed

	Low gait speed (n = 21)	Normal gait speed (n = 28)	p-value
SarQoL D1 Physical and mental health	51.04 ± 12.18	68.27 ± 16.94	< 0.001[a]
SarQoL D2 Locomotion	44.44 (27.78–62.50)	79.17 (63.89–94.44)	< 0.001[b]
SarQoL D3 Body composition	41.67 (35.42–54.17)	72.92 (58.33–83.33)	< 0.001[b]
SarQoL D4 Functionality	56.07 ± 16.25	78.72 ± 12.80	< 0.001[a]
SarQoL D5 Activities of daily living	43.33 (35.42–54.17)	75.00 (65.00–80.00)	< 0.001[b]
SarQoL D6 Leisure activities	33.25 (24.94–49.88)	41.57 (33.25–49.88)	0.081[b]
SarQoL D7 Fears	87.50 (75.00–87.50)	87.50 (78.13–100)	0.084[b]
Overall score	49.93 ± 12.23	73.40 ± 11.29	< 0.001[a]

Values are presented as mean±standard deviation or median (25th percentile–75th percentile).
[a]Student t-test for independent samples.
[b]Mann–Whitney U-test.

of single domains showed Cronbach's alpha values ranging from 0.861 to 0.912, indicating that no domain had a disproportionate influence on the homogeneity of the questionnaire (Table 5).

Correlations between overall and individual domain scores

The correlations between each domain and the total score of the SarQoL questionnaire were also assessed using Spearman coefficients. All domains showed a strong significant positive correlation with the overall score of the SarQoL, except for domain 6 (Table 5).

Floor and Ceiling Effects

No participants (n = 49) presented with the lowest score to the questionnaire (0 points) or the maximal score (100 points) on the Overall QoL score. A ceiling effect was present for domain 7, where 14 people (28.6%) scored 100 points.

Construct Validity

Assessment of the convergent validity in the complete sample showed three strong and significant and one moderate and significant correlation, confirming the convergent validity of the Ukrainian SarQoL questionnaire (Table 6). Assessment of the divergent validity showed two strong and one moderate correlation (Table 6).

Analysis of the 28 participants categorized as probably sarcopenic showed good convergent validity, with four strong correlations but inadequate divergent construct validity.

Test-Retest Reliability

The test-retest reliability indicated near-perfect results (Table 7), with an ICCs of 0.997 (0.994–0.998) for the overall quality of life score of the SarQoL questionnaire in the complete sample and 0.998 (0.995–0.999) in the probably-sarcopenic group. The lowest ICC was observed in the analysis of the probably-sarcopenic sample, in which domain 6 showed an ICC of 0.912 (0.821–0.958), still considered to be an excellent degree of test-retest reliability.

The rest-retest reliabilities of the SF36 PCS and MCS scores were of the same order as that of the SarQoL (ICC > 0.9) and slightly lower in the EQ-VAS (ICC = 0.829 for the complete sample and 0.876 in the probably-sarcopenic sample). However, the test-retest reliability of the EQ-VAS in this sample was still considered acceptable, as it was above the cutoff of 0.7.

DISCUSSION

The results of our study showed that the Ukrainian version of the original SarQoL is a valid and discriminant questionnaire that is useful to determine the quality of life of patients with sarcopenia. The SarQoL is the first quality of life questionnaire specific to sarcopenia available in the Ukrainian language. The population of Ukraine is 43 million, of whom 6.9 million (15.32%) are aged over 65 years;[24] thus, the SarQoL-UA questionnaire can be a reliable, and cost-effective tool for assessing QoL among older Ukrainian patients possibly affected by sarcopenia.

Because of the cost and complexity of measuring muscle mass using a DEXA instrument, we used the Ishii screening test[16] to screen patients for sarcopenia, which is much easier, faster, and cheaper and does require a specific apparatus. The Ishii test has excellent sensitivity and specificity compared with to other diagnostic definitions of sarcopenia such as the two-step algorithm of the EWGSOP, the SARC-F questionnaire, the screening grid, and the anthropometric prediction equation.[15] We observed that people with low grip strength or gait speed generally showed lower quality of life scores on the SarQoL questionnaire (except for domains 6 and 7), which might be because these domains have low numbers of items (and thus less precision) in combination with a relatively

Table 5. Correlations between overall and domain scores and Cronbach's alpha

	Correlations between overall and domain scores (n = 48)		Cronbach's alpha if domain deleted (n = 49)	Overall Cronbach's alpha
	r	p-value		
SarQoL D1 Physical and mental health	0.848	< 0.001	0.872	0.898
SarQoL D2 Locomotion	0.911	< 0.001	0.874	
SarQoL D3 Body composition	0.779	< 0.001	0.874	
SarQoL D4 Functionality	0.915	< 0.001	0.861	
SarQoL D5 Activities of daily living	0.880	< 0.001	0.875	
SarQoL D6 Leisure activities	0.389	0.006	0.912	
SarQoL D7 Fears	0.587	< 0.001	0.901	

All values are Spearman correlation coefficients.

Table 6. Convergent and divergent construct validity, and correlation with overall SarQoL score

	Complete sample (n = 49)		Probably sarcopenic sample (n = 28)	
	r	p-value	r	p-value
Convergent validity				
EQ-5D Mobility	-0.794	< 0.001	-0.793	< 0.001
EQ-5D Usual activities	-0.677	< 0.001	-0.605	0.001
SF-36 PCS	0.833	< 0.001	0.869	< 0.001
EQ-VAS	0.466	0.001	0.599	0.001
Divergent validity				
SF-36 MCS	0.295	0.039	0.177	0.367
EQ-5D Self-care	-0.632	< 0.001	-0.700	< 0.001
EQ-5D Pain/discomfort	-0.650	< 0.001	-0.684	< 0.001
EQ-5D Anxiety/depression	-0.454	0.001	-0.423	0.025

All correlation coefficients obtained using Spearman method.
EQ-5D, EuroQoL 5-dimension; PCS, physical component summary; MCS, mental component summary; VAS, visual analog scale.

Table 7. Test-retest reliability in the complete sample

	Complete sample (n = 50)		Probably sarcopenic sample (n = 28)	
	ICC	95% CI	ICC	95% CI
SarQoL D1 Physical and mental health	0.992	0.985–0.995	0.991	0.980–0.996
SarQoL D2 Locomotion	0.995	0.990–0.997	0.994	0.988–0.997
SarQoL D3 Body composition	0.990	0.982–0.994	0.996	0.991–0.998
SarQoL D4 Functionality	0.986	0.976–0.992	0.994	0.988–0.997
SarQoL D5 Activities of daily living	0.995	0.991–0.997	0.995	0.990–0.998
SarQoL D6 Leisure activities	0.950	0.913–0.971	0.912	0.821–0.958
SarQoL D7 Fears	0.933	0.884–0.961	0.897	0.791–0.951
SarQol Overall score	0.997	0.994–0.998	0.998	0.995–0.999
SF-36 PCS	0.966	0.940–0.980	0.970	0.937–0.986
SF-36 MCS	0.905	0.838–0.945	0.940	0.876–0.972
EQ-VAS	0.829	0.714–0.948	0.876	0.749–0.941

ICC, intra-class correlation coefficient; CI, confidence interval; PCS, physical component summary; MCS, mental component summary; VAS, visual analog scale.

low number of study population.

Similar publications of validations of the SarQoL are available for the English, French, Dutch, Romanian, Polish, Lithuanian, Greek, and other language versions,[7-10,13,25] with similar results in terms of the reliability and validity of the SarQoL questionnaire.

The Cronbach's alpha of the Ukrainian version of the SarQoL was 0.898. The recommended values are 0.7–0.9, with an upper limit of 0.95.[17,26] The Cronbach's alpha value in our study is similar to those reported for the French, English, and Dutch versions (0.87, 0.88, and 0.883, respectively).[5,7,8] The alpha value in our study was lower than those in the Greek, Lithuanian, Romanian, and Polish validation studies (0.960, 0.950, 0.946, and 0.920, respectively) suggesting that some questions in the SarQoL may be redundant.[9,10,13,25] However, although the internal consistency of the Ukrainian was excellent, this does not mean that cross-cultural effects are, therefore, excluded. Although we paid particular attention to cross-cultural equivalence, Ukrainian participants may have responded differently to certain questions. We hope that the data from this study and future data collected with the SarQoL-UA can be used in combination with data from other countries to analyze the questionnaire with Item Response Theory to detect any differential item functioning effects.

Test-retest reliability was excellent in our study and the same as reported in French, English, Dutch, Polish, Greek and Lithuanian studies.[6-8,10,13,25] The validation of the Romanian version did not perform test-retest reliability because of the limited number of sarcopenic subjects (n = 13). Overall, the results have indicated that the SarQoL questionnaire is a reliable instrument.[25]

The construct validity of the SarQoL-UA was examined with eight hypotheses on the correlation between the domains of the SF-36 and EQ-5D questionnaires that were theorized to measure a similar (convergent) or dissimilar (divergent) construct from that of the SarQoL-UA. The results showed that the questionnaire possessed good convergent validity; however, the results of the divergent validity were not as expected. It may be that the constructs represented in the SF-36 MCS and the self-care and pain/discomfort items of the EQ-5D are more closely aligned with the overall quality of life, the construct measured by the SarQoL-UA.

The major limitation of our study was related to the absence of a muscle mass assessment because we were not able to determine appendicular muscle mass using DEXA. In our study group, sarcopenia status was estimated using the Ishii equation (described above). However, anthropometric measurements are prone to errors and may produce pitfalls; thus, they are not recommended for routine use according to the EWGSOP.[3] Nevertheless, the equation provided by Ishii et al. for the estimation of sarcopenia was previously validated and showed a high level of corresponding sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios (84.9%, 88.2%, 54.4% and 97.2%, and 7.19 and 0.17 for men and 75.5%, 92.0%, 72.8% and 93.0%, and 9.44 and 0.27 for women, respectively).[16] A second possible limitation was the low number of participants. Although there are no fixed requirements for minimum sample size in validation studies, a commonly used benchmark is a sample of 100 participants, of whom 50 should have the condition in question.[17] The present study included a total of 49 participants, 28 of whom were probably sarcopenic based on the Ishii test; however, because of the relative precision of the obtained values (i.e., small standard deviations or 95% confidence intervals), we obtained statistically significant results in most if not all of our analyses. While this study falls short of the arbitrary sample size of 100 participants, the results should not be discounted given the significant p-values obtained throughout.

In summary, this first Ukrainian version of the SarQoL questionnaire is equivalent to the available original version. Thus, this tool may be used for clinical and research purposes. This questionnaire had higher sensitivity than that of other standard QoL questionnaires. The availability of the SarQoL questionnaire to the Ukrainian scientific community gives physicians speaking this language the chance to better follow and monitor sarcopenic patients in Ukraine. Thus, the Ukrainian version of SarQol may be potentially incorporated in the routine geriatric curriculum designated for the assessment of sarcopenic Ukrainian-speaking individuals.

ACKNOWLEDGEMENTS

We thank Pr. JY Reginster, Pr. O Bruyère, and Pr. C Beaudart for their permission to adapt the questionnaire to a Ukrainian setting and for their help and advice during this process.

CONFLICT OF INTEREST

OB, JYR, and CB are shareholders of SarQoL sprl. The authors declare no conflict of interest. The study was conducted in the absence of any financial or other relationships that could be construed as a potential conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization, JYR; Methodology, MD, CB, OB; Validation, MD-Jr, KCh, MK, MM, and HM; Formal analysis, MB, AG; Investigation, ET, LM, MD; Resources: OB, JYR; Data curation: MD-Jr, KG; Writing-original draft, MD; Writing-review and editing, MD, CB; Supervision, OB, JYR, CB.

REFERENCES

1. Cooper C, Dere W, Evans W, Kanis JA, Rizzoli R, Sayer AA, et al. Frailty and sarcopenia: definitions and outcome parameters. Osteoporos Int 2012;23:1839-48.
2. Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, et al. Epidemiology of sarcopenia among the elderly in New Mexico. Am J Epidemiol 1998;147:755-63.
3. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16-31.
4. Janssen I. Influence of sarcopenia on the development of physical disability: the cardiovascular health study. J Am Geriatr Soc 2006;54:56-62.
5. Beaudart C, Biver E, Reginster JY, Rizzoli R, Rolland Y, Bautmans I, et al. Development of a self-administrated quality of life questionnaire for sarcopenia in elderly subjects: the SarQoL. Age Ageing 2015;44:960-6.
6. Beaudart C, Biver E, Reginster JY, Rizzoli R, Rolland Y, Bautmans I, et al. Validation of the SarQoL, a specific health-related quality of life questionnaire for Sarcopenia. J Cachexia Sarcopenia Muscle 2017;8:238-44.
7. Beaudart C, Edwards M, Moss C, Reginster JY, Moon R, Parsons C, et al. English translation and validation of the SarQoL, a quality of life questionnaire specific for sarcopenia. Age Ageing 2017;46:271-6.
8. Geerinck A, Scheppers A, Beaudart C, Bruyere O, Vandenbussche W, Bautmans R, et al. Translation and validation of the Dutch SarQoL, a quality of life questionnaire specific to sarcopenia. J Musculoskelet Neuronal Interact 2018;18:463-72.
9. Gasparik AI, Mihai G, Beaudart C, Bruyere O, Pop RM, Reginster JY, et al. Psychometric performance of the Romanian version of the SarQoL®, a health-related quality of life questionnaire for sarcopenia. Arch Osteoporos 2017;12:103.
10. Konstantynowicz J, Abramowicz P, Glinkowski W, Taranta E, Marcinowicz L, Dymitrowicz M, Reginster JY, Bruyere O, Beaudart C. Polish Validation of the SarQoL, a Quality of Life Questionnaire Specific to Sarcopenia. J Clin Med 2018;7:323.
11. Hodinka L, Vereckei E, Gasparik AI. Sarcopenia and quality of life: the validated Hungarian translation of the Sarcopenia Quality of Life (SarQoL) questionnaire. Orv Hetil 2018;159:1483-6.
12. Safonova YA, Lesnyak OM, Baranova IA, Suleimanova AK, Zotkin EG. Russian translation and validation of SarQoL – quality of life questionnaire for patients with sarcopenia. Rheumatol Sci Pract 2019;57:38-45.
13. Tsekoura M, Billis E, Gliatis J, Tsepis E, Matzaroglou C, Sakkas GK, et al. Cross cultural adaptation of the Greek sarcopenia quality of life (SarQoL) questionnaire. Disabil Rehabil 2020;42:1006-12.
14. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine (Phila Pa 1976) 2000;25:3186-91.
15. Locquet M, Beaudart C, Reginster JY, Petermans J, Bruyere O. Comparison of the performance of five screening methods for sarcopenia. Clin Epidemiol 2017;10:71-82.
16. Ishii S, Tanaka T, Shibasaki K, Ouchi Y, Kikutani T, Higashiguchi T, et al. Development of a simple screening test for sarcopenia in older adults. Geriatr Gerontol Int 2014;14 Suppl 1:93-101.
17. Terwee CB, Bot SD, de Boer MR, van der Windt DA, Knol DL, Dekker J, et al. Quality criteria were proposed for measurement properties of health status questionnaires. J Clin Epidemiol 2007;60:34-42.
18. Cronbach LJ. Coefficient alpha and the internal structure of tests. Psychometrika 1951;16:297-334.
19. Syddall HE, Martin HJ, Harwood RH, Cooper C, Aihie Sayer A. The SF-36: a simple, effective measure of mobility-disability for epidemiological studies. J Nutr Health Aging 2009;13:57-62.
20. Feshchenko YI, Mostovoy YM, Babiychuk YV. The procedure of adaptation of international quality of life questionnaire MOS SF-36 in Ukraine: the experience of administration in asthma patients. Ukrainian Pulm Mag 2002;3:9-11.
21. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med 2001;33:337-43.
22. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res 2011;20:1727-36.
23. EuroQol Group. EQ-5D-5L: Ukrainian version for Ukraine [Internet]. Rotterdam, The Netherlands: EuroQol Group; c2010 [cited 2020 May 23]. Available from: https://cumming.ucalgary.ca/sites/default/files/teams/122/research/ESCAPE-NA1/pdf_ukraine-ukrainian-eq-5d-5l-paper-self-complete-v1.0.pdf.
24. State Statistics Service of Ukraine. Population statistics of Ukraine [Internet]. Kyiv, Ukraine: State Statistics Service of Ukraine; c2019 [cited 2020 May 23]. Available from: http://database.ukrcensus.gov.ua/Mult/Database/Population/database-tree_uk.asp.
25. Alekna V, Kilaite J, Tamulaitiene M, Geerinck A, Mastaviciute A, Bruyere O, et al. Validation of the Lithuanian version of sarcopenia-specific quality of life questionnaire (SarQoL). Eur Geriatr Med 2019;10:761-7.
26. Tavakol M, Dennick R. Making sense of Cronbach's alpha. Int J Med Educ 2011;2:53-5.

AGMR
Annals of Geriatric Medicine and Research

Case Report
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):148-151
https://doi.org/10.4235/agmr.20.0012

Primary Cutaneous Cryptococcosis in an Older Immunocompetent Patient: A Case Report

Hoon Choi, Yong Il Kim, Chan Ho Na, Min Sung Kim, Bong Seok Shin

Department of Dermatology, Chosun University College of Medicine, Gwangju, Korea

Corresponding Author:
Bong Seok Shin, MD, PhD
Department of Dermatology, Chosun University College of Medicine, 309 Pilmun-daero, Dong-gu, Gwangju 61452, Korea
Email: derm75@chosun.ac.kr
ORCID:
https://orcid.org/0000-0001-9618-1763

Received: March 18, 2020
Revised: May 2, 2020
Accepted: May 4, 2020

Cryptococcus neoformans is an encapsulated yeast that can be found in pigeon droppings, hay, and dust. Primary cutaneous cryptococcosis (PCC) without systemic involvement is recognized as a distinct clinical condition and is rarely reported in immunocompetent patients. A 78-year-old woman with no history of other diseases except for hypertension presented with a painful diffuse erythematous plaque along with oozing on left forearm that had lasted for 7 weeks. She was treated with cefoperazone/sulbactam for 3 weeks under suspicion of bacterial cellulitis, although the lesions aggravated without any improvement. We performed bacterial and fungal cultures as well as incisional biopsy. The pathogen was identified as *Cryptococcus neoformans* following sequence analysis of the internal transcribed spacer gene. The patient was treated with fluconazole 400 mg/day for 3 months, and there was no evidence of recurrence after 3 months of follow-up.

Key Words: *Cryptococcus neoformans* infection, Fungal skin diseases

INTRODUCTION

Cryptococcus neoformans is an encapsulated yeast that can be found in decaying wood, hay, dust, and feces of birds, especially pigeons.[1] Cryptococcosis is considered an opportunistic infection in immunocompromised people, such as patients with malignancy, human immunodeficiency virus (HIV) infection, and those on long-term treatment with glucocorticoids and immunosuppressive agents after organ transplantation.[2] The infections mainly involve the lungs and central nervous system, with skin invasion considered a sign of dissemination.[3] Primary cutaneous cryptococcosis (PCC) without systemic involvement is recognized as a distinctive clinical disease and is rarely reported in immunocompetent patients.[4] Herein, we report a case of PCC misdiagnosed as cellulitis in an older immunocompetent patient.

CASE REPORT

A 78-year-old woman living in rural South Korea and with no history of other diseases except for hypertension presented with a painful erythematous plaque with oozing ulcers on the left forearm that had lasted for 7 weeks (Fig. 1). She did not complain of any systemic symptoms such as fever and myalgia. Before the lesions developed, she was injured by a sickle while cutting grass. She was treated for 3 weeks with cefoperazone/sulbactam under the suspicion of cellulitis; however, the lesions became wider and worsened. We performed bacterial and fungal cultures, as well as an incisional biopsy. The biopsy specimen was stained with the following: Gomori methenamine silver stain (GMS), periodic acid-Schiff stain (PAS), and acid-fast stain. Histopathologically, granulomatous inflammation with aggregated histiocytes and multinucleated giant cells were observed in the dermis, along with multiple intracytoplasmic yeasts (Fig. 2A, 2B). Furthermore, the yeasts were also identified on staining with GMS and PAS (Fig. 2C, 2D). No specific findings were observed on other investigations such as complete blood cell count; serum chemistry analysis; and tests for HIV infection, beta-D-glucan, and *C. neoformans* antigen in the blood. C-reactive protein level was elevated at 3.95 mg/dL. No abnormalities were observed on radiography of the chest, computed tomography (CT) of the thorax and brain, and cerebrospinal fluid (CSF)

examinations for evaluation of systemic cryptococcosis. The patient was treated with intravenous fluconazole at doses of 400 mg/day for 4 days and 200 mg/day for 10 days. Two weeks later, several cream-colored smooth colonies were observed in cultures, which were identified as *Cryptococcus neoformans* var. grubii by sequence analysis of the internal transcribed spacer gene. Thus, the anti-fungal agent was changed to oral fluconazole 200 mg/day. One week later, however, her symptoms became aggravated, and the dose was increased to 400 mg/day, that maintained for 3 months. After 3 months of follow-up, the lesions improved with post-inflammatory hyperpigmentation (Fig. 3) and without evidence of recurrence.

The informed consent was obtained for the use of patient information and photographs.

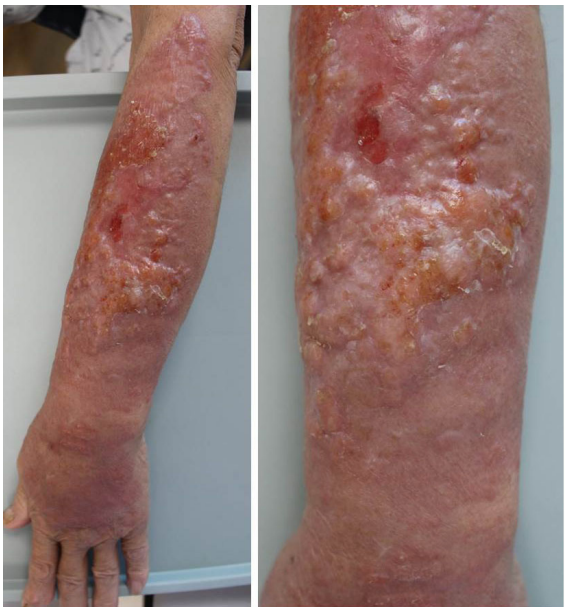

Fig. 1. Erythematous plaque with ulcers and oozing on left forearm.

DISCUSSION

PCC is a rare condition that is distinct from secondary cutaneous infections developing after infection of other organs.[5] The diagnostic criteria of PCC are confined to the skin and the condition can be diagnosed without clinical evidence of systemic involvement during follow-up for at least 4 weeks after confirmation of *C. neoformans* infection through skin biopsy or culture.[1] Neuville et al.[2] also reported diagnostic characteristics of PCC, which included rural residency, susceptible environment for trauma, localized lesions, no systemic symptoms, and no antigen detection. Our patient was also living in a rural area, had a history of trauma, and had no systemic symptoms.

The most common skin lesions of PCC are whitlow, cellulitis, and nodules or ulcerations on unclothed areas.[2] The lesions in our

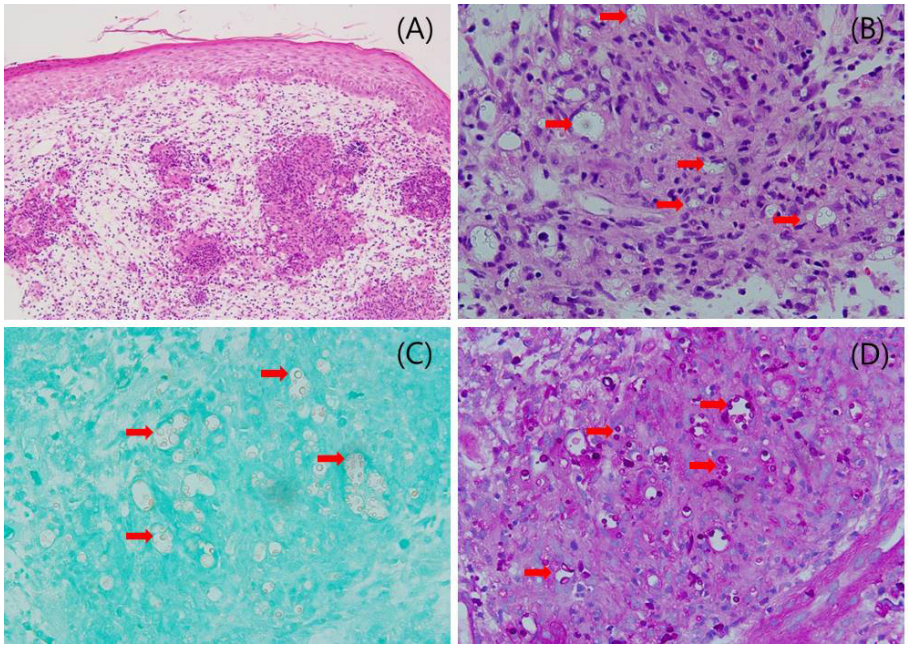

Fig. 2. Histopathologic findings. (A) There was granulomatous inflammation with aggregated histiocytes and multinucleated giant cells in the dermis (H&E, ×100). (B) Multiple intracytoplasmic yeasts (red arrows) were observed (H&E, ×400). (C, D) The yeasts (red arrows) were also identified with Gomori methenamine silver stain (GMS, ×400) and periodic acid-Schiff stain (PAS, ×400).

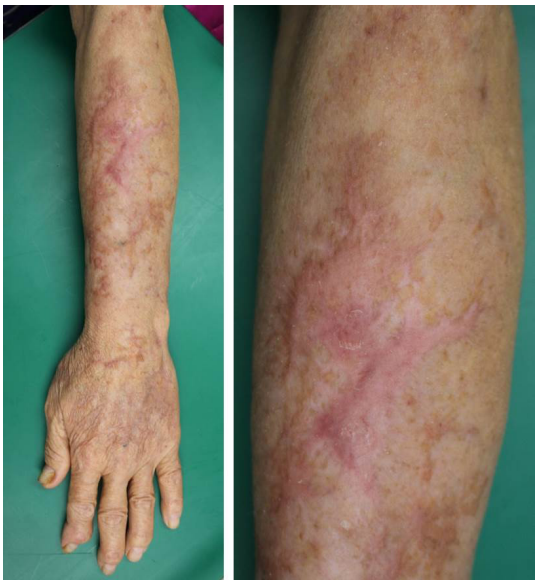

Fig. 3. After 3 months of follow-up. The lesions improved with post-inflammatory hyperpigmentation and scar.

patient developed as cellulitis and did not improve with empirical antibiotic treatments. Cutaneous lesions not successfully treated by antibiotics require additional tests to determine whether it is a fungal or mycobacterial infection. In addition, if cryptococcocus is identified by biopsy or culture, other investigations such as chest radiography, thorax CT, serologic tests for HIV, tests of CSF, and blood and urine cultures should be performed to rule out systemic infection, as skin lesions are markers of systemic cryptococcosis.[4]

PCC is usually treated with fluconazole (200–400 mg/day), itraconazole (200–400 mg/day), and amphotericin B (0.5–1 mg/kg/day), with the dosage and treatment duration depending on the patient's immune status and extent of involvement.[3] In the present case, we started treatment with 400 mg of fluconazole and then reduced the dosage to 200 mg. We assumed that 200 mg of oral fluconazole would be an adequate therapeutic dose because the bioavailability of oral fluconazole is over 90% and kidney functions are decreased in older adults.[6] However, the reduced dose was insufficient considering aggravated symptoms were alleviated by increasing the dosage of fluconazole. We believe that the insufficient dose of fluconazole was due to the necrotic lesions, poor blood supply, insufficient drug exposure at the infection site, and age-related reduction in patient immunity.[7,8]

Older adults are vulnerable to infections because of reduced T cell and cytokine activities.[8] In addition, as the skin microbiome changes with age, the role of the microbiome in inhibiting the growth of fungus may decrease.[9,10] The aged population (older than 65 years) in Korea is expected to increase, with corresponding increases in age-related diseases such as infections.[9] Therefore, accurate diagnosis and treatment are important and clinicians should be aware that even older adults without underlying diseases are vulnerable to various infectious pathogens.

In this case, because PCC appeared as bacterial cellulitis, it was difficult to clinically suspect this infection. If the lesions do not respond to antibiotics, it is important to perform additional tests to rule out other pathogens, such as fungi. In conclusion, we reported a case of PCC misdiagnosed as cellulitis in an older immunocompetent patient.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

This study was supported by grants from the Clinical Medicine Research Institute at Chosun University Hospital in 2019.

AUTHOR CONTRIBUTIONS

Conceptualization, HC, YIK, BSS; Funding acquisition, HC; Supervision, HC, CHN, MSK, BSS; Writing original draft, HC, YIK; Writing review & editing, HC, YIK.

REFERENCES

1. Noble RC, Fajardo LF. Primary cutaneous cryptococcosis: review and morphologic study. Am J Clin Pathol 1972;57:13-22.
2. Neuville S, Dromer F, Morin O, Dupont B, Ronin O, Lortholary O, et al. Primary cutaneous cryptococcosis: a distinct clinical entity. Clin Infect Dis 2003;36:337-47.
3. Saag MS, Graybill RJ, Larsen RA, Pappas PG, Perfect JR, Powderly WG, et al. Practice guidelines for the management of cryptococcal disease. Clin Infect Dis 2000;30:710-8.
4. Kosaraju K, Mukhopadhyay C, Vandana KE, Yagain K, Rao NR. Multiple cutaneous swellings in an immunocompetent host: cryptococcosis overlooked. Braz J Infect Dis 2011;15:394-6.
5. Lu YY, Wu CS, Hong CH. Primary cutaneous cryptococcosis in an immunocompetent man: a case report. Dermatol Sin 2013;31:90-3.
6. Pfizer Inc. Diflucan (fluconazole) [Internet]. New York, NY: Pfizer Inc.; c2019 [cited 2020 May 16]. Available from: https://www.pfizer.com/products/product-detail/diflucan.
7. Nucci M, Perfect JR. When primary antifungal therapy fails. Clin Infect Dis 2008;46:1426-33.
8. Choi H, Kim YI, Na CH, Kim MS, Shin BS. Mycobacterium ab-

scessus skin infection associated with shaving activity in a 75-year-old man. Ann Geriatr Med Res 2018;22:204-7.
9. Choi YJ, Lee DH. Microbiota: a key for healthy aging. Ann Geriatr Med Res 2016;20:168-76.
10. Mayer FL, Kronstad JW. The spectrum of interactions between Cryptococcus neoformans and bacteria. J Fungi (Basel) 2019;5:31.

AGMR
Annals of Geriatric Medicine and Research

Letter to the Editor
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2020;24(2):152-153
https://doi.org/10.4235/agmr.20.0033

How Can We Evaluate Disability without Bias?

Sunyoung Kim, Chang Won Won

Department of Family Medicine, Kyung Hee University Medical Center, Seoul, Korea

We read the article by Jang and Kawachi[1] regarding cultural and sexual differences in activities of daily living (ADLs) and instrumental activities of daily living (IADLs) with great interest. The authors concluded that cross-national comparisons of ADL and IADL disabilities need to consider item response bias stemming from culture- or education-based gender differences in household type and cognitive IADLs. While we agree that IADLs have gender- or culture-specific biases by nature, the results of this paper did not seem to demonstrate these biases in ADL items; thus, questions still remain for the conclusion.

We also agree with the author's suggestion that "unless corrected for, cross-national variations in disability rates may reflect item-response bias rather than real differences in disability levels". However, the last sentence "If possible, a culture-neutral ADL and IADL measurement that does not require DIF analyses should be developed" leaves room for consideration. Again, ADLs are not culture dependent, and IADL items should be based on each country's culture.[2] For example, the IADL items in the UK include whether one can brew tea and bring ashtrays, while those in New Zealand include gardening.[3,4] Therefore, national differences are inevitably a part of considering the cultural life of the residents and should be selected as an item that considers the characteristics of each country rather than simple translation-reverse translation in that country.

Meanwhile, Jung et al.[5] reported that men were more dependent on cooking and doing laundry, while women were more dependent on going out, using transportation, shopping, managing money, and using cell phones. However, this dependence was not significant in multiple regression analysis, and after adjusting for age, education, and comorbidities, IADLs showed a significantly lower dependence rate in women.[5] These results differed from those of previous studies[6-10] that reported many ADL functional disorders in older women. Indeed, Sheehan et al.[11] reported significant negative cohort slopes for men and women for not using a map and for men in preparing meals and shopping even after adjusting for age, ethnicity, education, and marital status. These results were consistent with those of a previous research that suggests that households are becoming more egalitarian and that by assuming increasing gender egalitarianism in household tasks, going forward, there should be less potential bias in IADL measures.[12]

As proposed by Jang et al.,[1] owing to gender bias, the assessment in some studies included only 5–6 items after excluding items not implemented in men.[13] As the initial IADL assessment by Lawton and Brody et al. comprised seven items (telephone, transportation, shopping, meal preparation, household chores, taking medicine, and money management), they did not investigate food preparation, housework, or laundry in men.[14]

Finally, one important thing to consider is that disability (capability) of IADL and dependency of IADL are somewhat different. By definition, disability is any condition that makes it more "difficult" for a person to perform certain activities, which encompasses impairments, activity limitations, and participation restrictions.[15] In this paper, if the respondents were partly or totally dependent for a given activity, they were categorized as having IADL disability. However, we would propose that IADL dependency is more correct in these instances. A man can be dependent on others for cooking even though he actually can perform this task.

For example, when performing the K-ADL and K-IADL questionnaire, rather than asking "whether it is possible (ability)", the question should be "whether it is actually being done (implementation)" to determine how much help (care) is needed rather than potential capabilities. In particular, men will often not report "performing household chores", "preparing meal", "doing laundry", and "managing money" items based on social conventions or because others perform these tasks for them. To cope with these problems, those who answered "don't do" to these items were instructed to further ask "if they could" or "they had never done so" in the original K-IADL.

Overall, we should carefully assess disability measures and utilize, clearly consider, and investigate how changes in the social expectations of engaging in the queried activities can affect outcomes. As society rapidly changes its individuals' roles, expectations, environments, and other characteristics, developing new measures without bias will become increasingly important to understand the health of aging populations.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The authors claim no conflicts of interest.

REFERENCES

1. Jang SN, Kawachi I. Why do older Korean adults respond differently to activities of daily living and instrumental activities of daily living? A differential item functioning analysis. Ann Geriatr Med Res 2019;23:197-203.
2. Brena SF, Sanders SH, Motoyama H. American and Japanese chronic low back pain patients: cross-cultural similarities and differences. Clin J Pain 1990;6:118-24.
3. Fillenbaum GG. Screening the elderly: a brief instrumental activities of daily living measure. J Am Geriatr Soc 1985;33:698-706.
4. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. JAMA 1963;185:914-9.
5. Jung JY, Kim JS, Choi HJ, Lee KY, Park TJ. Factors associated with ADL and IADL from the third Korea National Health and Nutrition Examination Survey (KNHANES III), 2005. Korean J Fam Med 2009;30:598-609.
6. Ng TP, Niti M, Chiam PC, Kua EH. Prevalence and correlates of functional disability in multiethnic elderly Singaporeans. J Am Geriatr Soc 2006;54:21.-9.
7. Dorantes-Mendoza G, Avila-Funes JA, Mejia-Arango S, Gutierrez-Robledo LM. Factors associated with functional dependence in older adults: a secondary analysis of the National Study on Health and Aging, Mexico, 2001. Rev Panam Salud Publica 2007;22:1-11.
8. Lee KJ, Park HS. A study on the perceived health status, depression, and activities of daily living for the elderly in urban areas. Korean J Women Health Nurs 2006;12:221-30.
9. Murtagh KN, Hubert HB. Gender differences in physical disability among an elderly cohort. Am J Public Health 2004;94:1406-11.
10. Leveille SG, Resnick HE, Balfour J. Gender differences in disability: evidence and underlying reasons. Aging (Milano) 2000;12:106-12.
11. Sheehan C, Domingue BW, Crimmins E. Cohort trends in the gender distribution of household tasks in the United States and the implications for understanding disability. J Aging Health 2019;31:1748-69.
12. Artis JE, Pavalko EK. Explaining the decline in women's household labor: Individual change and cohort differences. J Marriage Fam 2003;65:746-61.
13. Jekel K, Damian M, Wattmo C, Hausner L, Bullock R, Connelly PJ, et al. Mild cognitive impairment and deficits in instrumental activities of daily living: a systematic review. Alzheimers Res Ther 2015;7:17.
14. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179-86.
15. World Health Organization. Disability [Internet]. Geneva, Switzerland: World Health Organization; c2020 [cited 2020 Jun 10]. Available from: https://www.who.int/health-topics/disability#tab=tab_1.

Corresponding Author: Chang Won Won, MD, PhD
Department of Family Medicine, Kyung Hee University Medical Center, 23 Kyungheedae-ro, Dongdaemun-gu, Seoul 02447, Korea
E-mail: chunwon@khmc.or.kr
ORCID: https://orcid.org/0000-0002-6429-4461

Received: May 21, 2020; Accepted: June 2, 2020

AGMR
Annals of Geriatric Medicine and Research

The Korean Geriatrics Society News

Courses and Conferences

The academic events in 2020 of the Korean Geriatrics Society are as follows.
We would like to invite members of the Korean Geriatric Society and anyone who are interested.

[**The 66th Annual Meeting of the Korean Geriatrics Society**]
August 15-16, 2020.
KimDaeJung Convention Center
30, Sangmunuri-ro, Seo-gu, Gwangju, Republic of Korea.
For more information please contact kgskorea1968@gmail.com

[**The 40th Review Training Course**]
August 23, 2020
Seoul National University Hospital Innovation Center Seo-Hwan Seo Research Hall.
71, Daehak-ro, Jongno-gu, Seoul, Republic of Korea.
For more information please contact kgskorea1968@gmail.com

[**The 20th Geriatric Medicine Certification Exam**]
August 30, 2020
SC Convention 12F Anais Hall.
KOFST Managing the Science and Technology Center, 22 Teheran-ro 7-gil, Gangnam-gu, Seoul, Republic of Korea.
For more information please contact kgskorea1968@gmail.com

[**The 67th Annual Meeting of the Korean Geriatrics Society**]
November 14-15, 2020
KOFST Managing the Science and Technology Center, 22 Teheran-ro 7-gil, Gangnam-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.

AGMR
Annals of Geriatric Medicine and Research

AGMR Information

The Korean Geriatrics Society [Geriatric Disease] 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
   → Confimation 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/subscribtion fee" to speficy 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.

AGMR
Annals of Geriatric Medicine and Research

Instructions to authors

Enactment December 27, 2013
Revision January 31, 2020

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/what-we-do/medical-ethics/declaration-of-helsinki/). 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 Edi-

tor 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-ofinterest/).

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, pla-giarism, fraudulent or fabricated data, changes in authorship, un-disclosed 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://publicationeth-ics.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 web-

site. 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, editorial, and letters in geriatric medicine. 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

Type of article	Abstract (word)	Text (word)[a]	Reference	Table & figure
Original article	Structured[b], 250	3,500	30	7
Review	150	6,000	100	7
Case report	150	1,500	20	7
Editorial	No	1,200	15	7
Letter to the editor	No	1,200	15	1

AGMR, Annals of Geriatric Medicine and Research; NL, no limited.
[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, place of publication, publisher, year of copyright, and Internet address. Other types of references not described below should follow ICMJE Recommendations (https://www.nlm.nih.gov/bsd/uniform_requirements.html). Authors are responsible for the accuracy and completeness of their references and for ensuring that their text citations are correct. Papers still in press may be listed among the references using the journal name and a tentative year of publication. Unpublished data and personal communications may be listed only with the author's written permission.

Reference Style

- Journal article:

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

- Book:

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

- Book chapter:

4. Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension pathophysiology, diagnosis, and management. 2nd ed. New York, NY: Raven

Press; 1995. p. 465-78.

- Website:

5. AMA: helping doctors help patients [Internet]. Chicago, IL: American Medical Association; c2019 [cited 2019 Dec 22]. Available from: http://www.ama-assn.org.

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 GIFF 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.

AGMR
Annals of Geriatric Medicine and Research

Author's checklist

Date : _____

No. of Manuscript : AGMR- _____

Title of Manuscript : _____

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.

Corresponding Author _____ _____
Print Name Signiture

AGMR
Annals of Geriatric Medicine and Research

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/Job title/Company: _____

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 derivate 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

Jan 2020–Dec 2021

President
Hak Chul Jang, *Seoul National University*

Chairperson
Chang Won Won, *Kyung Hee University*

Honorary Committee
Haeng Il Koh, *Inje University*
In Soon Kwon, *Inje University*
Jong Chun Park, *Chonnam National University*
Hyun Wook Baik, *Bundang Sacrificial Hospital*
Seok Whan Shin, *Inha University*
Jun Hyun Yoo, *Sungkyunkwan University*
Hyung Joon Yoo, *Hallym University*
Jong Lull Yoon, *Hallym University*
Young-Soo Lee, *University of Ulsan*
Jung Ae Rhee, *Chonnam National University*
Hong Soon Lee, *Inje University*
Young Soo Jin, *Konkook University*
Hyun Rim Choi, *Kyung Hee University*
Il Woo Han, *The 1st Daejeon Municipal Geriatric Hospital*
Cheol Ho Kim, *Seoul National University*

Vice-President
Yong Deuk Jeon, *National Medical Center*

Secretary General
Seung-Jae Hong, *Kyung Hee University*

Vice-Secretary General
Sang Youl Rhee, *Kyung Hee University*

Treasurer
Doo Soo Jeon, *Catholic University*

Director, Scientific Committee
Eun Ju Lee, *University of Ulsan*

Director, Board Exam Committee
Dae Yul Kim, *University of Ulsan*

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

Director, Public Relations and Informational Committee
Hyuk Ga, *Incheon Eun-Hye Hospital*

Director, Research Committee
Ki Young Son, *University of Ulsan*

Director, Ethics Committee
Sam Gyu Lee, *Chonnam National University*

Director, International Cooperation Committee
Nam-Jong Paik, *Seoul National University*

Director, Planning Committee
Il-Young Jang, *University of Ulsan*
Heewon Jung, *Seoul National University*

Director, Medical Policy Planning Committee
Be Long Cho, *Seoul National University*
Kwang-Il Kim, *Seoul National University*

Director, Training Committee
Sol ji Yoon, *Kangwon University*

Director, Education Committee
Chang-Oh Kim, *Yonsei University*

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

Director, External Cooperation Committee
Dong-Woo Lee, *Inje University*

Director, Medical Insurance Policy
Jae Kyung Choi, *Kyung Hee University*

Director, Educational (Specialist Policy Planning) Committee
Young jung Cho, *National Medical Center*

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, Future Development TFT
Dong Ho Lee, *Seoul National University*

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

Director, CP and Guidelines Development Committee
Soo Lim, *Seoul National University*

Auditor
Seok Yeon Kim , *Seoul Metropolitan Dongbu Hospital*
Min Ho Chun , *University of Ulsan*

Special Appointment Director
SangYun Kim, *Seoul National University*
Hong Woo Nam, *National Medical Center*
Kang Seo Park, *Eulji University*
Young-Kyu Park, *DMC Bundang Jesaeng Hospital*
Sang Ah Lee, *Jeju University*
Yun Hwan Lee, *Aju University*
Yoon-Ho Choi, *Sungkyunkwan University*
Jong-Soon Choi, *Kosin University*
Yong-Chan Ha, *Chung Ang University*
Sung Hee Hwang, *Hallym University*
Hwan Sik Hwang, *Hanyang University*

[보건의료전문가용]

초기부터 진행된 당뇨병까지

T2DM Solution Partner

The Optimized
Zemiglo®
(Gemigliptin)

Once daily
Zemimet® SR
(Gemigliptin/Metformin)

제미글로®정 (제미글립틴) 50 mg

[효능·효과] 인슐린 비의존성(제2형) 당뇨병환자의 혈당조절을 향상시키기 위해 식사요법 및 운동요법의 보조제로 투여. 1. 단독요법으로 투여. 2. 다음의 경우 병용요법으로 투여. – 메트포르민 단독요법으로 충분한 혈당조절을 할 수 없는 경우. – 이전 당뇨병 약물치료를 받은 경험이 없으며 단독요법으로 충분한 혈당조절이 어려운 경우 메트포르민과 병용투여. – 메트포르민과 설포닐우레아 병용요법으로 충분한 혈당조절을 할 수 없는 경우. - 인슐린 요법(인슐린 단독 또는 메트포르민 병용)으로 충분한 혈당조절을 할 수 없는 경우. **[용법·용량]** 1일 1회 1정 투여하며, 1일 최대용량은 50 mg로 식사와 관계없이 투여 가능. 신장애 환자 및 경증 및 중등도의 간장애 환자에서 용법·용량 조절이 필요하지 않음. **[사용상 주의사항]** 금기-본제 또는 다른 dipeptidyl-peptidase 4(DPP4) 저해제에 중대한 과민반응을 보인 환자, 제1형 당뇨병 및 당뇨병성 케톤산증 환자. **[이상반응]** 임상시험(단독요법)에서 3% 이상의 환자에서 보고된 이상반응은 관절통, 코인두염, 세균뇨이었음. 시판 후 추가로 확인된 이상사례로 구토, 두드러기, 말초부종, 발진, 스티븐스-존슨증후군, 얼굴부종, 입술부기, 저혈당 반응, 췌장염, 폐렴이 보고되었으나, 불특정 다수의 인구집단에서 자발적으로 보고된 것이기 때문에 신뢰성 있는 발생빈도의 예측 및 약물과의 인과관계 확립은 일반적으로 가능하지 않음. **[최신 제품정보 개정일 2019.09.04]**

제미메트®서방정 (제미글립틴/메트포르민) 25/500 mg, 25/1000 mg, 50/500 mg, 50/1000 mg

[효능·효과] 제미글립틴과 메트포르민의 병용투여가 적절한 성인 제2형 당뇨병 환자의 혈당조절을 개선시키기 위해 식사요법 및 운동요법의 보조제로 투여. 제미메트서방정 25/500 mg, 25/1000 mg, 50/1000 mg: 1. 이전 당뇨병 약물치료를 받은 경험이 없으며 단독요법으로 충분한 혈당조절이 어려운 환자, 2. 메트포르민 단독요법으로 충분한 혈당조절을 할 수 없는 환자, 3. 메트포르민과 설포닐우레아 병용요법으로 충분한 혈당조절을 할 수 없는 경우 설포닐우레아와 이 약을 병용투여, 4. 인슐린과 메트포르민 병용요법으로 충분한 혈당조절을 할 수 없는 경우 이 약을 병용투여, 5. 제미글립틴과 메트포르민 병용요법을 대체하는 경우 투여. 제미메트서방정 50/500 mg: 1. 이전 당뇨병 약물치료를 받은 경험이 없으며 단독요법으로 충분한 혈당조절이 어려운 환자, 2. 제미글립틴과 메트포르민 병용요법을 대체하는 경우 투여. **[용법·용량]** 이 약은 일반적으로 저녁식사와 함께 투여하며, 메트포르민과 관련된 위장관계 부작용을 줄이기 위해 단계적으로 용량 증량. 50/500 mg 또는 50/1000 mg은 1일 1회 1정 복용, 25/500 mg 또는 25/1000 mg은 1일 1회, 1회 2정을 동시에 복용. 1일 최대 권장용량은 제미글립틴 50 mg 및 서방성 메트포르민 2000 mg이며, 이 약은 통째로 삼켜야 하며 절대로 부수거나 자르거나 또는 씹어서는 안 됨. **[사용상 주의사항]** 이 약 성분 또는 다른 dipeptidyl-peptidase 4(DPP4) 저해제에 중대한 과민반응을 보인 환자, 신기능부전, 울혈성 심부전, IV 조영제 검사자, 제1형 당뇨병, 유산산증 및 당뇨병성 케톤산증, 당뇨병성 전혼수, 이 약의 성분 또는 비구아니드계 약물에 과민반응의 병력이 있는 환자, 중증 감염증, 수술 48시간 전, 영양불량상태, 간기능 장애, 임부/수유부 등에서는 금기. **[이상반응]** 임상시험(제미글립틴과 메트포르민과 초기병용)에서 3% 이상의 환자에서 보고된 이상반응은 소화불량, 코인두염, 어지럼증, 설사, 이상지질혈증, 두통, 변비, 요통임. 시판 후 추가로 확인된 이상사례로 가려움증, 두드러기, 발진이 보고되었으나, 불특정 다수의 인구집단에서 자발적으로 보고된 것이기 때문에 신뢰성 있는 발생빈도의 예측 및 약물과의 인과관계 확립은 일반적으로 가능하지 않음. **[최신 제품정보 개정일 2020.03.04]**

GEM-BR-A063-01-JUN20

[제조 및 판매원] ㈜LG화학 **[공동판매원]** ㈜대웅제약 **※자세한 정보는 최신의 제품설명서 전문을 참고하시기 바라며, 홈페이지 (www.lgchem.com)에서 확인하실 수 있습니다.**

LG화학 | [07795] 서울특별시 강서구 마곡중앙10로 70, LG사이언스파크 2차부지 E14동 • 고객 상담 전화 080-023-5757 / www.lgchem.com

대웅제약