

# AGMIR

Annals of Geriatric Medicine and Research

December 2021 Vol. 25, No. 4

## Special Contribution

Challenges and Opportunities for Academic Journals to Serve the Older Population in Western Pacific Region

## Original Articles

Development of Guidelines on the Primary Prevention of Frailty in Community-Dwelling Older Adults

A Descriptive Study of Emergency Department Visits Within 30 Days of Discharge

Association of Preoperative Risk Factors and Mortality in Older Patients following Emergency Abdominal Surgery: A Retrospective Cohort Study

Utilization of Digoxin among Hospitalized Older Patients with Heart Failure and Atrial Fibrillation in Thailand: Prevalence, Associated Factors, and Clinical Outcomes

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Association between Health Literacy, Self-care Behavior, and Blood Sugar Level among Older Patients with Type 2 Diabetes in Rural Thai Communities

## Letter to the Editor

Health Literacy among Older Adults during COVID-19 Pandemic



# AGMIR

Annals of Geriatric Medicine and Research



The Korean Geriatrics Society



The Korean Society for Gerontology

## 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

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# Challenges and Opportunities for Academic Journals to Serve the Older Population in Western Pacific Region

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*Annals of Geriatric Medicine and Research* held its inaugural international editorial board virtual meeting on September 16, 2021, to brainstorm ideas for sustainable growth. This special article summarizes the key concepts obtained from the webinar proceedings, with further development of ideas from ensuing discussions occurring after the meeting. From the initial discussion points provided by eight editorial board members, including six presenters, email discussions further enriched these ideas to construct the current special article. The key points discussed were: impactful research and impact factors, international and Asian perspectives, and challenges to sustainable growth. The editors noted the existing gap between the impact factor and research impact as a challenge for the growth paths of regional journals. However, they agreed that persevering with impactful research would ultimately translate into parallel and gradual gains in impact, which is, therefore, consistent with the organic growth of the journal. Acknowledging challenges in navigating between unique Asian perspectives and international outlooks, the editors encouraged academic journals to serve as bridges linking international evidence with the richness of local perspectives. For sustainable growth, the editors suggested that journals may be forged into the academic ecosystems of the region, diversify value streams, and establish themselves as reputable brands in disciplines. By combining these discussions, we proposed the "IMPACT" strategy for journals on the growth path in the region, which stands for Immersive user experience encompassing authors, reviewers, and readers; Pasteur's quadrant use-inspired research; Asia-Pacific context; Collaborative; and Translation to practice and policy.

**Key Words:** Publishing, Journals, Regional health planning, Aging, Cultural diversity

## INTRODUCTION

As a journal focused on aging and age-related conditions, *Annals of Geriatric Medicine and Research* (AGMR) has aspired to address

disparities by representing the rapidly growing older populations of Asian and emerging countries since its inception.<sup>1)</sup> While the journal has experienced substantial growth in terms of volume and visibility,<sup>2)</sup> challenges remain for AGMR in its quest to become a

highly impactful arena for discussion. Therefore, to brainstorm ideas regarding design strategies for sustainable growth to adequately address the current challenges, AGMR held its inaugural international editorial board virtual meeting on September 16, 2021. The webinar included two lectures from the editors-in-chief of AGMR (JYL) and the *Journal of Frailty and Aging* (MC), four short talks from panelists, and fruitful discussion/brainstorming among editorial board members.

This special article summarizes the key concepts originating from the webinar proceedings, with further development of these ideas from ensuing discussions after the meeting. From the initial discussion points provided by eight editorial board members, including six presenters, email discussions further developed these ideas to construct the current special article. The key points discussed were: (1) impactful research and impact factors; (2) international and Asian perspectives; and (3) challenges to sustainable growth. Inputs from these eight participants were collected and drafted by HWJ and circulated for further enrichment. In particular, the authors aimed to encompass potential issues for academic journals on aging in general, not limiting the scope to AGMR itself. The participants felt that the accrued insights might be salient and potentially transferable to other journals in the Western Pacific region that may be experiencing similar challenges.

## CURRENT STATUS OF THE ANNALS OF GERIATRIC MEDICINE AND RESEARCH

AGMR has undergone a significant transformation in recent years. Changing its language from Korean to English in 2016 heralded a significant shift in the focus of AGMR to grow from a national journal of geriatrics to a more international one, with a broader spectrum of topics spanning geriatrics and gerontology. In addition, noting the challenge of addressing the tremendous research gaps in Asian countries experiencing the rapid aging of their populations, AGMR sought to become a high-profile journal to first serve and support this region with evidence-based material. After being indexed in SCOPUS (2019) and PubMed Central (2020), submissions to the journal have doubled annually. The number of contributions from outside Korea has also skyrocketed. As AGMR remains a non-profit, open-access platform operating on funding support from the Korean Geriatrics Society, the editorial board has been overwhelmed by the growing volume of submissions and the need to maintain a reasonable turnaround time for each submitted manuscript. In this process, editorial board members face new potential conflicts and challenges in balancing the diverse goals for journal growth.

## IMPACTFUL RESEARCH AND IMPACT FACTOR

Indeed, there has been an ongoing debate over whether the impact factor adequately represents the real impact of publications in journals.<sup>3)</sup> The impact factor was initially established as a citation-based metric, a simple tool for ranking scientific journals from the standpoint of bibliometric influence.<sup>4)</sup> On the other hand, the Research Excellence Framework defined “impact” as “an effect on, change or benefit to the economy, society, culture, public policy or services, health, the environment or quality of life, beyond academia.”<sup>5,6)</sup> However, many countries and institutions have increasingly used the impact factor as the de facto metric in evaluating the track record of researchers. This environment creates pressure on researchers to study mature and crowded topics and is a disincentive to risky and potentially groundbreaking work requiring substantial lead time before obtaining citations. At the same time, the pressure to publish (for being cited) likely affects the general quality of the research output by prioritizing quantity.<sup>3)</sup>

This discrepancy between impact factor and research impact is particularly problematic in the Western Pacific region, where the fast pace of population aging underlines the pressing need for well-designed, impactful research that targets older persons.<sup>7)</sup> Unfortunately, the growth of academic journals (in addition to aging) in this region lags the pace of aging. There is a tendency for hysteresis—defined as a system with a rate-independent memory effect;<sup>8)</sup> hence, the state of the system is dependent on its history—in the relationship between the visibility of academic journals (commonly represented by the impact factor) and the research impacts of their published papers. As researchers in many countries are rewarded by their quantifiable research output, impetus exists to submit better-quality papers to journals with higher impact factors.

Therefore, a chicken-and-egg cycle ensues for journals based in developing countries, with lower visibility (vis-à-vis the more prominent journals in aging), leading to fewer submissions.

Editors recognize and often have to grapple with the potential conflict between publishing potentially impactful research for the target population of the journal in the long run and soliciting manuscripts that are more helpful in attracting mid-term citations to increase the journal’s impact factor. For example, although a small-scale hypothesis-generating study might have a substantial clinical impact on a specific population, the volume of researchers in the same milieu<sup>9)</sup> that potentially cite the work may be less than the critical mass required to establish sufficient visibility for the study (especially in the context of the relentless flood of academic literature). Furthermore, the stringency of current clinical research standards in a publication that often preclude real-world studies, even

in advanced societies,<sup>10)</sup> may likewise prevent researchers in smaller organizations from establishing a viable research agenda based on clinical observations. In our experience, editors face a growing volume of manuscripts from developing countries that can be meaningful and novel when contextualized at the national level but may tend to be incomplete or marginal in terms of scientific rigor or generalizability (thus failing to find resonance in terms of perceived impact with high-quality bibliographic databases). Therefore, in the current stage of AGMR, the editors often find themselves choosing between Scylla and Charybdis in our roles as advocates of aging research in developing countries, fostering promising early-stage works (but with the tradeoff of less comprehensive scientific data) vis-à-vis more established but potentially less novel research.

Notwithstanding these challenges, there is agreement that, beyond its inherent significance, persevering with impactful research will ultimately translate into parallel and gradual gains in visibility, which is, therefore, consistent with the organic growth of the journal. Therefore, it is critical to resist the gentle nudge of hysteresis towards the false dichotomy of impactful research versus impact factor, especially when the journal's growth in visibility may lag behind the academic impact. Instead, we must steer the discourse towards an alignment between impactful research and impact factor. To this end, the editorial board comprising international scholars plays an important role in shaping research priorities, pushing the frontiers of knowledge, and cultivating impactful research that addresses specific gaps for populations around the region.

## INTERNATIONAL AND REGIONAL PERSPECTIVES

Editors have also experienced a dilemma for a journal under development; that is, whether to steer the journal towards adopting a more international outlook or to retain its unique Asian perspectives. To be more global, journals aspire to reach a larger community of the target audience and play a more prominent role in guiding the direction of scientific research in general.<sup>9)</sup> In contrast, this goal is less attainable for lower-profile regional journals. While more regional journals may attract more research specifically designed for a certain population, in some cases, they may, ironically, grapple with a lower volume of regional research submissions.

This issue is especially problematic for academic journals focused on the health and social issues of the older population. The feasibility and effectiveness of specific healthcare delivery models for the older population may be primarily affected by social structure, cultural perception, and economic resources, as previously noted in AGMR.<sup>1)</sup> These factors might be less relevant for studying individual diseases with clearly defined biomedical definitions

and therapeutics. For example, deprescribing medications in older adults with polypharmacy and frailty might be more critical in established medical systems with fee-for-service than in developing countries where seeking medical attention per se is barely accessible for most populations (and the number of excessive prescriptions is probably lower). “What matters” (i.e., one of the four cornerstones of the age-friendly health system framework)<sup>11)</sup> is also affected by the social characteristics of populations. While research diversity in aging is considered a pressing issue in the United States,<sup>12)</sup> knowledge gaps among different societies have been less addressed globally.

The cultural characteristics of Asian countries have long been considered significant when dealing with the care issues of older persons. For instance, providing nutritional support through enteral access has been considered a default in many Asian societies, even in patients with advanced dementia, even though tube feeding in these patients is clinically controversial.<sup>12,13)</sup> Similarly, a recent study suggested that socio-cultural factors pose barriers in initiating discussions about advance care planning in older persons with dementia.<sup>14)</sup> Specifically, in Chinese culture, discussing matters related to death has been considered taboo.<sup>15)</sup> In addition, it is not uncommon in Asian cultures for older people to leave end-of-life decisions to their family members.<sup>16)</sup> Again, from the caregiving perspective, the traditional concept of filial piety has primarily served as a backbone for providing long-term caregiving for older adults with functional needs within the community.<sup>17)</sup>

However, the salience of filial piety and familial caregiving in many Asian societies is increasingly questioned as shrinking family size and urbanization make familial care of older adults less feasible and portend the growing unmet needs of social support for the older population. The evolving social structure and lifestyle of Asian countries might ultimately attenuate the importance of traditional cultural beliefs regarding the duty to care for older adults. Academic journals in this region may serve as bridges by linking international evidence with the richness of local perspectives, providing leadership to define research frontiers, and translating the findings of research studies to address the specific needs of target populations.<sup>18)</sup> Altogether, journals would again serve to move beyond the limitations of a “false dichotomy” mindset by embracing a dualistic outlook of achieving both research impact and impact factor and harnessing the eclectic richness of international and regional perspectives.

## CHALLENGES TO SUSTAINABLE GROWTH

Peer reviewers have long been considered the guardians of research quality.<sup>19)</sup> Regional independent journals are usually operated by

the voluntary support of editors and reviewers. Securing high-quality review standards for the growing volume of submitted manuscripts while simultaneously minimizing the turnaround time of peer review is particularly challenging in this context. Many regional scientific societies and organizations do not have sufficient resources to attract internationally renowned scholars. Even local scientists with competitive track records are less incentivized to support lower-profile journals.<sup>9)</sup> As a significant proportion of manuscripts submitted to regional journals are of low quality (in terms of writing, editing, and scientific rigor), the increasing volume of submissions aggravates the editorial team's workload.

Moreover, the general volume of scientific literature has been growing, with many publishers choosing open access systems to maximize their volume, impact, and profit. Indeed, one of the most notable changes in the ecosystem of scientific publications over the last decade is the rise in open access publications.<sup>20)</sup> Open access journals with extensive networks, standardized editing platforms, and existing brand premiums inherited from their flagship journals have enjoyed tremendous growth in terms of publication volume. However, unlike these journals, non-profit-independent journals backed by national scientific societies are experiencing ever-growing challenges in maintaining sustainable positive trajectories, both in quantity and quality.

Although attracting support from established scholars might be less feasible, regional journals can strategically leverage the uneven field of the research ecosystem. For example, while senior scholars have been primarily considered candidates for the role of peer reviewers, studies have shown that younger researchers tend to provide peer reviews of better quality.<sup>21,22)</sup> Moreover, for junior researchers in their growing career path, regional journals with a strong relationship with local academic societies can serve as stepping stones for participation in core groups of researchers in the field and as editorial board members. In this ecosystem, regional journals can play a role as an arena for developing fresh ideas, innovative methodologies, and high-quality work by junior researchers and faculty members. To this extent, this ecosystem can be forged into a community of committed and motivated reviewers, regular contributors, and active readership. Thus, regional journals can serve as stepladders in research career development and as conduits for participation within the discipline.<sup>23)</sup>

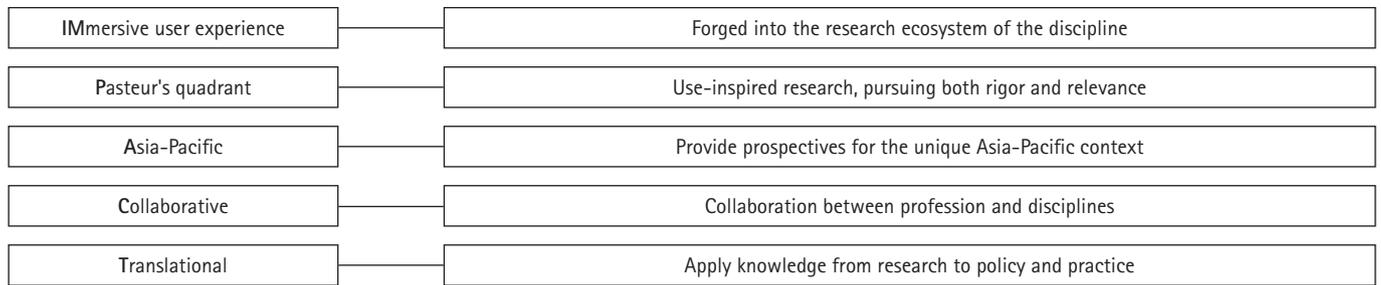
Currently, most regional journals are financially supported by governments and national academic societies. Inherently, the limited amount of such funding restricts the expansion of publication volumes if these journals do not request article processing charges (APC). At the same time, imposing an APC is difficult for these journals, presumably experiencing a scarcity of high-quality manuscripts. Indeed, securing funding sources is a challenge for these

journals, and a valley of death ensues before these journals get enough visibility to attract a sufficient number of authors to absorb the APC, similar to the experience of early-stage startup companies.<sup>24)</sup> On the other hand, journals may expand their available resources by establishing sustainable business models that balance academic, professional, and financial considerations. These efforts can be facilitated by advances in technology, journal administration, and the agile activities of supporting staff. One example might be granting discount vouchers for reviewers that can be used as APCs for future submissions. This strategy incentivizes reviewers, simultaneously alleviating resistance to APC among authors. In addition, journals may hold educational conferences on research methodologies, writing, and other issues on academic publications to diversify sustainable value streams.

Another consideration for attaining a sustainable growth trajectory is the development of reputable journals in research fields. Both brand and impact factor matter in academic publications. Many high-quality manuscripts are submitted to recently started franchise journals without an impact factor by researchers anticipating that gaining visibility for the journal (and, thus, for their article) is just a matter of time. To build robust reputations for journals, editors and reviewers should provide consistent experiences for contributors. A good reputation is, ultimately, dependent on the time-honored values of trust, dependability, timeliness, and respect.

## CALL TO ACTION: THE "IMPACT" STRATEGY

We discussed the challenges that regional journals on geriatrics and gerontology currently face in their growth trajectories in terms of research impact, regional characteristics, and sustainability. We agreed that dichotomies in these matters are not necessarily mutually exclusive and can be navigated through elaborations targeting the sweet spot of organic growth. We noted that these journals may serve as a critical platform for the academic ecosystem to provide immersive user experiences for members of academic disciplines in the region and attract meaningful and impactful research, thereby attaining visibility and completing a virtuous cycle of growth. Ironically, the disruption or cessation of research activities by the coronavirus disease 2019 (COVID-19) pandemic may represent a unique opportunity for regional journals to take advantage of well-conducted innovative research that will not reach the expected, high-level journals owing to incomplete data.<sup>25)</sup> By embracing a diverse array of possibilities, journals can steer towards pursuing research works that may translate into real-world practice in the region, from enriched perspectives driven by collaborations among professions and disciplines across regions. In navigating re-



**Fig. 1.** The proposed “IMPACT” strategy, a sustainable growth path for Western-Pacific regional journals on aging and age-related conditions.

search and real-world applications, journals may adopt the concept of Pasteur’s quadrant, pursuing both scientific excellence and usability in scientific research.<sup>26</sup> Putting these together, we call for an “IMPACT” strategy, an acronym for (1) IMmersive user experience encompassing authors, reviewers, and readers; (2) Pasteur’s quadrant use-inspired research; (3) Asia-Pacific; (4) Collaborative; and (5) Translational (Fig. 1). We hope that by adopting this strategy, journals in the region may position themselves as the nexus of the value chain of research, from hypothesis-generating to policymaking and practice.

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# Development of Guidelines on the Primary Prevention of Frailty in Community-Dwelling Older Adults

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**Background:** Despite the increasing number of older adults as the population ages, there is a lack of frailty prevention guidelines for community-dwelling older adults. The Korean Frailty and Aging Cohort Study conducted systematic review on contributors to frailty and developed guidelines on the primary prevention of frailty in community-dwelling older adults. **Methods:** This study updated a previous systematic review of contributors to frailty by adding the most recent articles. Based on this updated systematic review, experts in geriatrics and gerontology developed guidelines for preventing frailty using the Delphi method. **Results:** These guidelines categorized the recommendations into physical activity, resilience, oral health, management of non-communicable diseases, involvement in society, smoking cessation, and eating various kinds of food. **Conclusion:** Unlike previous frailty-related guidelines, this study developed evidence-based frailty prevention guidelines based on a systematic review. The guidelines are expected to contribute to the healthy aging of community-dwelling older adults by the primary prevention of frailty.

**Key Words:** Frailty, Primary prevention, Guideline, Aged, Independent living

## INTRODUCTION

The aging population is a global trend. The proportion of the world's population aged 65 years or older is projected to reach 15.9% of the total population by 2050.<sup>1)</sup> The results of several studies have shifted the perspective of aging from chronological to biological age, resulting in the concept of frailty.<sup>2)</sup>

Frailty is a vulnerable condition in which the intrinsic capacity

to respond to internal and external stressors is weakened, increasing the likelihood of adverse health outcomes such as disability, hospitalization, institutionalization, and death.<sup>3-6)</sup> Eventually, frailty is a state of declined biological homeostasis that resists entropy.<sup>2)</sup>

The prevalence of frailty is global. The reported community prevalence in high-income countries is 10%–12%<sup>7,8)</sup> and increases with age to 15.7% and 26.1% in those aged 80–84 and 85 years or

older, respectively.<sup>7)</sup> The prevalence of prefrailty is reported at 41.6%. Therefore more than half of the older population in high-income countries is related to frailty or prefrailty. The prevalence of frailty and prefrailty in middle-and low-income countries is 17.4% and 49.3%, respectively, higher than that in high-income countries.<sup>9)</sup> In Korea, the reported prevalence of frailty and prefrailty is 2.5%–12.4% and 27.7%–49.7%, respectively.<sup>10)</sup>

A recent meta-analysis reported an incidence of frailty and prefrailty in communities of 43.4 and 150.6 cases per 1,000 person-years, respectively. The change from robust to frailty was 12.0 cases per 1,000 person-years, whereas the change from prefrailty to frailty was 62.7 cases per 1,000 person-years.<sup>11)</sup>

The critical point in frailty is that it is a dynamic concept that frailty is preventable and can be reversed to robustness in some cases.<sup>12-14)</sup> Nevertheless, there remains a lack of frailty prevention guidelines for community-dwelling older adults. Moreover, despite the importance of self-care in frailty prevention, literature reviews of modifiable contributors to frailty are also lacking.

Therefore, this study conducted a systematic review on contributors to frailty and applied the Delphi method to develop frailty prevention guidelines for community-dwelling older adults. These evidence-based guidelines can contribute to the primary prevention of frailty by improving self-care among community-dwelling older adults.

## MATERIALS AND METHODS

### Purpose and Scope

The purpose of these guidelines is to prevent frailty by helping community-dwelling older adults avoid frailty risk factors and obtain/maintain protective factors. In this context, this study developed evidence-based guidelines with which older adults can comply in the real world (Table 1).

### Team

The guidelines were developed as part of the Korean Frailty and Aging Cohort Study (KFACS). The KFACS is a nationwide multi-center study that aimed to identify and analyze causes and effects of aging.<sup>15,16)</sup> The guideline development team comprised a multi-disciplinary group, including three geriatricians, three preventive medicine and public health experts, four nutritionists, three physical education experts, and one social welfare expert.

### Key Questions

The detailed contents of structured key questions for the article search are shown in Table 2. Since there has not been a clear summary of the contributors of frailty previously, the intervention/exposure items have been comprehensively set to cover as many contributors as possible. The outcomes were limited to physical frailty identified by validated tools based on the phenotype or cumulative deficit model. In addition, the study design was limited to cohort studies considering that randomized clinical trials that set outcomes as the occurrence of frailty are challenging to conduct and recommendations should be applicable to the community.

### Evidence Retrieval

The search strategy, including systematic reviews, was based on a decision tree of the systematic review in the *WHO Handbook for*

**Table 1.** Scope of developing the guideline

PIPOH	Scope
Population	Community-dwelling adults aged 60 years or older
Intervention	Avoidance of risk factors of frailty Acquisition/maintenance of factors protective against frailty
Professionals/patients	Community-dwelling adults aged 60 or older
Outcome	Physical frailty
Healthcare setting	Community

**Table 2.** PICOTSS framework for key questions

PICOTSS	Contents
Population	Community-dwelling adults aged 60 years or older
Intervention/exposure	Modifiable contributors (physical activity, nutrition, cognitive activity, social activity, and other lifestyles), management of non-communicable diseases
Comparison	A group not acquiring/maintaining modifiable protective factors A group not avoiding modifiable risk factors A group not managing non-communicable diseases
Outcome	Physical frailty
Time	A follow-up period of 1 year or more
Setting	Community
Study design	Cohort study

**Guideline Development.**<sup>17)</sup> First, a systematic review published in 2017 was identified as a result of searching for systematic reviews related to the key questions.<sup>18)</sup> The quality of this systematic review was evaluated by assessing the methodological quality of systematic reviews (AMSTAR 2)<sup>19)</sup> It was evaluated to be of high quality. Therefore, the development team used it for guideline development.

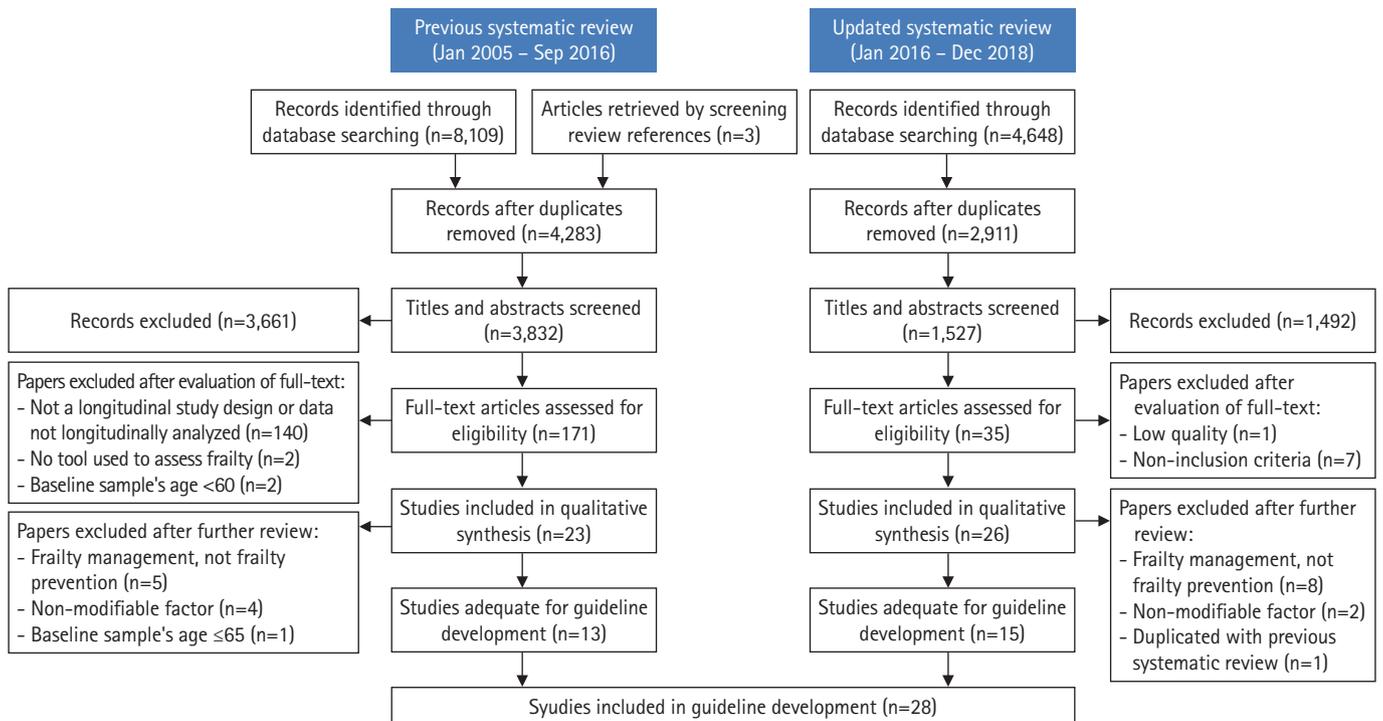
However, since this systematic review was conducted on articles published between January 2005 and September 2016, the development team updated the systematic review by adding more recent articles (January 2016–December 2018). To minimize missing articles, the overlapping period of 9 months was created.

For consistency, we used the same inclusion criteria as those used in a previous systematic review to search for updates. First, the included articles were as follows: (1) original articles, (2) articles related to contributors of frailty, (3) articles on community-dwelling older adults, and (4) articles whose outcome was frailty. Second, we included articles that used (1) a longitudinal study design, (2) a clear definition of frailty, and (3) specific tools to measure frailty and that included (4) subjects aged 60 years or older. The search formula was the same as that used in the previous systematic review. The search sources were the Embase on Ovid, Ovid MEDLINE, Cochrane Library, Web of Science, and CINAHL EBSCOhost databases.

Two public health experts (doctor 1, MPH 1) independently reviewed the titles and abstracts of the identified articles to select those that met the inclusion criteria. In the case of disagreement, the inclusion of an article was decided through discussion with a third party. Next, two experts independently conducted a full-text review of the selected articles, with disagreements resolved through discussion with a third party.

The quality of each article was also evaluated using the Quality of Reporting of Observational Longitudinal Research, as described in a previous systematic review.<sup>20)</sup> The total score for this tool was 30 points. As in the previous systematic review, articles with > 15 and > 20 points were judged to be of adequate and high quality, respectively. Likewise, two people evaluated each article independently and resolved disagreements through discussion with a third party.

The articles included in the previous systematic review were also reviewed. In addition, articles unsuitable for developing guidelines, such as articles irrelevant to frailty prevention and those about contributors that could not be modified, were removed. Finally, 28 articles were selected for guideline development (Fig. 1). All selected articles used the phenotype model, which evaluates physical functions such as gait speed and handgrip strength but does not evaluate other areas such as cognition, social status, and oral health. The list of all articles can be found in Supplement A.



**Fig. 1.** The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart.

### Draft Guideline Statements

From the 28 selected articles, 51 recommendations related to the prevention of frailty were prepared by organizing the contributors to frailty. However, the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was not applied. The GRADE is a representative grading system to evaluate articles according to the certainty of the evidence and strength of the recommendations. The certainty of the evidence is rated based on the study design, while the strength of the recommendations is rated according to the certainty of the evidence, benefit-harm assessment, preference and value, and cost-effectiveness.<sup>21)</sup>

These guidelines are based on cohort studies; therefore, the certainty of the evidence was homogenous and low. In addition, these guidelines have little harm, high applicability, and high cost-effectiveness; thus, the strength of the recommendations is also likely to be homogeneous and strongly recommended.

However, given that the target population is community-dwelling older adults, the gap between low certainty of evidence and strong recommendations is likely to confuse the target population. Moreover, information beyond the guideline text itself is likely to impair the applicability to community-dwelling older adults. Consequently, there was little benefit in the application of the grading system.

### Reaching Agreement on Recommendations

We applied the Delphi method to reach a consensus. A questionnaire was prepared for each recommendation, with answer sheets made on a 9-point Likert scale. The Delphi survey was conducted in two rounds. The second round included only recommendations that did not reach a consensus in the first round. Agreement was defined as 75% or more answers within 7–9 points, ambivalence as 75% or more answers within 4–6 points, and disagreement as 75% or more answers were 1–3 points.<sup>22,23)</sup>

Finally, a consensus was reached on 41 recommendations. Except for one recommendation, which reached ambivalence, all others reached an agreement. To improve the acceptability and usability among community-dwelling older adults, the recommendations are categorized into six domains: resilience, oral health, non-communicable disease management, involvement in society, smoking cessation, and eating various kinds of food.

However, no cohort study has assessed physical activity, which is a significant frailty intervention. As randomized clinical trials have evaluated physical activity, the guideline development team included physical activity recommendations from the Development of Clinical Intervention Guidelines on Prevention and Management of Frailty (unpublished) developed in the second year of the KFACS in these guidelines.

This unpublished guideline was developed by conducting a sys-

tematic review (Supplement B) and then implementing the Delphi method. It recommended exercise and combined interventions of exercise and nutrition to improve frailty (Supplement C). However, only one of the supporting evidence in this unpublished guideline included non-frail subjects in the study and could be a study related to primary prevention. Therefore, these prevention guidelines recommended physical activity based on supporting evidence.

Through this process, the present guidelines for frailty prevention were established. After external review, these guidelines comprising seven domains, including physical activity, were finalized.

## RESULTS

The guidelines for frailty prevention categorized the recommendations into seven domains: physical activity, resilience, oral health, management of non-communicable disease, involvement in society, smoking cessation, and eating various kinds of food. This study also created the “PROMISE” mnemonic to define and disseminate these guidelines (Table 3).

### Physical Activity

#### *Make multicomponent exercise a way of life*

The prevalence of frailty is 1.9 times higher among those who do not perform multicomponent exercise than among those who do. Multicomponent exercise refers to physical activities that include resistance, aerobics, balance, and flexibility training. The intensity of these multicomponent exercises should be increased incrementally over 2–3 weeks. Multicomponent exercise can reduce sedentariness, prevent frailty, and even prevent disability.<sup>24)</sup>

### Resilience

#### *Manage psychological problems with mental health professionals*

A positive effect reduced the risk of frailty by 8%.<sup>25)</sup> Additionally, the higher the number of depressive symptoms, the greater the risk of frailty,<sup>26)</sup> which increases by up to 2.2 fold.<sup>27)</sup> Moreover, ap-

**Table 3.** Frailty prevention mnemonics: PROMISE

PROMISE mnemonics
Physical activity
Resilience
Oral health
Management of non-communicable diseases
Involvement in society
Smoking cessation
Eating various kinds of food

athy and high levels of loneliness increase frailty risk by 2.9 and 1.9 times, respectively.<sup>28,29</sup> Therefore, psychological difficulties in old age should be managed with the help of mental health professionals.

## Oral Health

### *Take care of your teeth and gums*

Each additional tooth preserved in old age reduces the risk of frailty by 5%.<sup>30</sup> A weak maximum bite force increases the risk of frailty by 2.8 fold<sup>31</sup> and severe periodontitis increases the risk of frailty by 2.1 fold. Teeth should also be brushed three times daily to maintain oral hygiene, while dentures should be washed daily. Finally, oral health checkups and tartar removal should be performed every 6 months to manage oral health.

## Management of Non-communicable Diseases

### *Actively manage your chronic conditions*

High blood pressure,<sup>27,30</sup> diabetes, stroke, chronic obstructive pulmonary disease,<sup>27</sup> osteoporosis,<sup>30</sup> metabolic syndrome,<sup>32</sup> arthritis,<sup>27</sup> and chronic pain<sup>33</sup> increase the risk of frailty. In old age, non-communicable diseases must be actively managed by regularly seeing a doctor. Vision and hearing impairment are additional health challenges that are easily overlooked. The risk of frailty increases by 2.1 fold when vision is impaired<sup>34</sup> and by 1.4 fold when hearing is impaired.<sup>35</sup> Problems with vision or hearing should be managed by a doctor.

### *Review medications regularly*

The risk of frailty increases by 5.6 fold in people who take six or more drugs.<sup>36</sup> Older adults often take various drugs for multimorbidity. Regular medication reviews should be conducted to evaluate polypharmacy, and overlapping or unnecessary drugs should be discontinued.

## Involvement in Society

### *Meet people often*

Decreased social activities, social roles, or relationships (social frailty) increase the risk of frailty by 3.9 fold.<sup>37</sup> These guidelines recommend going out and visiting friends as often, in addition to talking to people every day, and if this is difficult, talking over the phone is recommended.

### *Take care of yourself and your partner*

A spouse's depressive symptoms increase the risk of one's depres-

sive symptoms; similarly, a spouse's frailty also increases an individual's risk of frailty.<sup>38</sup> Therefore, frailty prevention with a partner is more effective than alone.

## Smoking Cessation

### *Stop smoking*

Smoking increases the risk of frailty by 1.5–2.9 times.<sup>26,27,39</sup> Smoking cessation positively affects health, even in old age. Smoking causes various diseases and frailty; therefore, we recommend quitting smoking as soon as possible.

## Eating Various Kinds of Food

### *Maintain a balanced diet*

The consumption of fish,<sup>40</sup> fruits and vegetables,<sup>41</sup> low-fat milk, and low-fat yogurt<sup>42</sup> reduces the risk of frailty. In old age, eating habits are fixed, and preparing meals is challenging; therefore, older adults frequently eat simple meals such as rice, kimchi, or instant foods. These unbalanced diets increase the risk of frailty; therefore, we recommend the conscious eating of a variety of foods.

### *Eat sufficient food*

Lower intakes of protein and vitamin D increase the risk of frailty by up to 2.4 fold<sup>43</sup> and 1.6 fold,<sup>26</sup> respectively. Intakes of vitamin B6, folic acid, vitamin C, and vitamin E below the recommended dietary allowances (RDA) also increase the risk of frailty (Supplement D).<sup>44</sup> Among the 10 vitamins, older adults with < 5 RDAs have a 2.8-fold increased risk of frailty.<sup>44</sup> In addition, being underweight (body mass index < 18.5 kg/m<sup>2</sup>) increases the risk of frailty by 1.7 fold.<sup>27</sup> Therefore, eating can prevent frailty. However, as the risk of frailty increases by 1.4–4 fold in older adults with or at risk of obesity (body mass index ≥ 30 kg/m<sup>2</sup>),<sup>26,27</sup> food consumption should be reduced.

## DISCUSSION

This study developed guidelines for the primary prevention of frailty in community-dwelling older adults based on the results of a systematic review. Because older adults have complex medical conditions owing to physiological changes, multimorbidity, polypharmacy, and interactions,<sup>45</sup> the approach to frailty should be comprehensive.<sup>46</sup> By setting comprehensive key questions for the systematic review, the development team tried to capture the contributors of frailty as much as possible.

Based on the identified evidence, experts in geriatrics and gerontology derived recommendations using the Delphi method. As the

users of these guidelines are community-dwelling older adults and not health practitioners, this study attempted to improve the acceptability of the guidelines by organizing recommendations spanning various areas. Thus, we categorized the guidelines for preventing aging into seven areas: physical activity, resilience, oral health, chronic disease management, social participation, smoking cessation, and various food intake.

However, this study had some limitations. First, the evidence used to develop these guidelines was based on the results of cohort studies. Thus, the recommendations lacked certainty of the evidence and it was not easy to apply the GRADE system to the guidelines. Second, because the guidelines were developed based on known contributors to frailty, the recommendations were inevitably presented in a limited area.

In conclusion, these frailty prevention guidelines were developed by reflecting the contributors to frailty through a systematic review. The guidelines must be continuously updated by considering new scientific evidence. Therefore, the development team plans to update these guidelines through regular systematic reviews and also develop frailty management guidelines for health practitioners.

We hope that these guidelines based on scientific evidence will contribute to the prevention of frailty and help the healthy aging of community-dwelling older adults. A Korean version of the guideline is provided in [Supplement E](#).

## SUPPLEMENTARY MATERIALS

Supplementary materials can be found via <https://doi.org/10.4235/agmr.21.0072>.

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### CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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### AUTHOR CONTRIBUTION

Conceptualization, SK, JY, YL, CWW; Data curation, SKK, JHY; Funding acquisition, YL, CWW; Investigation, SK, JY; Methodology, SK, JY, JK; Project administration, SK, YL, JK; Resources, MK, COK, KYS, HP, SP, KEL, SJS, KK, MKK; Supervision, YL,

CWW, MK, COK, KYS, HP, SP, KEL, SJS, KK, MKK, JK; Writing—original draft, SK; Writing—review & editing, SK, JY, YL, JK.

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# A Descriptive Study of Emergency Department Visits Within 30 Days of Discharge

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## INTRODUCTION

In Korea, where geographic and financial accessibilities to tertiary hospitals are high, overcrowding of the emergency department (ED) of tertiary medical institutions is a serious problem. Such overcrowding, especially in the ED, leads to poor patient outcomes, increased length of stay, and increased risk of infectious dis-

**Background:** Unnecessary emergency department (ED) visits are a crucial consideration in discharge planning for acutely admitted patients. This study aimed to identify the reasons for unnecessary visits to the ED within 30 days of discharge from a medical hospitalist unit. **Methods:** We performed a retrospective review of patients discharged in 2018 from a medical unit of tertiary teaching hospital in Korea. The authors discussed in-depth and determined whether or not an ED visit was unnecessary, and further classified the causes of unnecessary visits into three categories. **Results:** The mean age of the patients was 62.9 years (range, 15–99 years), and among the 1,343 patients discharged from the unit, 720 (53.6%) were men. Overall, 215 patients (16.0%) visited the ED within 30 days after discharge; among them, 16.3% were readmitted. Of the 215 cases of ED visits within 30 days after discharge, 57 (26.5%) were considered unnecessary. Of these, 30 (52.6%) were categorized as having failed care transition, 15 (26.3%) had unestablished care plans for predictable issues, and 12 (21.1%) had insufficient patient education. **Conclusion:** A substantial number of short-term ED visits by discharged multimorbid or older medical patients were considered unnecessary. Discharging patients with a thorough discharge plan is essential to avoid unnecessary ED visits.

**Key Words:** Patient discharge, Patient readmission, Geriatrics, Multimorbidity, Hospital medicine

ease transmission.<sup>1-4)</sup> The rates of unplanned readmission of hospitalized patients after discharge range between 10% and 25%,<sup>5-10)</sup> with most patients readmitted through the ED. Thus, discharge planning to minimize unnecessary post-discharge ED visits should be considered an important medical issue to reduce ED overcrowding and consequent readmissions.

With the increasing prevalence of chronic diseases owing to ag-

ing, many patients have multimorbidities.<sup>11-13)</sup> The risks of readmission and ED visits are high among older or multimorbid patients. Hence, eliminating unnecessary hospital visits among these patients is a priority.<sup>14-18)</sup> Since the launch of the hospitalist system, older or multimorbid patients are often treated in hospital units by hospitalists who provide generalized medical care.<sup>5,6)</sup> Studies of medical hospitalist units in tertiary teaching hospitals in Korea have reported that the mean age of hospital inpatients is > 60 years, that most patients have multimorbidities, and that the average Charlson Comorbidity Index score is 6 or more.<sup>5)</sup> Hence, the readmission of patients from hospitalist units is of crucial concern when considering post-discharge ED visits.

To our knowledge, no published data have yet described the details and causes of ED visits after acute admission to hospitalist units in Korea. This study aimed to identify reasons for visiting the ED within 30 days of discharge and describe the reasons for unnecessary ED visits in multimorbid or older medical patients. We assessed cases in detail and proposed how physicians might prevent unnecessary ED visits, which could not only reduce ED overcrowding but also minimize unnecessary use of medical resources.<sup>19)</sup>

## MATERIALS AND METHODS

### Study Design and Participants

This retrospective database study collected information on ED visits of patients who were discharged from the hospitalist unit of a tertiary teaching hospital in Korea in 2018. The medical hospitalist unit services older or multimorbid inpatients as described in previous studies from the same unit.<sup>5,6)</sup> We then reviewed in detail medical records of patients who visited the ED within 30 days of discharge.

The study protocol was reviewed and approved by the Institutional Review Board of the Seoul National University Hospital (No. 2021-070-1180), which approved a waiver of consent because of the retrospective nature of the study. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

### Determination and Classification of Unnecessary ED Visits

Previous studies have proposed criteria for determining unnecessary ED visits based on diagnostic or procedural codes.<sup>20,21)</sup> However, criteria based on codes are insufficient to identify the cause of each case or suggest countermeasures. Thus, in this study, a roundtable discussion was performed with all authors who were board-certified internists and currently working in the ED or medical hospitalist units in the same hospital to discuss each case in

depth. First, unnecessary ED visits were determined based on the following criteria.

- (1) Primary care treatable: A patient visited the ED with symptoms that were not obvious or mild enough to be managed by the primary outpatient clinic of the community.
- (2) Preventable: If a patient's symptoms were reported during the index hospitalization, an appropriate plan was omitted at the time of discharge.
- (3) Hospice care suitable: If a patient's symptoms were worse than before or new, but could have been predicted while the underlying disease was progressing, and for which hospice care was recommended for patients during the index hospitalization.

Second, unnecessary ED visits were classified according to causes:

- (1) Failure of care transitions: Cases that returned to the ED owing to unmet medical or care needs after discharge to the community or that were admitted to medical institutions in the community. This category also included issues regarding discordance between physicians and patients regarding the therapeutic goal of index hospitalizations leading to ED visits.
- (2) Unestablished care plans for predictable issues: This category included unnecessary ED visits associated with previous discharge planning, such as predictable medical or caregiving issues after index discharge regarding symptoms (e.g., pain, dyspnea) of the underlying medical conditions.
- (3) Insufficient patient education: This category included issues such as education for the management of feeding tubes, drainage tubes, or intravenous catheters, as well as the administration of certain medications.

### Statistical Analysis

Data are expressed as mean  $\pm$  standard deviation or number (percentage), unless stated otherwise. Independent t-test and Pearson  $\chi^2$  test were used to compare continuous and categorical variables, respectively, between patients who visited the ED and those who did not. We considered two-sided p-values < 0.05 to be statistically significant. IBM SPSS Statistics for Windows version 23.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

## RESULTS

### Clinical Characteristics of Index Hospitalizations

A total of 1,343 patients were discharged from the medical hospitalist unit during the study period. Their mean age was 62.9 years (range, 15–99 years); 720 patients (53.6%) were men, and 323 pa-

tients (24.1%) were admitted to the ED. A total of 1,052 patients (78.3%) were initially admitted owing to cancer-related problems. Excluding patients with cancer, the common reasons for admission were respiratory tract infection, liver disease, and kidney disease. The mean length of stay was 11.3 nights, and 57 patients (4.2%) were transferred to long-term care hospitals after discharge.

A total of 215 patients (16.0%) visited the ED within 30 days of discharge. Among them, 16.3% were admitted from the ED to the ward. The mean age of patients did not differ significantly between those who did and did not visit the ED. Compared to those in the non-visiting group, patients in the visiting ED group had higher proportions of men and patients admitted to the ED for index hospitalization (63.3% vs. 51.8% and 34.0% vs. 22.3%;  $p = 0.002$  and  $p < 0.001$ , respectively). Patients in the visiting ED group also had longer hospital stays during the index hospitalization than those in the non-visiting group (mean, 13.4 nights vs. 10.9 nights;  $p = 0.001$ ). The proportions of patients with cancer or those who were transferred to long-term care hospitals did not differ between the two groups (Table 1).

### Clinical Characteristics and Causes of Unnecessary ED Visits

Of the 215 visits to the ED within 30 days of discharge, 57 (26.5%) were determined to be unnecessary (40 primary care treatable, 12

preventable, and 5 hospice care suitable). There were fewer men in the unnecessary visiting group than in the necessary visiting group (49.1% vs. 68.4%;  $p = 0.010$ ), and no significant differences in age, route of index hospitalization, proportion of patients with cancer, length of hospital stay, and proportion of patients transferred were noted between the two groups (Table 2).

Categorization of unnecessary ED visits according to causes revealed 30 (52.6%) visits for failure of care transition, 15 (26.3%) for unestablished care plans for predictable issues, and 12 (21.1%) for insufficient patient education (Fig. 1).

#### First cause: failure of care transitions

This category was the most common reason for unnecessary ED visits. Most cases in this category (24 of 30 visits) were treatable by primary care institutions. The cases in this category largely involved communication issues related to discharge planning or insufficient information about the local health system's coping capabilities. Several patients wanted parenteral nutrition, paracentesis, medications to control non-serious symptoms, and reassurance regarding insignificant symptoms. For example, a 49-year-old male patient returned to the ED 3 weeks after transfer seeking a prescription for laxatives. This category also included patients and their caregivers who were dissatisfied with the local medical insti-

**Table 1.** Clinical characteristics of the study population

Variable	Non-visiting	Visiting ED	p-value
Number of patients	1,128 (84.0)	215 (16.0)	
Age (y)	62.9 ± 13.6	62.8 ± 13.2	0.978
Sex, male	584 (51.8)	136 (63.3)	0.002
Index hospitalization through the ED	250 (22.3)	73 (34.0)	< 0.001
Malignancy-associated problems	876 (77.7)	176 (81.9)	0.171
Length of stay (nights)	10.9 ± 10.1	13.4 ± 9.3	0.001
Transfer to LTCHs	51 (4.5)	6 (2.8)	0.248

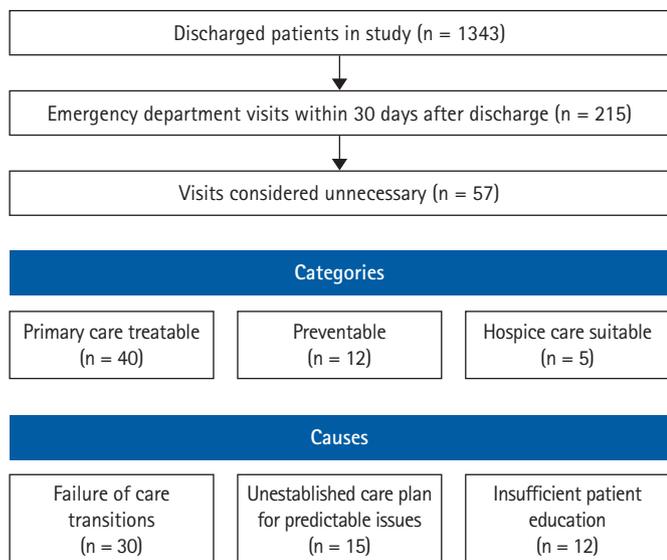
Values are presented as number (%) or mean ± standard deviation. ED, emergency department; LTCH, long-term care hospital.

**Table 2.** Clinical characteristics of patients who visited the ED within 30 days of discharge

Variable	Necessary	Unnecessary	p-value
Number of patients	158 (73.5)	57 (26.5)	
Age (y)	63.6 ± 12.7	60.6 ± 14.7	0.136
Sex, male	108 (68.4)	28 (49.1)	0.010
Index hospitalization through ED	57 (36.1)	16 (28.1)	0.274
Malignancy-associated problems	133 (84.2)	43 (75.4)	0.142
Length of stay (nights)	13.5 ± 9.3	12.9 ± 9.3	0.680
Transfer to LTCHs	4 (2.5)	2 (3.5)	0.657*

Values are presented as number (%) or mean ± standard deviation. ED, emergency department; LTCH, long-term care hospital.

\*Fisher exact test.



**Fig. 1.** Classification according to causes of unnecessary emergency department visits.

tutions who instead visited the ED of a tertiary hospital seeking admission. In this category, three patients returned to the ED after being discharged home and were eventually transferred to a medical institution at which hospice care was available.

**Second cause: unestablished care plans for predictable issues**

The most common reason for ED visits in this category was deficient analgesics for predictable pain (9 of 15 visits), such as breakthrough cancer pain. A patient revisited the ED complaining of abdominal pain only 3 days after discharge. The patient had stage IV intrahepatic cholangiocarcinoma and was discharged after undergoing biopsy of the newly detected neoplasm found on computed tomography. Since the patient complained of persistent pain in the right upper quadrant during hospitalization, it was predictable that the pain would continue even after discharge. There were also several cases of ED revisits owing to diet-related problems (3 of 15 visits). For instance, a 58-year-old man was brought to the ED because of seizures. During index hospitalization, the patient had a seizure for the first time and was prescribed an antiepileptic drug. However, pills were prescribed at the time of discharge despite the patient having difficulty swallowing. As the patient could not take oral medication, the blood level of the antiepileptic drug decreased, resulting in more seizures.

**Third cause: insufficient patient education**

A total of 12 patients returned to the ED owing to a lack of training in drug administration and management of feeding or drainage tubes. One patient also visited the ED because of hypoglycemia. During the previous hospitalization, the patient started taking in-

sulin for the first time and thus was not familiar with insulin administration. Another patient returned to the ED because the percutaneous transhepatic biliary drainage (PTBD) catheter had disconnected from the drainage bag. The patient was discharged in the morning and had to return to the ED within several hours. The patient returned home immediately after the healthcare staff reconnected the PTBD catheter to the drainage bag. Most cases in this category (10 of 12) were treatable by primary care.

**DISCUSSION**

Consistent with the literature, the results of this study revealed that a substantial number of patients returned to the ED shortly after discharge. Of these, 26.5% of ED visits were unnecessary. Unnecessary ED visits cost patients, consume their physical strength, and risk the acquisition of infectious diseases. More importantly, unnecessary ED visits may lead to wasted medical resources and prevent the efficient use of these resources for patients who require emergency treatment. In this study, we classified the causes of unnecessary ED visits after discharge into three categories.

In this study population, the most common type of unnecessary ED visits was primary care treatable, often caused by a failure of transition care. It is essential to link patients to community medical institutions at or before discharge so that they can visit primary or secondary medical institutions rather than tertiary hospitals for mild symptoms. It is also important to create a referral detailing the patient’s condition for local primary or secondary medical institutions. Patients also return to the ED after discharge because of a lack of communication between the staff of medical institutions. If a patient is discharged from a tertiary hospital and transferred to a nursing home or another hospital, the attending physician must fully explain the patient’s condition to the medical staff at the hospital. For instance, if no additional treatment plan and hospice care are needed, ED visits for worsening medical conditions can be a futile process. Patients may experience unnecessary suffering from being repeatedly transferred to the ED, even when death is imminent. Sharing information and ensuring two-way open communication between medical service providers are important for reducing unnecessary ED visits.<sup>22,23)</sup> In addition, a system that allows hospitals to share medical records for a certain period before and after transfer is also worth considering.

Patient factors often negate efforts for effective care transitions. This may be because of current medical delivery systems in Korea. Patients in Korea can receive treatment at a tertiary hospital for a similar fee, even for common mild chronic disease, with a simple request from the primary clinic.<sup>24)</sup> Medical institutions at each level are trying to attract patients through competition rather than co-

operation. Most patients, regardless of their degree of discomfort, tend to seek treatment at large tertiary hospitals. A similar trend has been reported in emergency care.<sup>25,26)</sup> Therefore, successful care transitions should always also inform patients about the capabilities of local primary or secondary medical institutions. Attending physicians must also explain to patients the disease course and prognosis and provide a list of indications for when he or she should visit the ED of the tertiary hospital at which they had previously received treatment. The patients in this study tended to visit the ED even for mild symptoms that did not require treatment at a tertiary hospital. When a patient is discharged from a tertiary medical institution, the attending physician may instruct the patient to visit a local primary or secondary medical institution for minor problems.<sup>27,28)</sup>

Predicting and responding to potential health-related situations in patients are important roles of attending physicians upon discharge. Unless told how to properly cope with their situation, patients will likely return to the ED every time unexpected symptoms occur. When a meticulous care plan is not available, patients will likely return to the ED after discharge for inappropriate issues such as hydration, additional nutritional supplementation, or drug prescription. When a physician prescribes discharge medications, it is necessary to follow a process that reflects the opinions of pharmacists, nurses, caregivers, and patients.<sup>29-32)</sup>

Patient education must be provided to empower their self-care ability upon discharge.<sup>27,29,32)</sup> Such education may include information on daily life, such as eating and bathing, or medical information such as the name, dose, and method of taking medications. In particular, healthcare professionals must educate patients who are discharged from the hospital with indwelling medical devices such as urinary catheters, nasogastric tubes, or PTBD on proper management procedures. Training these patients to adjust their insulin dose or manage drainage tubes would avoid visits to the ED. If education encompassing instructions for patients who are discharged from acute hospitals could be reimbursed, unnecessary ED visits associated with this issue might be alleviated.

Discharging patients from hospitals is a complex process, as observed for each case in this study. Meticulous and individualized discharge plans may reduce unnecessary post-discharge ED visits. Previous studies have proposed various approaches to improve the discharge process and reduce unnecessary ED visits, including pre-discharge interventions (including discharge planning, patient education, and scheduling follow-up appointments) or post-discharge interventions (follow-up phone calls after discharge, communication by telemedicine, etc.).<sup>33-35)</sup> Bridging interventions, such as transition coaches and continuity of care between inpatient and outpatient departments, may also be helpful. Reducing un-

necessary ED visits may improve both patient quality of life and the financial status of the healthcare system. Furthermore, the burden on medical personnel may decrease.

The findings of this study should be considered in light of the following limitations. First, the study sample was limited to data from the medical hospitalists-operated unit of a tertiary hospital, in which most patients were older or had serious underlying diseases such as cancer. The results of this study might be difficult to apply to primary or secondary local hospital situations. Second, cases of ED visits other than the hospital where the patients were discharged were not investigated. Third, this study depended on the accuracy of the documented data, which was retrospective and administrative in nature. Finally, although there have been suggestions on ways to reduce ED visits, none of them were assessed for their efficacy in this descriptive study.

In conclusion, a significant number of short-term ED visits after the discharge of multimorbid or older medical patients were unnecessary. Comprehensive discharge procedures, including care transition, planning for predictable issues, and patient education, are essential. Further interventional and prospective studies are needed to investigate the effects of discharge interventions on ED visits.

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### CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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None.

### AUTHOR CONTRIBUTION

Conceptualization, HK; Data curation, HK, SJH, JHL, SM, HM, SYL, SWY, HWJ; Formal analysis, HK, SJH, JHL, SM, HM, SYL, SWY, HWJ; Investigation, SJH; Methodology, SJH, HWJ; Software, SJH; Visualization, HK; Writing – original draft, HK, SJH; Writing – review & editing, SJH.

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# Association of Preoperative Risk Factors and Mortality in Older Patients following Emergency Abdominal Surgery: A Retrospective Cohort Study

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**Background:** Older patients undergoing emergency laparotomy have high morbidity and mortality rates. Preoperative risk assessment with good predictors is an appropriate measure in this population. Frailty status is significantly associated with postoperative outcomes in older adults. This study aimed to investigate the effect of preoperative risk factors and frailty on short-term outcomes following emergency surgery for acute abdomen in older patients. **Methods:** This study included older patients ( $\geq 65$  years of age) who underwent emergency abdominal surgery. We retrospectively analyzed their demographic and clinical variables and used the modified Frailty Index-11 to evaluate their frailty status. The primary outcome was the 30-day mortality rate. We also analyzed risk factors of mortality in these patients. **Results:** The study included 150 patients with a median age of 74 years. The mortality rate was 17.3% (n=26). We observed significantly higher mortality rates in patients who were obese and who had higher American Society of Anesthesiology (ASA grades) ( $p < 0.05$ ). Frailty status was worse in deceased group ( $p < 0.001$ ), when compared to individuals who survived. Septic shock was associated with the development of mortality ( $p < 0.001$ ). Multivariate regression analysis revealed that ASA grade was the only independent risk factor for mortality (odds ratio=19.642; 95% confidence interval, 3.886-99.274;  $p < 0.001$ ). **Conclusion:** Older patients with obesity and frailty presenting with higher ASA grades and septic shock had the worst survival following emergency abdominal surgery. The ASA grade was an independent risk factor for mortality.

**Key Words:** Acute abdomen, Aged, Frailty, Mortality rate

## INTRODUCTION

The life expectancy of the older adult population is increasing globally.<sup>1)</sup> The number of emergency laparotomies performed for geriatric patients increases similar to other surgical procedures in an aging population.<sup>2)</sup> Although the definition of older adult is controversial, many authors agree on an age over 65 years.<sup>3)</sup> Patients who undergo emergency laparotomy have high morbidity and mortality rates with additional high risks.<sup>4,5)</sup> In addition, older patients undergoing abdominal surgery in emergency settings usu-

ally require intensive care and longer hospital stays. Therefore, compared to younger patients, it is essential to provide a safe, beneficial, and effective surgical assessment system to evaluate medical risks of consequent illness and clinical competence in older patients.

Chronological age alone may not be a good predictor for poor outcomes in emergency operations of older adults.<sup>6,7)</sup> Preoperative risk assessment is an appropriate measure for decision-making and preemptive resource allocation.<sup>4)</sup> Previous studies assessed in detail morbidity and mortality rates in older patients following emer-

gency laparotomy.<sup>8-10</sup> Several perioperative risk scoring systems have been developed to assess the outcomes in surgical patients in elective or emergent situations.<sup>5</sup> These systems of identifying high-risk patients and providing them with the appropriate level of care include the American Society of Anesthesiology (ASA) grades, Portsmouth Physiological and Operative Severity Score (P-POSSUM) for the enumeration of mortality and morbidity, American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) surgical risk calculator, and National Emergency Laparotomy Audit (NELA) risk prediction calculator.<sup>4,6,11-14</sup>

The strengths and weaknesses of these tools have been reported.<sup>15</sup> The major criticisms include various parameters that may not be routinely performed and the overestimation of mortality and morbidity.<sup>4,6</sup> Moreover, there remains no consensus regarding the reliability of these tools in geriatric populations subjected to emergency laparotomy.<sup>16</sup> Because of differences among institutions in their risk prediction of mortality, detailed analyses are needed to determine the reproducibility of the variables used for these tools. Thus, identifying more accurate predictors of mortality in older patients could help identify a surgical assessment tool.<sup>11,16</sup>

There is a lack of consensus on the definition of frailty in the literature, and this term has been used subjectively.<sup>4,12,17</sup> It often denotes unintentional weight loss, exhaustion, weakness, slow walking, low physical activity, and lack of phenotype.<sup>4,18</sup> The Clinical Frailty Scale has been used to apply a more consistent definition.<sup>6,17</sup> Because of the lack of a uniform definition and a tool to identify frailty in older patients, several tools have been proposed in different patient groups. Among these, the Clinical Frailty Scale has the advantage of being fast and straightforward to perform.<sup>17,18</sup> However, a prospective clinical observation is needed, which includes comorbidities, ability to perform specific activities of daily living, oxygen supplementation, and presence of a terminal illness. The modified Frailty Index-11 (mFI-11) comprises 11 possible comorbidities/deficits that can be recorded retrospectively.<sup>6</sup>

As frailty is significantly reportedly associated with 90-day mortality and postoperative morbidity in patients undergoing emergency laparotomy,<sup>19</sup> we examined the effect of preoperative frailty on the loss of functional independence following emergency abdominal surgery in older adults.

The present retrospective cohort study aimed to investigate the associations of some preoperative predictive factors, including frailty, with morbidity, mortality, management strategies, and short-term outcomes of emergency surgery for acute abdomen in patients aged 65 years and older.

## MATERIAL AND METHODS

### Study

This retrospective cohort study included all consecutive older patients who underwent emergency abdominal surgery at Bagcilar Training and Research Hospital in Istanbul, Turkey, between February 2016 and January 2020. The Bagcilar Training and Research Hospital Local Ethics Committee approved the study (No. 2020.10.2.01.162). We conducted this study in accordance with the principles of the Declaration of Helsinki. Written consent could not be obtained due to the retrospective design of the study and the anonymity of the data.

### Patients

We retrospectively searched all emergency general surgery admissions using the hospital information system and medical records to include patients aged  $\geq 65$  years. We identified a total of 831 patients. The exclusion criteria were age  $< 65$  years on the day of surgery ( $n = 647$ ) and incomplete data ( $n = 11$ ). All types of gynecological and urological procedures in non-trauma or trauma surgery settings ( $n = 23$ ) were also excluded. Thus, we evaluated data from 150 admissions.

We collected data on patient characteristics, including demographic data, body mass index (BMI), comorbidities, ASA score, perioperative features, and outcomes. The patients were grouped based on their age (65–74 or  $\geq 75$  years). Clinical data, including evidence of sepsis and systemic shock, systolic blood pressure (mmHg), and the lowest or highest values of the laboratory parameters in the initial 24-hour period, were obtained from emergency department records. Comorbidities included diabetes mellitus (DM), hypertension, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), and chronic renal failure (CRF). We also recorded perioperative characteristics, diseases requiring surgical treatment, surgical approach, type of surgery, duration, length of intensive care unit (ICU) and hospital stays, postoperative complications, and readmission data.

Frailty status was evaluated using mFI-11. This 11-point scoring system includes 11 possible comorbidities and deficits (Table 1). As a comorbidity-dominant scoring system, it requires binary non-subjective responses. The score can also be calculated without phenotypic measures of the patients, such as exhaustion, slowness, and reduced physical activity.<sup>6</sup> Each component is assigned one point with a total point range of 0–11. Frailty status is categorized as frail (score  $> 3$  points), pre-frail (1–2 points), and absence of frailty (0 points). For analysis, we grouped the patients as frail (frail and pre-frail) and non-frail.

Clinical decisions, including the decision to undergo surgery

**Table 1.** Modified Frailty Index-11 (mFI-11)

Comorbidities and/or deficits	
	Diabetes mellitus
	Congestive cardiac failure
	Hypertension requiring medication
	History of either transient ischemic attack or cerebrovascular accident
	A functional status that is non-independent
	History of myocardial infarction
	History of peripheral vascular disease or rest pain
	History of a cerebrovascular accident with neurological deficit
	History of either chronic obstructive pulmonary disease or pneumonia
	History of either prior percutaneous coronary intervention, previous coronary surgery, or history of angina
	History of impaired sensorium
Frailty status (total score)	
	> 3, frail
	1–2, pre-frail
	0, absence of frailty

and choice of operative technique (open or laparoscopic), were based on the discretion of the attending consultant surgeons. The surgical procedures were performed by the consultant surgeons or under their supervision.

All patients were followed up to 30 days postoperatively or to death.

### Statistical Analyses

The primary outcome was 30-day mortality. We grouped the patients based on the development of mortality (non-survivors and survivors).

We performed statistical analyses using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Continuous variables with or without normal distribution are presented as mean  $\pm$  standard deviation and median with interquartile range (IQR, 25% to 75%). Categorical variables are presented as frequencies with percentages. We applied the Kolmogorov-Smirnov test to check the normality of the numerical variables. We used the independent samples t-test to compare two independent groups with normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. We applied Pearson chi-square and Fisher exact tests in  $2 \times 2$  tables to compare the differences in categorical variables.

Multivariate logistic regression analyses were performed to analyze the factors affecting the development of mortality. Statistically significant factors in the univariate analyses were included in the multivariate analysis. Statistical significance was set at  $p < 0.05$ .

## RESULTS

**Table 2** presents the details of the patients' demographic and clinical characteristics. The median age of the 150 patients was 74 years. Of these, 124 patients (82.7%) survived to discharge (survivors), while 26 patients (17.3%) died (non-survivors) within a median length of 3 days (IQR, 2–6).

The numbers of female and male patients were similar (71 vs. 79). The mean BMI of the study group was  $26.7 \pm 4.2$  kg/m<sup>2</sup>. Most of the patients were classified as ASA III ( $n = 62$ ; 41.3%), followed by ASA II ( $n = 46$ ; 30.7%). Most patients (90%) had at least one type of comorbid disease. Hypertension and DM were the two most common coexisting diseases in the study group. Frailty was not observed in 126 patients (84.0%), 19 patients (12.7%) were pre-frail, and five (3.3%) were frail. Seventeen patients (11.3%) experienced septic shock. **Table 3** summarizes the laboratory findings of the study groups.

Gastrointestinal perforation was the most common diagnosis in the study group. Forty-four patients (29.3%) had perforation, followed by intestinal obstruction in 30 patients (20.0%). The other diagnoses are listed in **Table 4**. Intestinal resection with ostomy formation and anastomosis was the most frequently performed surgical procedure in 31 (20.7%) and 22 (14.7%) patients, respectively. The distribution of operations is presented in **Table 5**.

A total of 26 deaths occurred within postoperative 30 days (non-survivors), corresponding to a mortality rate of 17.3%. The median age of the non-survivors was significantly higher than that of the survivors ( $p < 0.001$ ). The rate of patients aged 75 years or more was significantly higher among the non-survivors than in the survivors (80.8% vs. 41.9%) ( $p < 0.001$ ). We observed significantly higher mortality rates in obese older patients with higher ASA grades (**Table 3**). Hypertension and CAD were more common in non-surviving patients ( $p = 0.040$  and  $p = 0.003$ , respectively). The absence of frailty was more frequently observed in the surviving patients than in non-surviving patients (91.1% vs. 50%;  $p < 0.001$ ). All patients with frailty ( $n = 5$ ) were non-survivors, whereas no patient in the survivor group was categorized as frail. Grouping based on frailty (frail and pre-frail) and the absence of frailty revealed a significant difference in mortality rates (54.2% vs. 10.3%;  $p < 0.001$ ). In non-survivors, the incidence of septic shock was higher than that in survivors ( $p < 0.001$ ).

Patients with frailty (frail and pre-frail) were likely to be older ( $p < 0.001$ ); have higher ASA grades ( $p < 0.001$ ); and have higher incidences of hypertension ( $p = 0.001$ ), DM ( $p = 0.046$ ), and septic shock ( $p = 0.001$ ). Other demographic and clinical variables were not significantly associated with frailty ( $p > 0.05$ ).

We observed significant differences in laboratory parameters be-

**Table 2.** Demographic and clinical characteristics of the study groups (n=150)

Variable	Overall (n = 150)	Non-survivors (n = 26)	Survivors (n = 124)	p-value
Age (y)	74 (69–79)	81 (76–85)	73 (69–77)	< 0.001
65–74	77 (51.3)	5 (19.2)	72 (58.1)	< 0.001
≥ 75	73 (48.7)	21 (80.8)	52 (41.9)	
Sex				1.0
Female	71 (47.3)	12 (46.2)	59 (47.6)	
Male	79 (52.7)	14 (53.8)	65 (52.4)	
BMI (kg/m <sup>2</sup> )	26.1 (23.8–29)	27.5 (25.7–31.6)	25.9 (23.7–28.6)	0.025
ASA grade				< 0.001
1	10 (6.7)	0 (0)	10 (8.1)	
2	46 (30.7)	1 (3.8)	45 (36.3)	
3	62 (41.3)	2 (7.7)	60 (48.4)	
4	26 (17.3)	17 (65.4)	9 (7.3)	
5	6 (4.0)	6 (23.1)	0 (0)	
Comorbidity				0.470
Present	135 (90)	25 (96.2)	110 (88.7)	
Absent	15 (10)	1 (3.8)	14 (11.3)	
Types of comorbidity				
Hypertension	103 (68.7)	22 (84.6)	81 (65.3)	0.040
DM	61 (40.7)	13 (50)	48 (38.7)	0.198
CAD	25 (16.7)	10 (38.5)	15 (12.1)	0.003
COPD	16 (10.7)	1 (3.8)	15 (12.1)	0.191
CRF	14 (9.3)	4 (15.4)	10 (8.1)	0.206
Frailty				< 0.001
Absence of frailty	126 (84.0)	13 (50)	113 (91.1)	
Pre-frail	19 (12.7)	8 (30.8)	11 (8.9)	
Frail	5 (3.3)	5 (19.2)	0 (0)	
Septic shock				< 0.001
Present	17 (11.3)	12 (46.2)	5 (4.0)	
Absent	133 (88.7)	14 (53.8)	119 (96.0)	
SBP (mmHg)	140 (120–160)	135 (90–150)	145 (120–160)	0.075

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

BMI, body mass index; ASA, American Society of Anesthesiologists; DM, diabetes mellitus; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; SBP, systolic blood pressure.

**Table 3.** Laboratory features of the study groups (n=150)

Variable	Overall (n = 150)	Non-survivors (n = 26)	Survivors (n = 124)	p-value
Hemoglobin (g/dL)	12.4 (10.5–13.5)	12.1 (8.4–13.2)	12.4 (11.1–13.5)	0.075
WBC ( $\times 10^9/L$ )	11.1 (7.3–14.5)	16.0 (10.5–18.7)	10.4 (7.2–13.5)	0.003
Glucose (mg/dL)	109 (89–139.3)	120 (100–190)	101 (88–134)	0.013
Creatinine (mg/dL)	1.4 (1–3.1)	3.6 (1.9–4.4)	1.3 (1.0–1.75)	< 0.001
Sodium (mEq/L)	138.8 $\pm$ 4.6	138.0 $\pm$ 5.3	139.0 $\pm$ 4.5	0.444
Albumin (g/dL)	3.9 (2.9–4.9)	2.35 (2–3.4)	4.15 (3.3–4.95)	< 0.001
CRP (mg/dL)	52.0 (18.8–123.6)	183.5 (114–245)	39 (13.8–80.5)	< 0.001
NLR	4.5 (3.0–7.7)	9.65 (6.5–11.9)	3.8 (2.9–5.9)	< 0.001

Values are presented as mean  $\pm$  standard deviation or median (interquartile range).

WBC, white blood cell; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio.

**Table 4.** Distribution of diagnoses in the study groups

Diagnoses	Overall (n = 150)	Non-survivors (n = 26)	Survivors (n = 124)	p-value
Perforation	44 (29.3)	16 (61.6)	28 (22.6)	
Intestinal obstruction	30 (20.0)	2 (7.7)	28 (22.6)	
Mesenteric ischemia	18 (12.0)	4 (15.4)	14 (11.3)	
Acute cholecystitis	17 (11.3)	0 (0)	17 (13.7)	0.004
Anastomotic problems	12 (8.0)	1 (3.8)	11 (8.9)	
Acute appendicitis	8 (5.3)	0 (0)	8 (6.5)	
Bleeding <sup>a)</sup>	7 (4.7)	2 (7.7)	5 (4.0)	
Hernia	3 (2.0)	0 (0)	3 (2.4)	
Others <sup>b)</sup>	11 (7.3)	1 (3.8)	10 (8.1)	

Values are presented as number (%).

<sup>a)</sup>Upper gastrointestinal (n=4), intra-abdominal (n=3); <sup>b)</sup>diagnostic laparotomy/laparoscopy (n=8), acute pancreatitis/gastrointestinal foreign body/invagination in each.

**Table 5.** Distribution of surgical procedures in the study group

Type of operation	n (%)
Intestinal resection with ostomy formation	31 (20.7)
Intestinal resection with anastomosis	22 (14.7)
Cholecystectomy	17 (11.3)
Diagnostic laparoscopy/laparotomy	16 (10.7)
Primary suturing	16 (10.7)
Ostomy formation	15 (10.0)
Adhesiolysis	10 (6.7)
Appendectomy	8 (5.3)
Others <sup>a)</sup>	15 (10.0)

<sup>a)</sup>Diagnostic laparoscopy/laparotomy, drainage, hemostasis, embolectomy, splenectomy, necrosectomy, hernia repair, and antrectomy.

tween the two groups (Table 3). Lower albumin values were significantly associated with the development of mortality ( $p < 0.001$ ). Non-survivors had significantly higher white blood cell (WBC) counts and glucose, creatinine, and C-reactive protein (CRP) values ( $p = 0.003$ ,  $p = 0.013$ ,  $p < 0.001$ , and  $p < 0.001$ , respectively). The median neutrophil-to-lymphocyte ratio (NLR) values differed significantly between the non-survivor and survivor groups (9.65 vs. 4.8;  $p < 0.001$ ).

We observed significant associations between the diseases requiring surgical treatment and the development of mortality ( $p = 0.004$ ) (Table 4). Perforation was detected in 61.6% of the non-survivors compared to 22.6% of the survivors. No patients with acute cholecystitis or appendicitis died. Intestinal obstruction was more frequently observed in survivors (22.6% vs. 7.7%, respectively). The disease-related mortality rates for perforation, bleeding (intra-abdominal or gastrointestinal), and mesenteric ischemia were 36.4%, 28.6%, and 22.2%, respectively. The distribution of the most frequently performed surgical procedures is presented in Table 5.

The overall morbidity rate was 52%, with a significant difference

between groups (100% vs. 41.9%, respectively;  $p < 0.001$ ). The median operation times differed significantly between non-survivors and survivors (118 vs. 85 minutes;  $p = 0.001$ ). Although the length of hospital stay was shorter in non-survivors than in the survivors ( $p = 0.027$ ), the length of the ICU stay was significantly longer in non-survivors ( $p < 0.001$ ).

Overall, 184 complications occurred in 77 patients (51.3%). In other words, 73 patients (48.7%) had no complications. Surgical site infection and renal failure were the most common complications. Cardiac complications were observed only in patients who died. The types of complications are detailed in Table 6.

The univariate regression analysis identified frailty status, shock, and ASA grade as significant risk factors for mortality. In the multivariate regression analysis, ASA grade was the only independent risk factor for mortality (odds ratio = 19.642; 95% confidence interval, 3.886–99.274;  $p < 0.001$ ) (Table 7).

## DISCUSSION

The present retrospective study examined the effect of clinical factors and preoperative frailty on morbidity and mortality following emergency abdominal surgery in older patients. We found that 17.3% of patients died within 30 days of surgery. Older patients who were obese and frail with higher ASA grades were the most vulnerable to mortality following emergency abdominal surgery.

Given the increasing incidence of older patients requiring emergency laparotomy, there is an urgent need for a detailed understanding of the outcomes after this surgery because of the higher risks of mortality.<sup>2)</sup> Consistent with previous studies,<sup>2,10,12,18,19)</sup> the most significant predictors for mortality in the present study were age, ASA grade, frailty status, and presence of septic shock. It was not unexpected that these variables were associated with death as they represent the degree of preoperative physiological derange-

**Table 6.** Distribution of complications in the study groups

Complication	Overall (n = 150)	Non-survivors (n = 26)	Survivors (n = 124)
SSI	45 (24.5)	11 (12.5)	34 (35.4)
ARF	30 (16.3)	11 (12.5)	19 (19.8)
Sepsis	23 (12.5)	20 (22.7)	3 (3.1)
Respiratory	20 (10.9)	4 (4.5)	16 (16.7)
Cardiac	16 (8.7)	16 (18.2)	0
UTI	14 (7.6)	1 (1.1)	13 (13.5)
Bleeding	11 (6.0)	8 (9.1)	3 (3.1)
Evisceration	10 (5.4)	8 (9.1)	2 (2.1)
Anastomotic leakage	8 (4.3)	4 (4.5)	4 (4.2)
Stoma related	7 (3.8)	5 (5.7)	2 (2.1)
Total	184	88	96

Values are presented as number (%).

SSI, surgical site infections; ARF, acute renal failure; UTI, urinary tract infection.

**Table 7.** Results of univariate and multivariate logistic regression analyses for mortality

Variable	Univariate				Multivariate			
	OR	95% CI		p-value	OR	95% CI		p-value
		Lower	Upper			Lower	Upper	
Age ( $\geq 75$ vs. 65–74 y)	0.005	-0.098	0.105	0.943	0.772	0.115	5.193	0.790
BMI	0.080	-0.004	0.018	0.198	1.157	0.950	1.409	0.148
Hypertension (yes vs. no)	-0.038	-0.132	0.071	0.553	0.711	0.134	3.773	0.689
CAD (yes vs. no)	0.102	-0.021	0.229	0.101	3.400	0.723	15.976	0.121
Frailty (yes vs. no)	0.158	0.022	0.305	0.024	1.806	0.340	9.589	0.487
Septic shock (yes vs. no)	0.268	0.165	0.475	< 0.001	4.040	0.499	32.723	0.191
ASA grade	0.415	0.110	0.227	< 0.001	19.642	3.886	99.274	< 0.001

BMI, body mass index; CAD, coronary artery disease; ASA, American Society of Anesthesiologists; OR, odds ratio; CI, confidence interval.

ment. Although there are controversial findings regarding the effect of advancing age on mortality, the mortality rates in the present study were higher in older patients aged  $\geq 75$  years. Thus, like other investigators,<sup>2,3,9,10,20</sup> we recommend considering patient age in the decision-making process for emergency abdominal surgery in older patients.

The results of multivariate regression analysis in the present study identified ASA grade as the only independent risk factor for mortality. Although this finding was contrary to those of other studies in which the ASA grade was not associated with mortality after emergency colectomy,<sup>21,22</sup> this may be due to differences in population characteristics. Due to the possible reciprocal relationships between aging and morbidity, it is difficult to determine the specific effect of each factor on mortality. With increasing age, patients are more likely to have comorbidities and experience polypharmacy.<sup>19,23</sup> Hypertension and CAD were significant risk factors for the development of mortality in the present study. Therefore, physicians should be aware of the higher risk of adverse events leading to mortality in older patients with hypertension and CAD.

Frailty has been studied as a preoperative risk assessment variable to identify high-risk patients for mortality.<sup>3,19,24</sup> Although there is no universal definition of frailty, it may be defined as a phenotype that includes any combination of unintentional weight loss, self-reported exhaustion, grip strength weakness, slow walking speed, and low physical activity.<sup>4</sup> However, not all frail patients are old; thus, frailty can be considered a risk factor independent of age.<sup>23,24</sup> Different scales or indices have been developed to assess frailty.<sup>4,6,17,23</sup> Many of these tools evaluate phenotypic measures such as physical strength, speed, activity, nutritional status, and fatigue. The main advantage of the mFI-11 is its comorbidity-dominant scoring system.<sup>6</sup> Because of the present study's retrospective design and unavailability of data to measure these phenotypic measures, we used the mFI-11 to assess frailty status. However, the clinical significance of each system has not been proven satisfactorily, and more research is needed to determine the optimum frailty assessment tool.

Previous studies have reported significant associations between frailty and several outcomes such as mortality, increased risk of

complications, and length of hospital stay in older patients undergoing emergency laparotomy.<sup>3,17,18</sup> Frailty is also considered an independent risk factor for readmissions and post-discharge deaths. In the present study, frailty was also a significant risk factor for inpatient mortality during the postoperative 30 days. This result may be due to the use of the mFI-11 scale, which is a comorbidity-dominant scoring system.<sup>6</sup> The results of the present study showed that higher ASA grades were significantly associated with mortality. Additionally, hypertension and CAD were predictive factors for mortality. Therefore, both the number and severity of comorbid diseases associated with frailty were crucial variables for the development of mortality in this patient group.

Multi-dimensional phenotypic manifestations of frailty, such as physical strength, walking speed, activity, nutritional status, and fatigue, could be better indicators of the physiological reserve. However, owing to the retrospective design of the present study, it was not possible to collect such data. The most common indication for surgical treatment in the present study was gastrointestinal perforation. Various etiological causes have been attributed to gastrointestinal perforation in different study populations, such as bowel obstruction secondary to cancer or adhesions.<sup>19</sup> Although the mortality rates vary based on the diagnoses, peritonitis is generally regarded as the most severe intra-abdominal pathology associated with high mortality rates.<sup>19</sup> However, we did not evaluate peritonitis as a separate diagnostic category in this study because there is some degree of subjectivity in grading peritonitis and the condition can result from various etiologies, such as perforation and ischemia.

The major limitation of the present study was that it assessed only 30-day mortality and did not include 90-day mortality. The other limitations were the use of data from a single-center, retrospective design, lack of standardization for postoperative care protocols, and relatively small sample size.

In conclusion, older patients with obesity and frailty with higher ASA grades and septic shock had worse survival following emergency abdominal surgery. Early recognition of these high-risk groups necessitates dedicated and detailed follow-up after emergency abdominal surgery.

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### CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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None.

## AUTHOR CONTRIBUTION

Conceptualization, NAH, AA; Data curation, YA, SM; Investigation, NAH, YU, MT, GE; Methodology, NAH, YU, MT, GE; Writing-original draft, NAH, TVA, OK; Writing-review & editing, NAH, AA, YU, TVA, SM, MT, OK, GE, YA.

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# Utilization of Digoxin among Hospitalized Older Patients with Heart Failure and Atrial Fibrillation in Thailand: Prevalence, Associated Factors, and Clinical Outcomes

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**Background:** Digoxin is used to control heart rate in patients with heart failure (HF) and atrial fibrillation (AF). However, its use is often limited in older patients, as they are prone to digoxin toxicity. This study aimed to determine the prevalence of digoxin use, investigate the factors associated with digoxin use, and explore the association between digoxin use and clinical outcomes in older Thai patients with HF and AF. **Methods:** This cross-sectional study used data obtained from an electronic medical records database. We performed logistic regression analysis to determine the prevalence of digoxin use at index discharge and the factors associated with its use. The Cox proportional hazard model was used to determine the association of all-cause mortality and HF rehospitalization with digoxin use. **Results:** Of the 640 patients assessed, 107 (16.72%) were prescribed digoxin before discharge. The factors negatively associated with digoxin use included high serum creatinine level (adjusted odds ratio [AOR]=0.38; 95% confidence interval [CI], 0.22–0.65) and ischemic heart disease (IHD) (AOR=0.52; 95% CI, 0.30–0.88). The factors positively associated with digoxin use were the use of diuretics (AOR=2.65; 95% CI, 1.60–4.38) and mineralocorticoid receptor antagonists (MRAs) (AOR=2.24; 95% CI, 1.18–4.27). We observed no significant association between digoxin use and clinical outcomes (adjusted hazard ratio=1.00; 95% CI, 0.77–1.30). **Conclusion:** Digoxin use was prevalent among older patients with HF and AF. Patients with high serum creatinine or IHD were less likely to be prescribed digoxin, whereas those using diuretics or MRAs were more likely to be prescribed digoxin. Although digoxin use was not uncommon among older patients, it was prescribed with caution among Thai patients hospitalized with HF and AF.

**Key Words:** Frail older adults, Prevalence, Drug utilization, Digoxin, Heart failure, Atrial fibrillation

## INTRODUCTION

Atrial fibrillation (AF) typically coexists with heart failure (HF), especially in older adults. The coexistence of both conditions at the time of discharge from the hospital is frequently reported among hospitalized older adults.<sup>1,2)</sup> The prevalence of AF among

patients with HF increases with age.<sup>1,3)</sup> A report on older Thai patients (mean age, 64 ± 14 years) hospitalized for acute HF revealed that 24.1% had a history of AF.<sup>4)</sup> Additionally, combined HF and AF occurred in 20.8% of patients aged ≥ 65 years.<sup>5)</sup> The coexistence of both conditions in older adults was not only associated with increased adverse outcomes such as mortality, hospitalization,

and healthcare costs<sup>4,5)</sup> but also necessitated complicated pharmacological therapies.<sup>1)</sup>

Digoxin is a therapeutic agent used for the treatment of HF and AF. Its use is dependent on the type of HF. HF is classified by ejection fraction (EF) as HF with reduced EF (HFrEF) (EF < 40%), HF with mid-range EF (HFmrEF) (EF 41%–49%), and HF with preserved EF (HFpEF) (EF ≥ 50%). In the treatment of HF alone, digoxin is recommended as an add-on therapy in symptomatic patients with HFrEF to reduce HF-related hospitalization but is not recommended for use in patients with HFmrEF and HFpEF due to a lack of clinical benefit.<sup>6-8)</sup> However, digoxin still plays an important role in AF therapy in patients with HF. In the treatment of AF in these patients, the three common therapeutic agents recommended for heart rate control are beta-blockers (BBs), non-dihydropyridine calcium channel blockers (non-DHP CCBs), and digoxin.<sup>9-11)</sup> While any of these three options can be used in patients with HFmrEF and HFpEF, non-DHP CCBs are contraindicated in patients with HFrEF.<sup>9,11)</sup> Although BBs and non-DHP CCBs are considered first-line therapy, their synergistic negative inotropic effect on the heart is a significant clinical concern for older adults, who are vulnerable to this effect. Avoidance of non-DHP CCBs is also recommended for patients with severe HF.<sup>12)</sup> Thus, digoxin has become an alternative treatment choice for older patients with both HF and AF, resulting in its broad prescription in clinical practice.

The prevalence of digoxin use in previous studies varied depending on the study population. Digoxin was more likely to be prescribed to patients with HF and AF than to patients with HF alone. For example, prevalence rates of 20.84%<sup>13)</sup> and 11.0%<sup>14)</sup> were reported in patients with HF with and without AF, respectively. This is because digoxin is used as an add-on therapy in HFrEF but is used as mainstream therapy in AF. Nevertheless, digoxin use is not considered to be highly prevalent in patients with both conditions. Advanced age and renal function are important factors that limit the use of digoxin in clinical practice because they are associated with an increased risk of digoxin toxicity that is common among older patients and patients with impaired renal function.

Among clinical outcomes, a randomized trial demonstrated the relationship between digoxin treatment and decreased risk of rehospitalization in HFrEF patients without concurrent AF<sup>15)</sup> and that the relationship was not age-dependent.<sup>16)</sup> However, the clinical benefits of digoxin for older adults with both HF and AF remain controversial. Both post-hoc analyses of randomized controlled trials (RCTs)<sup>17-19)</sup> and well-designed observational studies<sup>13,20-25)</sup> have reported conflicting evidence on the risk-benefit profile of digoxin. Some studies observed an association of digoxin and increased risk of mortality in AF patients with or without HF.<sup>17-20)</sup> Conversely, several other studies did not report such find-

ings.<sup>13,21-25)</sup> Recently, studies in Asians have evaluated the safety and benefits of digoxin use in older patients.<sup>26,27)</sup> A study in Taiwan showed that digoxin use was related to increased ischemic stroke and mortality in AF patients without HF but not in those with HF.<sup>26)</sup> Another study in China found that digoxin use was related to an increased likelihood of mortality and rehospitalization in HFrEF patients with or without AF.<sup>27)</sup> These results varied according to differences in the prevalence of digoxin use and outcomes in each clinical setting.

In Thailand, the national HF guidelines suggest the use of digoxin as a therapeutic agent for heart rate control in patients with HF and coexisting AF.<sup>9)</sup> However, the prescribing rate, contributing factors, and clinical outcomes of digoxin use in older adults with both conditions have not been reported. Thus, the primary objective of the present study was to determine the prevalence and identify factors associated with digoxin use. The secondary objective was to explore the association between digoxin treatment and clinical outcomes.

## MATERIALS AND METHODS

### Study Design and Settings

This cross-sectional study included data on patients diagnosed with both HF and AF, which were obtained from the electronic medical records (EMR) database of a tertiary care teaching urban hospital (a 1,100-bed public hospital) in Phitsanulok Province. The study hospital is an academic referral center for the lower northern region of Thailand. The EMR database included patient demographics, clinical characteristics, and medication information. At the time of the study, well-trained hospital staff entered patient information into the EMR database.

The research protocol was approved by the Research Ethics Committee of Buddhachinaraj Hospital (IRB No. 067/63, Approval data: March 26, 2020) before retrieval of patient data.

### Subjects

The analysis included patients aged ≥ 60 years (based on a definition of “older adult” of 60 years)<sup>28)</sup> and diagnosed with HF and AF who were hospitalized for HF for the first time between January 2014 and December 2018 (defined as the patient’s index hospitalization). Patients were identified as having HF and AF using the following International Statistical Classification of Disease and Related Health Problems 10th Revision (ICD-10) codes: I50.0, I50.1, or I50.9 (for HF) and I48.0 (for AF). Patients with serum creatinine concentrations > 3 mg/dL or serum potassium concentrations < 3.2 or > 5.5 mEq/L were excluded from the analysis.

Among the eligible patients discharged alive, those who were

prescribed oral digoxin at index predischARGE were assigned to the exposed group (i.e., patients treated with digoxin). The remaining patients were assigned to the unexposed group (i.e., patients not treated with digoxin). The patients in the unexposed group were examined for digoxin prescription post-discharge to ensure that none were exposed to digoxin during the follow-up period. Both patient groups were followed up until December 10, 2020, for clinical outcome measurement.

### Data Collection

All study factors and outcomes were obtained from the EMR database. The study factors were categorized as patient demographics, including sex and age (calculated on the index date of admission); clinical characteristics, including echocardiogram results, last laboratory findings, length of stay (LOS); cardiovascular (CV) comorbidities and comorbidity score calculated using the Charlson Comorbidity Index (CCI);<sup>29,30</sup> and discharge medication lists. Data on disease severity (e.g., New York Heart Association [NYHA] classification or brain natriuretic peptide [BNP] level) were not routinely recorded in the EMR database. As one study suggested that LOS, which might indicate HF severity or complex conditions, was a positive predictor of rehospitalization,<sup>31</sup> we used this factor to determine HF severity in this study. All medications used for the treatment of AF and HF were identified using the drug codes of the study hospital.

### Definitions of Clinical Outcomes

The primary outcome was a composite outcome of all-cause mortality and HF rehospitalization occurring after the index discharge. The primary discharge diagnosis, which was defined based on ICD-10 codes related to HF diagnoses (I50.0, I50.1, or I50.9), was used to identify HF rehospitalization. The cause of death, which was recorded in the database, was used to identify in-hospital deaths from any cause. The secondary outcomes were all-cause mortality and HF rehospitalization. Digoxin toxicity was identified according to ICD-10 code T46.0.

### Statistical Analysis

Continuous variables with normal distribution were presented as mean  $\pm$  standard deviation, and independent sample t-tests were used for comparisons between patient groups. Continuous variables with non-normal distribution were presented as median and interquartile range (IQR), and Mann-Whitney U tests were used for between-group comparisons. Categorical variables were presented as frequencies and percentages, and either the chi-square test or Fisher exact test was used for between-group comparisons, as appropriate.

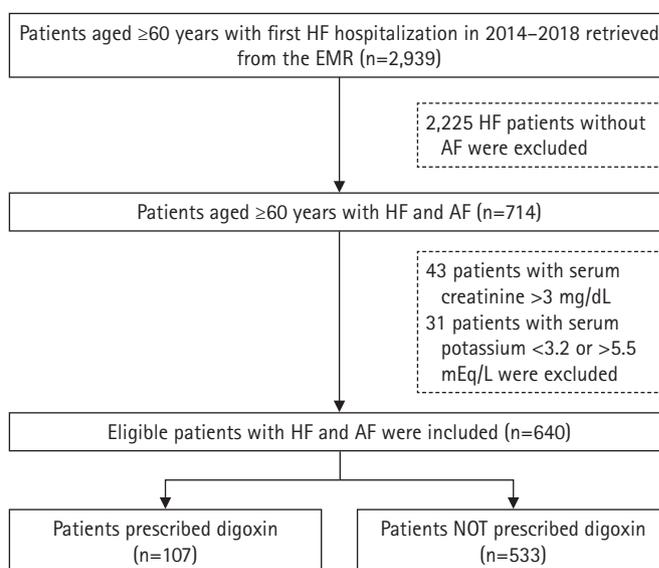
The prevalence of digoxin use was calculated by dividing the number of patients who were prescribed digoxin by the total number of patients and presented as a percentage (%). To determine the factors affecting digoxin prescription, we performed univariable and multivariable binary logistic regression analyses and calculated crude odds ratios (ORs), adjusted ORs, and 95% confidence intervals (CIs). In univariate analysis, we selected factors with  $p < 0.1$  for multicollinearity tests. In the multicollinearity tests, in which independent variables in a binary logistic regression model are highly correlated, we excluded factors with a variance inflation factor (VIF)  $> 10$ .<sup>32</sup> In the multivariate analysis, we applied the backward elimination method, in which the least significant variable was discarded at each step until all remaining variables in the model reached a significance level of  $\leq 0.05$ .

We also assessed clinical outcomes, including all-cause mortality and rehospitalization due to HF, and calculated hazard ratios (HRs) using the Cox proportional hazards model between patients treated and not treated with digoxin. The cohorts were adjusted using the most frequently reported factors associated with all-cause mortality and rehospitalization due to HF, including sex, age, comorbidity score, and LOS. All analyses were conducted using Stata release 14.0 (Stata Corporation, College Station, TX, USA). Statistical significance was set at  $p < 0.05$ . All p-values were two-tailed.

## RESULTS

### Patient Characteristics

From the EMR database, we included a total of 640 older adults with HF and AF (Fig. 1). Characteristics of the total patient group,



**Fig. 1.** Flowchart showing the process of data retrieval. HF, heart failure; EMR, electronic medical records; AF, atrial fibrillation.

patients treated with digoxin, and those not treated with digoxin are shown in Table 1. Overall, the average age of the patients was  $74.42 \pm 8.23$  years and they were mostly female (55.62%). Among patients with EF (46.72%), almost three-fourths had an EF  $\geq 40\%$ . The mean serum potassium and serum creatinine concentrations were  $3.9 \pm 0.42$  mmol/L and  $1.25 \pm 0.50$  mmol/L, respec-

tively.

The most frequently reported cardiovascular comorbidity was hypertension, followed by dyslipidemia and ischemic heart disease (IHD). Almost all patients (93.44%) were treated with oral anti-coagulants (OACs), and BBs were the primary agents used to control heart rate. Among HF medications, 44.84%, 36.57%, and

**Table 1.** Characteristics of all patients with heart failure and atrial fibrillation

Characteristic	Total patients (n = 640)	Patients treated with digoxin (n = 107)	Patients not treated with digoxin (n = 533)	p-value
<b>Demographics</b>				
Sex, male	284 (44.38)	42 (39.25)	242 (45.40)	0.243
Age (y)	$74.42 \pm 8.23$	$72.94 \pm 7.75$	$74.71 \pm 8.33$	0.044
$\geq 80$	193 (30.16)	24 (22.43)	169 (31.71)	0.058
<b>Clinical characteristics</b>				
EF <sup>a)</sup> (%)	$53.97 \pm 18.84$	$51.44 \pm 18.15$	$54.54 \pm 18.98$	0.271
HF with EF				0.666
HF <sub>r</sub> EF (EF < 40%)	84 (28.09)	17 (30.91)	67 (27.46)	
HF <sub>m</sub> rEF (EF 40%–49%)	31 (10.37)	4 (7.27)	27 (11.07)	
HF <sub>p</sub> EF (EF $\geq 50\%$ )	184 (61.54)	34 (61.82)	150 (61.48)	
Serum sodium (mmol/L)	$138.28 \pm 4.58$	$137.83 \pm 4.79$	$138.37 \pm 4.53$	0.266
Serum potassium (mmol/L)	$3.90 \pm 0.42$	$3.89 \pm 0.40$	$3.90 \pm 0.42$	0.920
Serum creatinine (mg/dL)	$1.25 \pm 0.50$	$1.08 \pm 0.36$	$1.28 \pm 0.52$	< 0.001
eGFR (mL/min)	$56.19 \pm 22.54$	$62.76 \pm 19.67$	$54.87 \pm 22.86$	0.001
LOS (day)	6 (3–10)	5 (4–9)	6 (3–10)	0.532
> 5	331 (51.72)	53 (49.53)	278 (52.16)	0.620
<b>Cardiovascular comorbidities</b>				
Hypertension	278 (43.44)	41 (38.32)	237 (44.47)	0.242
Dyslipidemia	198 (30.94)	27 (25.23)	171 (32.08)	0.163
Ischemic heart disease	189 (29.53)	21 (19.63)	168 (31.52)	0.015
Diabetes mellitus	157 (24.53)	24 (22.43)	133 (24.95)	0.580
Chronic kidney disease	50 (7.81)	5 (4.67)	45 (8.44)	0.192
Stroke	12 (1.88)	1 (0.93)	11 (2.06)	0.444
Comorbidity score $\geq 2$	350 (54.69)	53 (49.53)	297 (55.72)	0.015
Comorbidity score	2 (1–2)	1 (1–2)	2 (1–2)	0.241
<b>HF medications</b>				
OACs	598 (93.44)	107 (100.00)	491 (92.12)	0.003
Diuretics	391 (61.09)	83 (77.57)	308 (57.79)	< 0.001
BBs	287 (44.84)	43 (40.19)	244 (45.78)	0.289
ACEIs	172 (26.88)	37 (34.58)	135 (25.33)	0.050
ARBs	62 (9.69)	14 (13.08)	48 (9.01)	0.196
MRAs	51 (7.97)	18 (16.82)	33 (6.19)	< 0.001
Nitrates	50 (7.81)	7 (6.54)	43 (8.07)	0.592
DHP CCBs	41 (6.41)	4 (3.74)	37 (6.94)	0.224
Hydralazine	30 (4.69)	2 (1.87)	28 (5.25)	0.149
Non-DHP CCBs	18 (2.81)	5 (4.67)	13 (2.44)	0.210

Values are presented as number (%) or mean  $\pm$  standard deviation or median (interquartile range).

HF<sub>r</sub>EF, heart failure with reduced ejection fraction; HF<sub>m</sub>rEF, heart failure with mid-range ejection fraction; HF<sub>p</sub>EF, heart failure with preserved ejection fraction; eGFR, estimated glomerular filtration rate; LOS, length of stay; OACs, oral anticoagulants; BBs, beta-blockers; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor blockers; CCBs, calcium channel blockers; MRAs, mineralocorticoid receptor antagonists.

<sup>a)</sup>Data were available for 55 and 244 patients with and without digoxin, respectively.

7.97% of the patients were receiving BBs, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs), and mineralocorticoid receptor antagonists (MRAs), respectively.

### Prevalence and Associated Factors of Digoxin Use

Our review of the index discharge medication lists of all study patients showed that 107 patients (16.72%) were prescribed oral digoxin at the index hospital discharge. The prevalence rate of digoxin use in patients with EF < 40%, with EF ≥ 40%, and with no EF were 20.24%, 17.67%, and 15.25%, respectively. Among patients treated with digoxin, most (90.65%) received oral digoxin at a daily dose of 0.125 mg, and only a few received a daily dose of 0.0625 mg and 0.250 mg (4.67% each).

The results of univariate and multivariate analyses are shown in Table 2. In the univariate analysis, the factors negatively associated with digoxin use included older age (crude OR = 0.97; 95% CI, 0.95–0.99), higher serum creatinine (crude OR = 0.37; 95% CI, 0.22–0.62), IHD (crude OR = 0.53; 95% CI 0.32–0.88), and higher CCI (crude OR = 0.74; 95% CI, 0.59–0.95). The factors positively associated with digoxin use were higher estimated glomerular filtration rate (eGFR) (crude OR = 1.02; 95% CI, 1.01–1.03), use of diuretics (crude OR = 2.53; 95% CI, 1.55–4.11), and use of MRAs (crude OR = 3.06; 95% CI, 1.65–5.68).

In the multivariate analysis, the factors negatively associated with digoxin use included higher serum creatinine (adjusted OR = 0.38; 95% CI, 0.22–0.65) and IHD (adjusted OR = 0.52; 95% CI, 0.30–0.88). The two medication classes positively associated with digoxin use were diuretics and MRAs (adjusted OR = 2.65; 95% CI, 1.60–4.38 and adjusted OR = 2.24; 95% CI, 1.18–4.27, respectively).

### Relationships between Digoxin Treatment and Clinical Outcomes

The results of the analysis of the associations between digoxin treatment and clinical outcomes are shown in Table 3. The study outcomes occurred in 413 patients (64.53%) during a median follow-up period of 4.7 (IQR 3.3–5.8) years. In an unadjusted analysis, we observed no statistically significant decrease in the risk of the primary outcome among patients treated with digoxin compared to the risk in those who did not receive digoxin (HR = 0.91; 95% CI, 0.70–1.18). Patients treated with digoxin had a longer mean survival time (850 ± 69 vs. 789 ± 30 days; *p* = 0.414). In addition, we observed no statistically significant association after adjusting for sex, age, comorbidity score, and LOS (adjusted HR = 1.00; 95% CI, 0.77–1.30) (Fig. 2).

Among the secondary outcomes, all-cause mortality and rehospitalization due to HF occurred in 372 (58.13%) and 139 (21.72%) patients, respectively. In the univariate analysis, we observed no statistically significant decreases in the risks of all-cause mortality (crude HR = 0.91; 95% CI, 0.70–1.83) and rehospitalization due to HF (crude HR = 0.99; 95% CI, 0.64–1.53) in patients treated with digoxin compared to those in patients who did not receive this treatment. After controlling for pre-specified covariates, the association remained the same for all-cause mortality (adjusted HR = 1.02; 95% CI, 0.77–1.35) and rehospitalization due to HF (crude HR = 0.96; 95% CI, 0.62–1.50).

A subgroup analysis performed according to EF categories showed that treatment with digoxin was not significantly associated with the primary outcome in patients with EF < 40% and in patients with EF ≥ 40% (adjusted HR = 0.87; 95% CI, 0.43–1.76; *p* = 0.692 and adjusted HR = 1.10; 95% CI, 0.71–1.71; *p* = 0.669, respectively). Similarly, we observed no statistically significant association between treatment with digoxin and all-cause mortality

**Table 2.** Results of univariable and multivariable analyses for the identification of study factors associated with digoxin treatment

Study factors <sup>a)</sup>	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age (y)	0.97 (0.95–0.99)	0.044		
Age, ≥ 80 y	0.62 (0.38–1.02)	0.058		
Serum creatinine (mg/dL)	0.37 (0.22–0.62)	< 0.001	0.38 (0.22–0.65)	< 0.001 <sup>b)</sup>
eGFR (mL/min)	1.02 (1.01–1.03)	0.001		
Ischemic heart disease	0.53 (0.32–0.88)	0.015	0.52 (0.30–0.88)	0.015 <sup>b)</sup>
Comorbidity score	0.74 (0.59–0.95)	0.015		
Diuretics	2.53 (1.55–4.11)	< 0.001	2.65 (1.60–4.38)	< 0.001 <sup>b)</sup>
ACEIs	1.56 (0.99–2.42)	0.050		
MRAs	3.06 (1.65–5.68)	< 0.001	2.24 (1.18–4.27)	0.014 <sup>b)</sup>

OR, odds ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate; ACEIs, angiotensin-converting enzyme inhibitors; MRAs, mineralocorticoid receptor antagonists.

<sup>a)</sup>Factors with p-value < 0.1 were included in the multivariable model.

<sup>b)</sup>After adjusting for serum creatinine, ischemic heart disease, diuretics, and MRAs in the adjusted model with a mean variance inflation factor of 1.83.

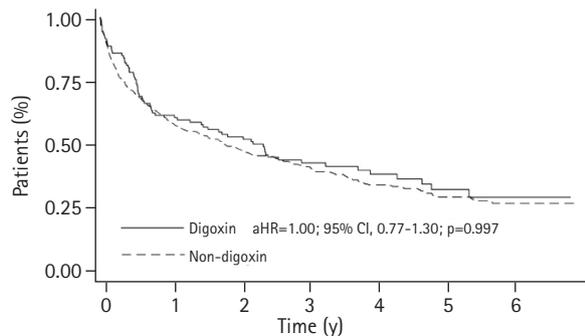
**Table 3.** Results of the analysis of associations between digoxin treatment and clinical outcomes

Study outcomes	Crude HR (95% CI)	p-value	Adjusted HR <sup>a)</sup> (95% CI)	p-value
All-cause mortality and HF rehospitalization				
All patients	0.91 (0.70–1.18)	0.484	1.00 (0.77–1.30)	0.997
EF <sup>b)</sup> < 40%	0.76 (0.38–1.50)	0.422	0.87 (0.43–1.76)	0.692
EF ≥ 40%	1.15 (0.75–1.76)	0.521	1.10 (0.71–1.71)	0.669
All-cause mortality				
All patients	0.91 (0.70–1.83)	0.507	1.02 (0.77–1.35)	0.874
EF < 40%	0.79 (0.39–1.64)	0.533	0.92 (0.43–1.94)	0.822
EF ≥ 40%	1.06 (0.67–1.68)	0.813	1.09 (0.68–1.74)	0.730
HF rehospitalization				
All patients	0.99 (0.64–1.53)	0.963	0.96 (0.62–1.50)	0.872
EF < 40%	0.95 (0.35–2.57)	0.924	0.99 (0.35–2.74)	0.979
EF ≥ 40%	1.04 (0.48–2.23)	0.923	0.82 (0.38–1.80)	0.628

HR, hazard ratio; CI, confidence interval; HF, heart failure; EF, ejection fraction.

<sup>a)</sup>When controlling for sex, age, comorbidity score, and length of stay.

<sup>b)</sup>EF data were available for 84 and 215 patients with EF <40% and ≥40%, respectively.



Number at risk							
Digoxin	533	318	257	172	100	57	21
Non-digoxin	107	66	57	35	24	14	5

**Fig. 2.** Kaplan-Meier survival plot of all-cause mortality and heart failure rehospitalization according to digoxin prescription. aHR, adjusted hazard ratio; CI, confidence interval.

and HF rehospitalization in patients with EF < 40% and EF ≥ 40% (Table 3).

## DISCUSSION

The safety of digoxin treatment for heart rate control in older patients with HF and AF has been questioned due to its adverse clinical effects, including mortality, hospitalization, and digoxin toxicity. Given the safety concerns in this population, direct evidence on digoxin treatment among older Thai patients with both conditions is required to understand digoxin use in real-world clinical practice. Our results indicated that digoxin use was relatively prevalent. Both positively and negatively associated factors contributed to the use of digoxin. However, we observed no sta-

tistically significant association between adverse clinical outcomes and digoxin use.

Despite advances in procedure-based AF therapies, pharmacological therapy still plays a major role in controlling the heart rate in AF treatment. The results of the present study revealed that BBs and digoxin were the primary agents for heart rate control in the study cohort, with 44.84%, 16.72%, and 6.72% of patients receiving BBs, digoxin, and a combination of both agents, respectively, whereas only 2.81% of patients received non-DHP CCBs (verapamil and diltiazem). According to the AF status in HF guidelines, either BBs, digoxin, or a combination can be used in all HF types (EF < 40% and ≥ 40%), while non-DHP CCBs should be avoided in patients with EF < 40%.<sup>9)</sup> Less than half of the patients (46.72%) in this study had known EF, with 28.09% and 71.91% having EF < 40% and EF ≥ 40%, respectively. These data suggested that BBs and digoxin were safer than non-DHP CCBs for older patients with known and unknown EF. Additionally, the combination of BBs and non-DHP CCBs is inappropriate for older patients with EF ≥ 40% because of their negative inotropic effect, which is high among these patients.<sup>12)</sup> This is why digoxin is the second choice of therapeutic agent for heart rate control in older patients with HF and AF.

The prevalence of digoxin use in our study was slightly lower than that reported previously (16.72% vs. 20.84%).<sup>13)</sup> Although we excluded patients with a contraindication to digoxin use (serum creatinine concentration > 3 mg/dL or serum potassium concentration < 3.2 or > 5.5 mEq/L), we identified other factors contributing to digoxin. Patients with higher serum creatinine concentration or IHD were less likely to be treated with digoxin, whereas patients receiving diuretics or MRAs were more likely to be treated

with digoxin. Digoxin might not be considered for patients with increasing serum creatinine levels, which indicates worse renal function and a susceptibility to digoxin toxicity.<sup>33</sup> IHD may deteriorate due to the positive inotropic effect of digoxin. In addition, a recent study indicated that digoxin therapy was associated with an increased risk of all-cause and cardiovascular death in patients with ischemic heart failure.<sup>34</sup> Two medication classes were positively associated with digoxin use, including diuretics and MRAs. Current HF guidelines suggest digoxin as an adjunct to medical therapy for HF<sub>r</sub>EF; thus, digoxin may have been additionally prescribed in HF<sub>r</sub>EF patients receiving diuretics or MRAs, indicating persistent symptoms.<sup>9-11</sup> In addition to the previously mentioned factors, the low prevalence of digoxin use may be related to the clinicians' perception of increased mortality risk associated with digoxin use, as reported in previous studies.<sup>17-20</sup>

Among adverse clinical impacts of digoxin use, we observed no occurrence of digoxin toxicity in patients treated with digoxin. This is because most of the patients in our study were administered a daily dose of 0.125 mg, which is the recommended oral digoxin dose for older patients with HF.<sup>12</sup> We observed no significant relationship between digoxin treatment and all-cause mortality and HF rehospitalization in either unadjusted or adjusted analyses. Our study findings were consistent with those of previous studies that reported statistically insignificant results.<sup>13,21-25</sup> A retrospective propensity-matched analysis of a randomized trial found no evidence of increased mortality or hospitalization in patients with paroxysmal and persistent AF who received digoxin as baseline initial therapy.<sup>21</sup> In another observational propensity-matched study conducted by Singh et al.,<sup>13</sup> the authors reported that digoxin initiation was not positively related to mortality and HF readmission in hospitalized older patients with HF (HF<sub>r</sub>EF and HF<sub>p</sub>EF) and AF. Likewise, a previous study using data obtained from real clinical settings found no effect of digoxin use on mortality in AF patients with HF.<sup>23</sup> Although these observational studies applied several methods for controlling potential confounding factors, including propensity matching, multivariable adjustment, and stratified analysis, they did not consider disease severity or other issues related to clinical outcomes, which is an important limitation. Nevertheless, recent data from systematic reviews and meta-analyses support the continued use of digoxin as a heart rate control treatment for older patients.<sup>35</sup>

In clinical practice in Thailand, the decision to prescribe digoxin depends on the patient's characteristics as well as the physician's experience. Despite the lack of statistical significance, patients treated with oral digoxin were likely to have a longer survival time compared to those who did not receive digoxin. The current AF guidelines recommend digoxin as a second-line therapeutic agent for

heart rate control.<sup>9,11</sup> Our findings extend the knowledge that oral digoxin treatment for older patients with both HF and AF is safe when used at a proper dose ( $\leq 0.125$  mg/day).

This study has some limitations. First, this was a single-center study of a limited number of patients. Therefore, these findings cannot be generalized to other hospitals as the patient characteristics and prescribing patterns might vary. Although we tried to include all eligible patients, our sample size was adequate only for the primary objective and not the secondary objective. Second, we lacked data on HF severity (e.g., NYHA or BNP) and clinical status (e.g., heart rate, systolic blood pressure, diastolic blood pressure), which are potential factors associated with both digoxin prescription and clinical outcomes. Third, unlike RCTs, this observational study could not entirely explain the causal relationship because digoxin treatment was not randomly assigned to the patients. Although we adjusted for the difference in baseline characteristics between the two groups, the associations may also be affected by other residual confounding factors. Finally, we could not assess the association of clinical outcomes with the serum level of digoxin due to a lack of data on digoxin levels. Nevertheless, no patient was diagnosed with T46.0 (defined as digoxin toxicity) during the follow-up period.

In conclusion, the use of digoxin in clinical practice was not uncommon among older Thai patients with HF and AF. The factors negatively associated with digoxin use included higher serum creatinine level and IHD, whereas the positively associated factors included the use of diuretics or mineralocorticoid receptor antagonists. We observed no significant association between digoxin use and the risk of all-cause mortality and rehospitalization due to HF.

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## CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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## AUTHOR CONTRIBUTION

Conceptualization, NS; Data curation, YW, DP, SP, CS; Formal analysis, NS, YW; Investigation, DP, SP, CS; Methodology, NS, YW; Visualization, NS, YW; Project administration, NS; Supervi-

sion, NS; Writing—original draft, NS; Writing—review & editing, NS, YW.

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# Statin Supply and Polydrug Use in Older Adults: A Focus on Drug Combinations that Reduce Bone Density

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**Background:** We investigated the comorbidities of individuals who were prescribed statins to identify the use of bone mineral density (BMD)-reducing drugs, examine polydrug use trends involving these drugs, and explore their relationship with osteoporosis. **Methods:** We analyzed claims data from the Korean National Health Insurance Service (January 2014–December 2018). We sampled 20% of 8,379,419 patients aged  $\geq 50$  years who were prescribed statins. Among them, we analyzed the data of those who were administered two or more prescriptions for 14 days or longer within 6 months of the initial date of statin prescription. Data on comorbidities and drugs that can potentially reduce BMD were obtained. Osteoporosis-related diagnoses were obtained as an outcome measure. The relationship between statins and BMD-reducing drugs was analyzed using logistic regression. **Results:** Among the 4,138 statin users aged 50 years or older, 552 were diagnosed with osteoporosis. The most common comorbidity in statin users was hypertension, followed by ischemic heart disease, diabetes mellitus, and stroke. The most frequently administered BMD-reducing drugs were proton pump inhibitors (PPIs). The osteoporosis diagnosis rate was higher in patients who were prescribed both statins and PPIs or both statins and levothyroxine than in those using only a statin. **Conclusion:** PPIs and levothyroxine should be prescribed cautiously in statin users and bone densitometry should be proactively performed considering the increased risk of osteoporosis.

**Key Words:** HMG-CoA statins, Polydrug use, Bone density, Osteoporosis, Elderly patient

## INTRODUCTION

The proportion of older adults in South Korea is increasing, including that of individuals aged  $\geq 75$  years who often have complex health problems and show a functional decline. The older adult population is predicted to account for more than half of the total population by 2038.<sup>1)</sup> The incidence of “polydrug use” de-

defined as the use of more than one drug or multiple types of drugs at the same time or sequentially,<sup>2)</sup> is rising owing to extended life expectancy and the increasing occurrence of complex chronic diseases in the older adult population.<sup>3-7)</sup> Polydrug use can increase the risk of the prescription of potentially inappropriate medications (PIM) in older adults. A previous study that assessed the rate of PIM among Korean older adults observed the prescription of at

least one PIM in 80.96% of older patients and that polydrug use was a significant risk factor for PIM prescription.<sup>8)</sup>

The National Institutes of Health designated osteoporosis as a skeletal disorder with an elevated risk of fracture owing to weakening bone strength.<sup>9)</sup> The 2008–2011 Korea National Health and Nutrition Examination Survey (KNHANES) reported a prevalence of osteoporosis among individuals aged 50 years or older of 22.4%. The prevalence in women (37.3%) is approximately five-fold higher than that in men (7.5%). Moreover, the incidence of osteoporosis increases with age with 68.5% of women aged 70 years or older experiencing osteoporosis.<sup>10)</sup>

Dyslipidemia, a major risk factor for cardiovascular diseases, is a chronic disease that requires continuous management in older adults. Furthermore, an analysis of the 2002–2018 National Health Insurance Service (NHIS) dataset published in the Dyslipidemia Fact Sheet in Korea in 2020<sup>11)</sup> showed that 7.69 million people were prescribed medications for dyslipidemia. A recent study conducted outside of Korea reported that the risk of osteoporosis increases with the dosage of statin, a drug used to treat dyslipidemia.<sup>12)</sup> This finding called for an evaluation of the use of drugs that reduce bone mineral density (BMD) among statin users.

The use of proton pump inhibitors (PPIs) is increasing owing to the recent increasing prevalence of digestive diseases in patients with obesity and in older adults.<sup>13)</sup> Studies have reported adverse events such as reduced BMD and osteoporosis caused by the prolonged use of PPIs.<sup>14)</sup> A classic example of a potassium-competitive acid blocker is revaprazan. Although revaprazan has been gaining popularity as a medication for gastroesophageal reflux disease, patients often take other drugs for metabolic disorders, including non-steroidal anti-inflammatory drugs. Therefore, studies on the resultant adverse drug reactions are required.<sup>15)</sup>

Tenofovir is commonly used to treat hepatitis B and human immunodeficiency virus infections. It reportedly induces Fanconi syndrome and ultimately leads to reduced BMD, osteomalacia, and electrolyte imbalance.<sup>16)</sup> A retrospective cohort study reported that the risk of osteoporosis fracture increased by 12% with tenofovir use.<sup>17)</sup>

Levothyroxine is considered the standard of care for hypothyroidism and, thus, is widely prescribed. However, excessive levothyroxine use accelerates bone loss and may have deleterious effects, such as osteoporosis. This calls for its cautious prescription, particularly to older adults and postmenopausal women.<sup>18)</sup>

The recently introduced sodium-glucose co-transporter 2 (SGLT2) inhibitors are hypoglycemic agents involved in glucose resorption in the kidney.<sup>19)</sup> However, SGLT2 inhibitor users have been shown to result in significantly reduced hip BMD.<sup>20)</sup>

Therefore, we examined comorbidities in statin users and identified drugs that might reduce BMD. We also explored trends in polydrug use involving these drugs and investigated their relationship with osteoporosis.

## MATERIALS AND METHODS

### Identifying Statin Users

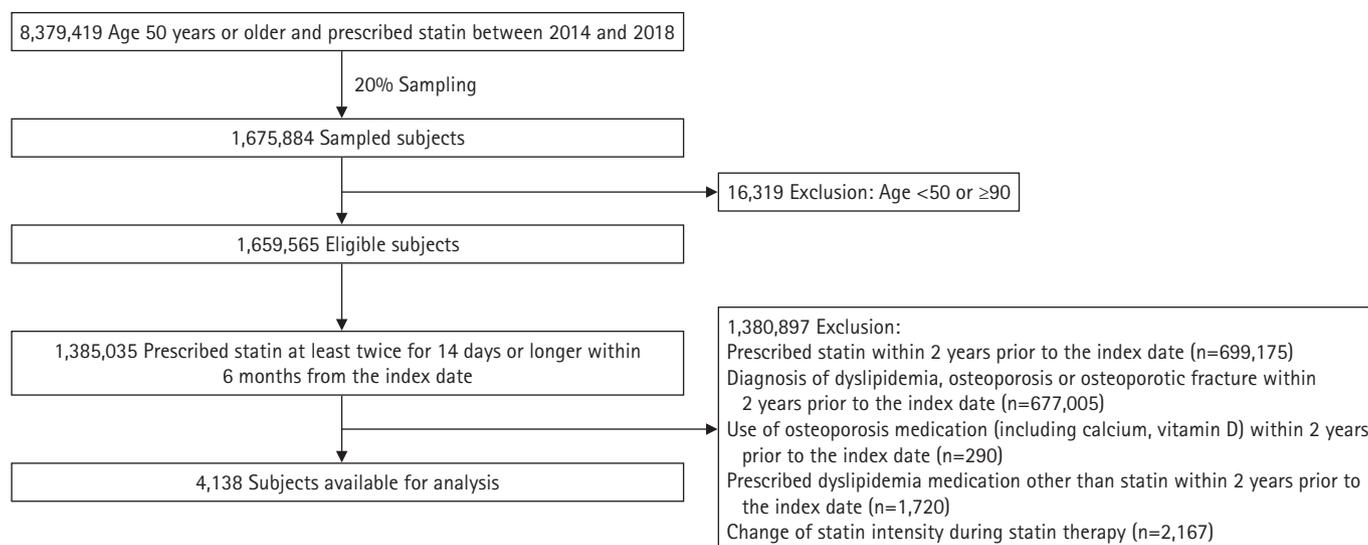
As the study subjects were older adults taking statins, “stain users” were defined based on previous cohort studies<sup>21,22)</sup> to extract as many users as possible. We enrolled patients prescribed any type of statin and with more than two prescriptions lasting 14 days or longer within 6 months of the initial statin prescription date (index date) between January 2014 and December 2018. The patients’ statin prescription history was determined using the active ingredient codes for each statin type. The following statins were analyzed: atorvastatin, rosuvastatin, lovastatin, simvastatin, pravastatin, fluvastatin, and pitavastatin. The total days of statin supplies were calculated based on the number of days in the prescription.

### Study Population

This retrospective cohort study used NHIS claims data and enrolled a total of 8,379,419 patients aged 50 years or older who were prescribed statins between January 2014 and December 2018. Of these patients, we sampled 20% ( $n = 1,675,884$ ). After excluding patients aged under 50 years and 90 years and older ( $n = 16,319$ ) based on the index date, 1,659,565 patients remained. Among them, we selected 1,385,035 patients who had been prescribed statins at least twice for 14 days or longer within 6 months of the index date. The additional exclusion criteria were (1) patients prescribed statins within 2 years before the index date; (2) patients diagnosed with dyslipidemia (I78.0–I78.9), osteoporosis (M81 and M82), or osteoporotic fracture (M80, S72.0, S72.1, S22.0, S22.1, S32.0, M48.4, M48.5, S52.5, and S52.6) within 2 years before the index date; (3) patients who had taken osteoporosis medication (including calcium and vitamin D) within 2 years before the index date; (4) patients prescribed dyslipidemia medications other than statins within 2 years before the index date; and (5) patients whose statin dose was adjusted during statin therapy. Both main and sub-diagnoses were checked (Fig. 1).

### Variables

We included sex and age as demographic factors in the analysis of osteoporosis incidence according to statin use. The analyzed comorbidities were rheumatoid arthritis (M06); hypertension (I10–I15); ischemic heart diseases (I20–I25); diseases of arteries, arterioles, and capillaries (I70–I79); stroke (I63, I64); diabetes (E10,



**Fig. 1.** Flow chart of study subjects.

E11); chronic renal insufficiency (N17–N19); nicotine dependency (F17); overweight and obesity (E65–E68), chronic obstructive pulmonary disease (J44); asthma (J45); and Crohn's disease (K50). We applied the Korean Standard Classification of Diseases codes, which follow the 10th revision of the International Statistical Classification of Diseases (ICD-10). We checked for cases in which these diagnosis codes appeared at least once between the index date and final date, regardless of whether it was a main diagnosis or sub-diagnosis. Among the drugs that potentially reduce BMD (PPIs, revaprazan, tenofovir, lithium, levothyroxine, and prednisone), oral (sulfonyleurea, glinide, metformin, alpha-glucosidase inhibitor, thiazolidinedione, DPP-4 inhibitor, and SGLT2 inhibitor) and injectable (insulin and GLP-1 inhibitor) drugs for treating diabetes mellitus (DM) that are associated with a high fracture risk among older adults with dyslipidemia were identified. We selected cases in which these drugs were prescribed for 3 months or longer between the index and final dates.

In this study, the outcome was osteoporosis-related diagnoses. Osteoporosis was defined as the presence of least one of the following codes: M81 (osteoporosis without current pathological fracture), M82 (osteoporosis in diseases classified elsewhere and defined as osteoporosis in multiple myelomatosis or endocrine disorders), M80 (osteoporosis with current pathological fracture), S72.0 or S72.1 (hip fracture), S22.0, S22.1, S32.0, M48.4, or M48.5 (spine fracture), and S52.5 or S52.6 (distal radius fracture).

The maximum follow-up period was 2 years. Follow-up was terminated if a patient was diagnosed with osteoporosis or died. Furthermore, because the data only covered health care utilization until December 31, 2018, all follow-up was terminated on this date. We set the maximum follow-up period to 2 years to eliminate po-

tential confounding effects, such as the passage of time, that may have contributed to the onset of osteoporosis.

#### Ethics Statement

This study was exempted for review by the Institutional Review Board at Seoul Medical Center (No. SEOUL 2020-01-004). Moreover, the data were obtained from the NHIS and were accessed in the analysis center.

#### Statistical Analyses

We analyzed the participants' general characteristics, comorbidities, and use of BMD-reducing drugs using descriptive statistics. The frequencies of comorbidities and BMD-reducing drug use were analyzed by sex, age, and statin type. We also analyzed the frequencies of patients undergoing bone density testing at the time of, or within 1 year of, osteoporosis diagnosis. The frequency of statin supply was analyzed by statin type; we also determined the frequency of use of each statin type according to comorbidity, as well as the frequency of polydrug use with BMD-reducing drugs by statin type. We then applied logistical regression to examine polydrug use trends in patients prescribed BMD-reducing drugs according to the prescribed statin type who were also diagnosed with osteoporosis. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) software with a statistical significance level set to 0.05.

## RESULTS

#### General Characteristics

A total of 4,138 patients aged 50 years or older were prescribed

statins between January 2014 and December 2018. Among these, 2,567 were male (62%) and 1,571 were female (38%), including 1,326 males aged 50–64 years (M50–64, 32.0%), 1,241 males aged 65–89 years (M65–89, 30.0%), 743 females aged 50–64 years (F50–64, 18.0%), and 828 females aged 65–89 years (F65–89, 20.0%). Statins were prescribed for 441.2, 427.4, 338.9, and 384.4 days in the M50–64, M65–89, F50–64, and F65–89 groups, respectively. The mean number of days of statin use among statin users was 441.2. A total of 552 patients were diagnosed with osteoporosis: 47 (8.5%) M50–64, 149 (27%) M65–89, 106 (19.2%) F50–64, and 250 (45.3%) F65–89. Seventy-five of these patients were advised to undergo dual-energy X-ray absorptiometry (DXA) within 1 year of their osteoporosis diagnosis: 5 (6.7%) M50–64, 19 (25.3%) M65–89, 15 (20.0%) F50–64, and 36 (48.0%) F65–89 (Table 1).

Most statin users showed no comorbidities (n = 2,078); among those with comorbidities, the most common was hypertension (n = 2,051), followed by ischemic heart disease (n = 1,326), DM (n = 1,207), and stroke (n = 1,183). Among statin types, rosuvastatin was the most frequently prescribed (n = 2,538; 61.3%), followed by atorvastatin (n = 1,001; 24.2%), and pitavastatin (n = 569; 13.8%) (Table 2).

**Table 2.** Analysis of comorbidities and statin type (n=4,138)

Variable	n (%)
Comorbidities (ICD-10)	
No disease	2,087 (50.43)
Rheumatoid arthritis (M06)	102 (2.46)
Hypertension (I10–I15)	2,051 (49.57)
Ischemic heart diseases (I20–I25)	1,326 (32.04)
Diseases of arteries, arterioles, and capillaries (I70–I79)	806 (19.48)
Stroke (I63, I64)	1,183 (28.59)
Diabetes (E10, E11)	1,207 (29.17)
Chronic renal insufficiency (N17–N19)	215 (5.20)
Nicotine dependency (F17)	6 (0.14)
Overweight and obesity (E65–E68)	1 (0.02)
Chronic obstructive pulmonary disease (J44)	251 (6.07)
Asthma (J45)	650 (15.71)
Crohn's disease (K50)	2 (0.05)
Generic name of statin	
Atorvastatin	1,001 (24.2)
Rosuvastatin	2,538 (61.3)
Pitavastatin	569 (13.8)
Lovastatin	17 (0.4)
Simvastatin	9 (0.2)
Pravastatin	4 (0.1)
Fluvastatin	0 (0.0)

ICD-10, International Statistical Classification of Diseases 10th revision.

**Table 1.** General characteristics of statin users by sex and age group (n=4,138)

Characteristic	Age group	Sex	Value
Number of participants	50–64 y	Male	1,326 (32.0)
		Female	743 (18.0)
	65–89 y	Male	1,241 (30.0)
		Female	828 (20.0)
Days of statin supply	50–64 y	Male	441.2 ± 235.9
		Female	338.9 ± 263.5
	65–89 y	Male	427.4 ± 243.5
		Female	384.4 ± 233.1
Number of medications taken that induce bone density reduction	50–64 y	Male	1.04 ± 1.06
		Female	1.09 ± 1.05
	65–89 y	Male	1.16 ± 1.07
		Female	1.14 ± 1.08
Osteoporosis diagnostic rate (n = 552)	50–64 y	Male	47 (8.5)
		Female	106 (19.2)
	65–89 y	Male	149 (27.0)
		Female	250 (45.3)
DXA prescription rate (n = 75)	50–64 y	Male	5 (6.7)
		Female	15 (20.0)
	65–89 y	Male	19 (25.3)
		Female	36 (48.0)

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

DXA, dual-energy X-ray absorptiometry.

### Distribution of Comorbidities and BMD-Reducing Drug Use by Statin Type

Among patients without comorbidities, the most frequently prescribed statin was rosuvastatin (n = 1,279), followed by atorvastatin (n = 528) and pitavastatin (n = 259). Among all patients with comorbidities, including hypertension, ischemic heart disease, DM, and stroke, the most frequently prescribed statin was rosuvastatin (n = 1,259, 812, 737, and 722, respectively), followed by atorvastatin (n = 473, 300, 276, and 270, respectively), and pitavastatin (n = 310, 209, 190, and 188, respectively) (Fig. 2).

Regarding BMD-reducing drug use among statin users, PPIs were the most frequently prescribed (n = 1,734), followed by levothyroxine (n = 136), tenofovir (n = 12), lithium (n = 9), and revaprazan (n = 6). None of the patients used prednisone. Oral DM drugs were prescribed to 2,501 patients and injectable DM drugs to 79 cases, whereas 384 patients were not prescribed any additional drugs. Among statin users who were diagnosed with osteoporosis, PPIs were the most frequently prescribed medications (n = 321), followed by levothyroxine (n = 22), revaprazan (n = 3), and tenofovir (n = 1). None of these patients were prescribed lithium or prednisone. Oral DM drugs were prescribed to 328 of the diagnosed patients and injectable DM drugs to 11 patients, whereas 34 of the diagnosed patients were not prescribed any additional medications (Fig. 3).

### Relationships between Osteoporosis and BMD-Reducing Drug Use among Statin Users

The prevalence of osteoporosis was 1.84 times higher among statin users concomitantly prescribed PPIs than among those who did not take additional drugs. This was particularly evident for pitavastatin (2.40-fold), rosuvastatin (1.83-fold), and atorvastatin

users (1.82-fold) concomitantly prescribed PPIs. The prevalence of osteoporosis was also higher among statin users concomitantly prescribed levothyroxine (1.81-fold) than among those who were not prescribed additional drugs, especially among concomitant pitavastatin-levothyroxine users (7.03-fold increase). We observed no significant differences in the prevalence of osteoporosis in patients prescribed revaprazan, tenofovir, oral DM drugs, or injectable DM drugs concomitantly with a statin (Table 3).

### DISCUSSION

In this study, we examined a nationwide sample of patients who were prescribed statins between January 2014 and December 2018 for the treatment of dyslipidemia, a major cause of mortality among older adults and a cardiovascular disease risk factor. We analyzed the rates of osteoporosis diagnosis, the prescription of DXA following diagnosis and treatment, and the use of BMD-reducing drugs among patients diagnosed with osteoporosis in two age groups: 50–64 (at 50 years of age, osteoporosis incidence begins to increase) and 65–89 years.

Statins, which are used to treat dyslipidemia, reduce low-density lipoprotein levels by inhibiting β-hydroxy β-methylglutaryl coenzyme A (HMG-CoA) reductase, the most important enzyme in cholesterol synthesis.<sup>23)</sup> However, they are associated with adverse events, such as hepatotoxicity, myalgia, hyperglycemia, and chronic renal insufficiency, as well as risks from drug interactions. These effects vary widely across different statin types and clinical dosages.<sup>23)</sup> A meta-analysis of 33 studies that examined the association between statins and osteoporosis reported that statins lowered the risk of fracture, particularly in men.<sup>24)</sup> In addition, a study that analyzed data from the NHIS in Taiwan reported that statins lowered

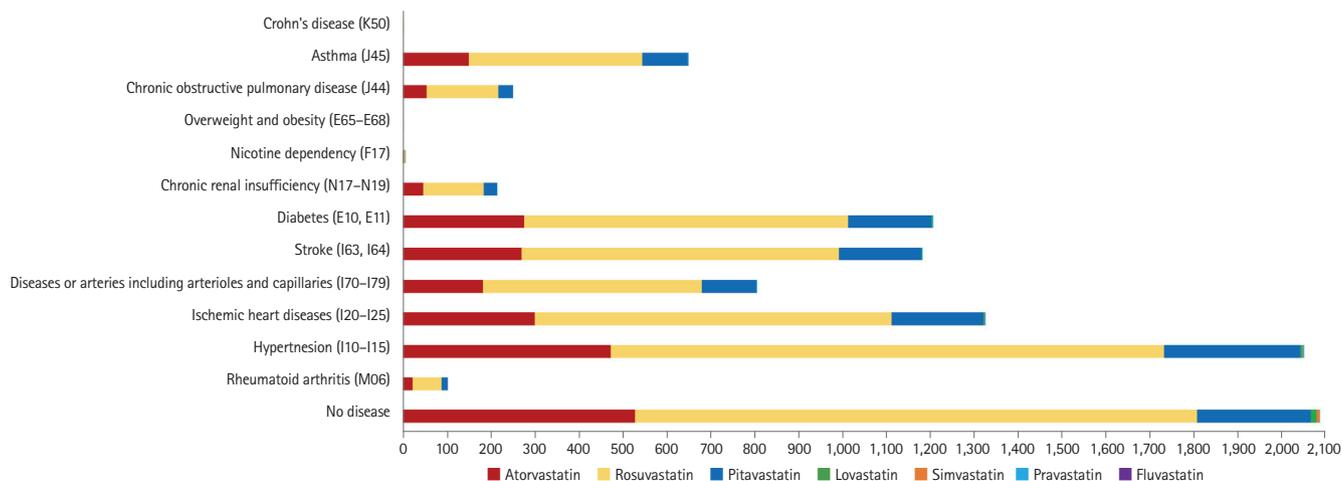
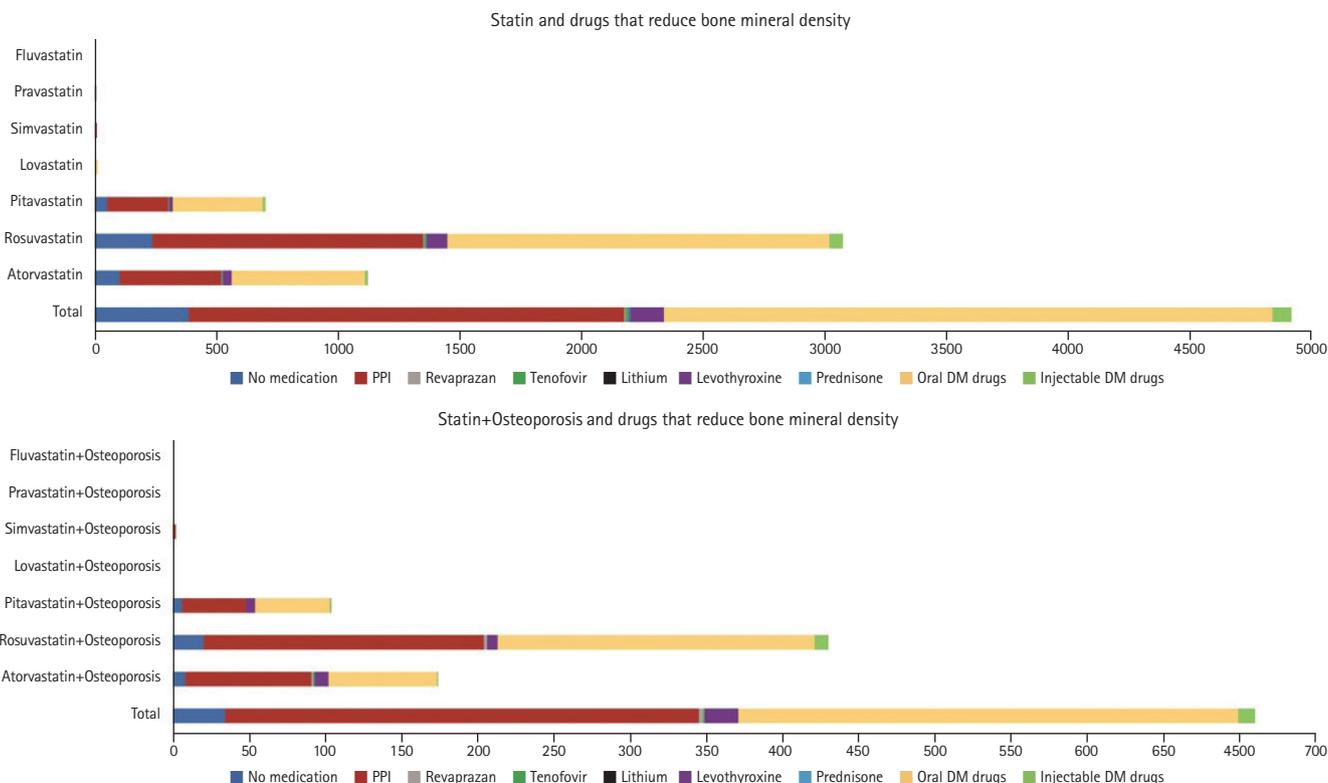


Fig. 2. Types of statin according to comorbidities.



**Fig. 3.** Bone mineral density-reducing drug use among statin users and statin users with osteoporosis.

the risk of osteoporosis and fracture.<sup>25)</sup> In an analysis of 350,000 Austrians who had taken statins for at least 1 year and 7.80 million Austrians diagnosed with osteoporosis from 2006 to 2007, the low-dose statin group had a low risk of osteoporosis, whereas the high-dose statin group had a 2.04-fold higher risk of osteoporosis.<sup>12)</sup> In the present study, we only enrolled patients who had been taking statins to eliminate the effect of statin use or non-use on BMD. The study in Austria<sup>12)</sup> only assessed the association (trend) of osteoporosis with varying doses of the same statin, without analyzing the rate of osteoporosis in relation to different intensities of statin use (high, moderate, or low). Hence, subsequent studies are needed to assess the associations between osteoporosis and statin type and intensity.

The results of previous studies on the associations between PPI use and osteoporosis are inconsistent;<sup>26,27)</sup> thus, the specific durations, doses, and use of PPIs that elevate the risk of fracture remain unknown. A previous study that analyzed health insurance claims data reported an increased risk of osteoporotic fracture with PPIs use in women who underwent their health check-ups at a transitional life phase at the age of 66 years. The odds ratio (OR) for fractures during the follow-up period was 1.13 for individuals who took PPIs compared to that in individuals who took histamine-2 receptor antagonists (H2RAs) and the OR for hip fracture was even higher (1.51). Moreover, the risk of fracture increased with

the duration of PPI use during follow-up.<sup>28)</sup> In our study, the OR for osteoporosis was 1.84 among statin users with concomitant PPI use compared with that in those who did not take any other prescribed drugs and was 2.40 among pitavastatin users, 1.82 among atorvastatin users, and 1.83 among rosuvastatin users. Furthermore, the OR for osteoporosis was 1.81 among statin users concomitantly prescribed levothyroxine and increased to 7.03 among those concomitantly prescribed pitavastatin and levothyroxine. Hence, bone density testing should be performed in patients prescribed these drugs. The tests would fall within the insurance coverage criteria (disease or use of drugs that may induce osteoporosis).

Among DM drugs, the use of SGLT2 inhibitors reduced hip BMD,<sup>20)</sup> whereas canagliflozin has been associated with increased fracture risk.<sup>29)</sup> In contrast, a meta-analysis of the risk of fracture linked to SGLT2 inhibitors in patients with DM reported fracture incidence rates of 1.59% and 1.56% in the SGLT2 inhibitor and control groups, respectively. Compared to a placebo, canagliflozin (OR=1.15; 95% confidence interval [CI], 0.71–1.88), dapagliflozin (OR=0.68; 95% CI, 0.37–1.25), and empagliflozin (OR=0.93; 95% CI, 0.74–1.18) did not significantly increase the risk of fracture.<sup>30)</sup> In our study, the prevalence of osteoporosis was not significantly higher among statin users who concomitantly took oral DM drugs. However, further studies are needed, as we

**Table 3.** Relationship between osteoporosis and bone mineral density-reducing drug use among statin users

	No medication	OR (95% CI)	p-value	Revaprazan	OR (95% CI)	p-value	Tenofovir	OR (95% CI)	p-value	Levothyroxine	OR (1.17-2.80)	p-value	Oral DM drugs	OR (95% CI)	p-value	Injectable DM drugs	OR (95% CI)	p-value
Statin	384	1.790 (1.52-2.23)	<0.0001	6	0.97 (0.26-3.70)	0.9663	12	0.68 (0.08-5.87)	0.7285	136	1.81 (1.17-2.80)	0.0072	2,501	1.25 (0.85-1.84)	0.254	79	1.04 (0.52-2.05)	0.9191
Statin + osteoporosis	34	311		3			3			22			328			11		
Atorvastatin	100	418 (1.25-2.65)	0.0018	2	2.22 (0.13-37.17)	0.5788	2	14.68 (0.73-29.59)	0.0798	36	2.34 (1.01-5.41)	0.048	547	0.89 (0.45-1.77)	0.7467	13	0.42 (0.05-3.40)	0.4131
Atorvastatin + osteoporosis	8	83		1			1			9			71			1		
Rosuvastatin	234	1,114 (1.43-2.35)	<0.0001	3	0.93 (0.19-4.65)	0.9295	8	NA		84	1.39 (0.77-2.49)	0.2742	1,571	1.55 (0.91-2.63)	0.1062	55	1.43 (0.65-3.15)	0.3711
Rosuvastatin + osteoporosis	20	184		2			0			7			208			9		
Pitavastatin	48	252 (1.36-4.26)	0.0027	1	NA		2	NA		14	7.03 (1.09-25.96)	0.0034	370	0.97 (0.30-3.10)	0.9555	11	0.44 (0.04-4.43)	
Pitavastatin + osteoporosis	6	42		0			0			1			49			1		0.4822

PPis, proton pump inhibitors; DM, diabetes mellitus; OR, odds ratio; CI, confidence interval; NA, not available. Adjusted for age, sex, comorbidities, and concomitant drugs.

did not conduct separate analyses according to the composition of the oral DM drugs.

This study differs from other studies in that it compared the prevalence of osteoporosis in patients taking a combination of statin—a hyperlipidemia drug used to lower the risk of cardiovascular and cerebrovascular disease that accounts for a large proportion of comorbidities osteoporosis—and drugs known to reduce BMD. We found that the risk of osteoporosis was higher in patients prescribed both statins and PPIs and those who received both statins and levothyroxine compared to those who took other drugs. Therefore, bone density tests should be performed. Moreover, when prescribing drugs that induce bone density reduction, alternative prescriptions should be considered. Regular bone density tests are also needed for patients diagnosed with osteoporosis or who have risk factors for bone density reduction. Furthermore, a study on the possible interactions of PPIs and levothyroxine with statins is needed. Our study results showed the negative effects of polydrug use by focusing on multiple drugs. Older patients are often prescribed a variety of drugs by different doctors and also take non-prescription drugs, various herbal medicines, and health supplements. The many cases of polydrug use underscore the need for a thorough monitoring system and caution to reduce the unnecessary use of drugs that may interact in older patients.

The number of patients was limited because this study only assessed older patients taking statins and it was difficult to apply the medication possession ratio (MPR) or the 12-month cumulative persistence rate relative to the persistence of dosing. To exclude the characteristics of the older adults and focus on drug interactions, the size of the population must be increased by including younger generations and ensuring the continuity of sufficient drug intake. In addition, a broader patient group rather than just those taking statins may be required to investigate the complex relationships among various drugs. In addition, additional studies on the effect of statin intensity on bone density are needed.

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**CONFLICT OF INTEREST**

The researchers claim no conflicts of interest.

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**AUTHOR CONTRIBUTION**

Conceptualization, KSK, HJH, KBK, JCH, KMY, AJH; Data cura-

tion, JCH, KMY, KDR, PYH, KBK; Funding acquisition, KSK; Investigation, HJH; Methodology, HJH, KBK, JCH, KMY, KDR, PYH, AJH; Project administration, KSK, HJH, KBK; Supervision, KSK; Writing-original draft, HJH, KBK, KSK; Writing-review & editing, HJH, KBK, JCH, KMY, KDR, PYH.

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# Non-achievement of the Low-Density Lipoprotein Cholesterol Goal in Older Patients with Type 2 Diabetes Mellitus and a Very High Cardiovascular Disease Risk: A Multicenter Study in Vietnam

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**Background:** Lowering the low-density lipoprotein cholesterol (LDL-c) level is important for reducing cardiovascular (CV) events. However, little is known about the management of LDL-c in older patients with type 2 diabetes mellitus (T2DM). This study investigated the prevalence and factors associated with the non-achievement of LDL-c goals in older T2DM patients with a very high risk of CV diseases. **Methods:** This multicenter cross-sectional study measured the LDL-c levels of 733 T2DM outpatients from December 2019 to July 2020. The patients were aged  $\geq 60$  years, had very high risks of CV disease, and had been on LDL-c-lowering therapy for 6 months or more. The goal of lipid concentrations were assessed based on the recent guidelines of the European Society of Cardiology. We applied logistic regression analysis to identify the factors associated with the non-achievement of the LDL-c goal. **Results:** The mean age of the patients was  $68.6 \pm 7.2$  years. In total, 654 patients (89.2%) did not achieve the aggressive LDL-c goal of  $< 1.4$  mmol/L. In the adjusted model, the factors associated with the non-achievement of the LDL-c goal were obesity defined by body mass index (odds ratio [OR]=2.33; 95% confidence interval [CI], 1.13–4.81;  $p=0.022$ ) and high-intensity statin therapy (OR=0.03; 95% CI, 0.01–0.05;  $p<0.001$ ), while age, sex, education level, smoking habit, and comorbidities were not associated. **Conclusion:** Older patients with T2DM who are at a very high CV disease risk are often unable to achieve their LDL-c goal. Obesity can increase the probability of not achieving the LDL-c goal, whereas high-intensity statin therapy can decrease this probability.

**Key Words:** Low-density lipoprotein (LDL) cholesterol, Diabetes mellitus, Older patients, Aged

## INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major global health burden in currently aging societies.<sup>1)</sup> Diabetes management in older adults is difficult owing to the coexistence of geriatric syndromes such as frailty, falling, delirium, polypharmacy, and polymorbidity.<sup>2)</sup> Vietnam has entered an aging phase: in 2019, people aged  $\geq 60$  years accounted for 12.3% of the total Vietnamese population.<sup>3)</sup> Furthermore, the country has been experiencing an epidemiological transition, with the health panorama shifting from infectious to

non-communicable diseases.<sup>4)</sup> Previous studies showed that 6% of the total population in Vietnam had diabetes,<sup>5)</sup> with the rate increasing to 12.5% among older individuals.<sup>6)</sup> Dyslipidemia was detected in 37.9%–60.2% of older adults with T2DM.<sup>7,8)</sup> Several factors reflecting risk-behavior changes drive these high rates, including smoking, unhealthy eating habits, and a sedentary lifestyle.<sup>9)</sup>

Until recently, atherosclerotic cardiovascular disease (ASCVD) was the principal cause of morbidity and mortality in patients with diabetes.<sup>10,11)</sup> Previous studies demonstrated that lowering the low-density lipoprotein cholesterol (LDL-c) level prevented and

reduced the rate of ASCVD events in patients with T2DM.<sup>12-15)</sup> The relative reduction in the rate of ASCVD events was also observed in older patients with T2DM.<sup>15)</sup> Notably, the approach to achieving lipid goals is an important part of the comprehensive ASCVD risk reduction strategy. In a cohort study of 69,942 patients in South Korea, Kim et al.<sup>16)</sup> reported a higher rate of ASCVD events among those who did not achieve the LDL-c goal compared to those who did. The LDL-c goal non-achievers were older and had higher cardiovascular (CV) risk levels compared to the LDL-c goal achievers.

The recent clinical guidelines of the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) for dyslipidemia and the European Society of Cardiology/European Association for the Study of Diabetes (ESC/EASD) for diabetes recommend an LDL-c goal of < 1.4 mmol/L for patients with T2DM who are at very high risk for CV disease.<sup>17,18)</sup> However, there is a lack of evidence of non-achievement of LDL-c goals in older patients with T2DM at very high risk for CV disease. Therefore, this cross-sectional study aimed to determine how often LDL-c goals are not achieved in very high-risk older patients with T2DM and identify the factors associated with non-achievement.

## MATERIALS AND METHODS

### Sample Size Calculation

The sample size was calculated using a single population proportion formula:

$$N = Z_{1-\alpha/2}^2 \times (p \times (1-p) / d^2),$$

where  $N$  is the required sample size;  $Z_{1-\alpha/2}$  is 1.96 (with  $\alpha = 0.05$  and 95% confidence interval [CI]);  $d$  is precision (assumed to be 0.04); and  $p$  is the prevalence of not achieving the LDL-c goal (< 1.4 mmol/L) in older T2DM patients at a very high CV disease risk. Because the prevalence was unknown, we set  $p = 0.5$  to obtain the maximum possible value of  $p \times (1-p)$  of 0.25. This study required a minimum of 600 participants.

### Ethical Statement

The study was carried out according to the ethical principles of the Declaration of Helsinki. All patients provided written informed consent. The study protocol was approved by the ethics committee of the University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam (No. 2545/QD-DHYD).

### Study Design and Data Collection

This multicenter cross-sectional study was conducted from De-

cember 2019 to July 2020 in outpatients with T2DM aged  $\geq 60$  years at three hospitals in Ho Chi Minh City, Vietnam. To ensure consistent management among the study sites, trained geriatricians treated all patients according to the ESC guidelines<sup>17,18)</sup> and all sites started recruitment at the same time. Patients met the inclusion criteria if they had been treated for hypercholesterolemia with LDL-c-lowering therapy for 6 or more months before enrollment. The CV risk category and lipid goals were assessed according to the recent ESC guidelines.<sup>17,18)</sup>

Patients were diagnosed with diabetes based on a fasting plasma glucose level of  $\geq 7.0$  mmol/L after no caloric intake for at least 8 hours and/or an HbA1c level of  $\geq 6.5\%$ .<sup>18)</sup> Hypercholesterolemia was diagnosed in our very-high-risk patients if their LDL-c levels were > 1.4 mmol/L before lipid management.<sup>17)</sup> In our study, all T2DM patients with hypercholesterolemia and at least two major risk factors (age  $\geq 65$  years, hypertension, smoking, and obesity) were classified as having a very high CV disease risk.<sup>17)</sup> For participants with very high CV disease risk, the lipid goal was an LDL-c level of < 1.4 mmol/L, a non-high-density lipoprotein cholesterol (non-HDL-c) level of < 2.2 mmol/L, and a triglyceride level of < 1.7 mmol/L.<sup>17)</sup> All blood samples for serum lipid estimation were obtained after a 12-hour fast. LDL-c levels were measured using a direct LDL-c assay kit (LDL-CHOLESTEROL, OSR6183; Beckman Coulter Ireland Inc., Clare, Ireland). The exclusion criteria were severe illnesses requiring hospital admission, serious mental conditions, and active malignancies.

The geriatricians managing the participating patients collected participant demographic data and clinical characteristics and measured their body weights and heights. The intensity of statin therapy was defined based on the last prescription within one month before enrollment. High-intensity statin therapy included 40–80 mg atorvastatin or 20–40 mg rosuvastatin, whereas low-to-moderate intensity statin therapy was defined based on lower doses of all statins.<sup>17)</sup> The participants' educational level was classified as lower ( $\leq 12$  years of education, including graduation from senior high school or lower) or higher (graduation from college or university or higher). Patients who had smoked any tobacco products over the previous year were considered current smokers. Body mass index (BMI) was calculated as the quotient between body weight (kg) and height ( $m^2$ ). Body weight and height were measured following the standardized protocol using identical equipment at all study sites. BMI was stratified per the World Health Organization's guidelines for the Asia-Pacific region, which defined underweight (< 18.5 kg/ $m^2$ ), normal weight (18.5–22.9 kg/ $m^2$ ), overweight (23.0–24.9 kg/ $m^2$ ), and obese ( $\geq 25$  kg/ $m^2$ ).<sup>19)</sup> The normal weight group was the reference group for regression analyses.

### Statistical Analyses

All data were analyzed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Qualitative data were described as frequencies and percentages. Quantitative data were represented as mean  $\pm$  standard deviation. Comparisons were conducted with chi-square or Fisher exact tests for non-numerical data and Student t-test for continuous variables. Univariate and multivariate logistic regression analyses using the enter method were performed to identify the predictors of non-achievement. Univariate logistic regression was performed on the potential risk factors for non-achievement. All variables were selected for multivariate logistic regression and examined for interaction and multicollinearity. The significance level was set at  $p < 0.05$ .

## RESULTS

### Patient Characteristics and the Prevalence of Not Achieving the Lipid Goal

We enrolled 733 patients with a mean age of  $68.6 \pm 7.2$  years (range, 60–94 years). The participants were predominantly male (51.3%). Overall, 71 patients (9.7%) were current smokers, 174 (23.7%) had completed college/university or higher education, 412 (56.2%) had documented coronary artery disease (CAD), and 575 patients reported hypertension (78.4%). Regarding BMI, 2.3% were underweight, 34.7% were of normal weight, 26.6% were overweight, and 36.4% were obese.

A total of 654 patients (89.2%) did not achieve the aggressive LDL-c goal ( $< 1.4$  mmol/L). Further, 644 (87.9%) did not achieve the non-HDL-c goal ( $< 2.2$  mmol/L), 412 (56.2%) did not meet the triglyceride goal ( $< 1.7$  mmol/L), and 355 (48.4%) did not meet the HbA1c goal ( $< 7\%$ ), indicating a high prevalence of non-achievement in older patients with T2DM with a very high CV disease risk.

### Differences between the Groups That Did and Did Not Achieve the LDL-c Goal

The participants were assigned to achieved or non-achieved LDL-c goal groups. Table 1 presents the baseline characteristics of all participants and compares the two groups. Age, sex, education levels, hypertension, and CAD did not differ between the groups. As expected, the non-achieved group had a significantly higher LDL-c level than that in the achieved group ( $2.9 \pm 1.0$  vs.  $1.1 \pm 0.2$  mmol/L;  $p < 0.001$ ), along with a higher non-HDL-c level ( $3.8 \pm 1.2$  vs.  $2.2 \pm 0.9$  mmol/L;  $p < 0.001$ ), a lower achievement rate for the non-HDL-c goal (5.4% vs. 68.4%;  $p < 0.001$ ), and a higher BMI ( $24.1 \pm 3.3$  vs.  $22.9 \pm 3.4$  kg/m<sup>2</sup>;  $p = 0.003$ ).

The distribution of patients according to BMI also differed sig-

nificantly between the two groups ( $p = 0.008$ ), with patients in the non-achieved group more likely to be obese compared to the achieved group (38.2% vs. 21.5%) (Fig. 1). Thus, obesity occurred more frequently in older patients with T2DM with a very high CV disease risk who did not achieve their LDL-c goal compared to those who did achieve the goal. The non-achieved group also had a significantly lower rate of high-intensity statin therapy than the achieved group (14.7% vs. 86.1%;  $p < 0.001$ ). We observed no significant difference in ezetimibe use between the two achievement groups (Supplementary Tables S1–S3).

### Factors Associated with Not Achieving the LDL-c Goal

The results of the univariate and multivariate logistic regression analyses are summarized in Table 2. In the adjusted model, obesity defined by BMI (odds ratio [OR] = 2.33; 95% CI, 1.13–4.81;  $p = 0.022$ ) increased the probability of not achieving the LDL-c goal, whereas the adjusted ORs were 0.78 (95% CI, 0.16–3.94;  $p = 0.775$ ) for underweight and 1.33 (95% CI, 0.66–2.68;  $p = 0.423$ ) for overweight participants (normal weight was the reference). High-intensity statin use (OR = 0.03; 95% CI, 0.01–0.05;  $p < 0.001$ ) decreased the probability of not achieving the LDL-c goal.

## DISCUSSION

The results of this multicenter cross-sectional study provided three key observations regarding the management of hypercholesterolemia in older patients with T2DM with a very high CV disease risk. First, a large proportion of patients did not meet the aggressive LDL-c goal. Second, obesity and the suboptimal use of high-intensity statin therapy were associated with not achieving the LDL-C goal. Third, those participants who did not meet the LDL-c goal also had lower achievement rates for the other goals, such as non-HDL-c, compared to those who achieved the LDL-c goal. According to these findings, we propose three discussion points.

### Non-achievement of the LDL-c Goal in Older Patients with T2DM at Very High CV Disease Risk

Our study is the first to assess the achievement of an aggressive LDL-c target value (according to the 2019 ESC/EAS guidelines) in older patients with T2DM with a very high risk of CV disease. We found that 89.2% of patients did not achieve the recommended LDL-c goal of  $< 1.4$  mmol/L, despite being at a very high risk of having an ASCVD event. For the more relaxed LDL-c goals of  $< 1.8$  mmol/L and  $< 2.6$  mmol/L, the non-achievement rates were 78.0% and 49.9%, respectively (Fig. 1), corroborating the

**Table 1.** Baseline characteristics of the patients according to the achievement of the goal LDL-c level

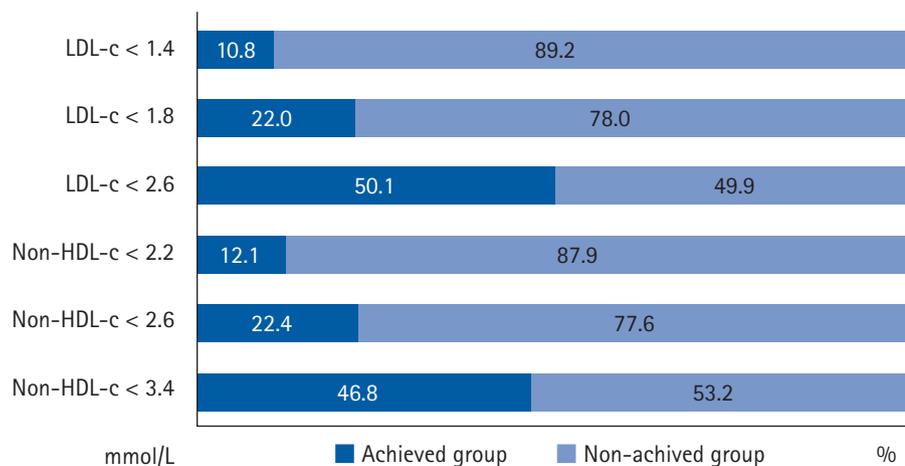
Characteristic	All (n = 733)	Achieved group (n = 79)	Non-achieved group (n = 654)	p-value <sup>a)</sup>
Sex, male	376 (51.3)	37 (46.8)	339 (51.8)	0.471
Age (y)	68.6 ± 7.2	69.4 ± 7.1	68.5 ± 7.2	0.260
≥ 75	153 (20.9)	18 (22.8)	135 (20.6)	0.767
Education				0.440
Lower education	559 (76.3)	57 (72.2)	502 (76.8)	
Higher education	174 (23.7)	22 (27.8)	152 (23.2)	
BMI (kg/m <sup>2</sup> )	23.9 ± 3.3	22.9 ± 3.4	24.1 ± 3.3	0.003
BMI groups				0.008
Underweight	17 (2.3)	3 (3.8)	14 (2.1)	
Normal	254 (34.7)	39 (49.4)	215 (32.9)	
Overweight	195 (26.6)	20 (25.3)	175 (26.8)	
Obese	267 (36.4)	17 (21.5)	250 (38.2)	
Smoking	71 (9.7)	6 (7.6)	65 (9.9)	0.640
Hypertension	575 (78.4)	64 (81.0)	511 (78.1)	0.658
Coronary artery disease	412 (56.2)	48 (60.8)	364 (55.7)	0.457
Lipid profile				
Total cholesterol (mmol/L)	4.8 ± 1.4	3.3 ± 0.9	5.0 ± 1.3	< 0.001
LDL-c (mmol/L)	2.7 ± 1.1	1.1 ± 0.2	2.9 ± 1.0	< 0.001
HDL-c (mmol/L)	1.1 ± 0.3	1.1 ± 0.4	1.1 ± 0.3	0.170
Non-HDL-c (mmol/L)	3.7 ± 1.2	2.2 ± 0.9	3.8 ± 1.2	< 0.001
Triglyceride (mmol/L)	2.2 ± 1.5	2.4 ± 1.9	2.2 ± 1.5	0.310
Non-HDL-c ≥ 2.2 mmol/L	644 (87.9)	25 (31.6)	619 (94.6)	< 0.001
Triglyceride ≥ 1.7 mmol/L	412 (56.2)	49 (62.0)	363 (55.5)	0.330
Diabetes profile				
HbA1c (%)	7.4 ± 1.8	7.3 ± 1.6	7.4 ± 1.8	0.700
HbA1c ≥ 7%	355 (48.4)	33 (41.8)	322 (49.2)	0.257
LDL-c-lowering therapy				
High-intensity statin therapy	164 (22.4)	68 (86.1)	96 (14.7)	< 0.001
Ezetimibe	27 (3.7)	2 (2.5)	25 (3.8)	0.758

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

BMI, body mass index; HbA1c, glycated hemoglobin; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol.

Comparisons were conducted using chi-square and Student t-tests for categorical and continuous variables, respectively.

<sup>a)</sup> Achieved group vs. non-achieved group.



**Fig. 1.** Prevalence of the achievement and non-achievement of low-density lipoprotein cholesterol (LDL-c) and non-high-density lipoprotein cholesterol (non-HDL-c) goals according to the levels of treatment goals.

**Table 2.** Factors associated with the non-achievement of LDL-c goal levels in logistic regression analysis

Variable	Univariate		Multivariate	
	OR (95% CI)	p-value	AOR (95% CI)	p-value
Age	0.98 (0.95–1.01)	0.262	-	-
Male	1.22 (0.77–1.95)	0.402	-	-
Lower education	1.28 (0.76–2.15)	0.364	-	-
BMI groups				
Normal	1 (Ref)		1 (Ref)	
Underweight	0.85 (0.23–3.08)	0.801	0.78 (0.16–3.94)	0.775
Overweight	1.59 (0.89–2.82)	0.115	1.33 (0.66–2.68)	0.423
Obese	2.67 (1.47–4.85)	0.001	2.33 (1.13–4.81)	0.022
High-intensity statin therapy	0.03 (0.01–0.06)	< 0.001	0.03 (0.01–0.05)	< 0.001
Smoking	1.34 (0.56–3.21)	0.507	-	-
Hypertension	0.84 (0.46–1.51)	0.557	-	-
Coronary artery disease	0.81 (0.50–1.30)	0.389	-	-

LDL-c, low-density lipoprotein cholesterol; BMI, body mass index; CI, confidence interval; OR, odds ratio; AOR, adjusted odds ratio.

findings reported in other diabetic populations. Two recent studies in France and Korea showed that 59% of patients with diabetes with very high CV disease risk and 87.8% with high CV disease risk did not achieve the LDL-c goal of < 1.8 mmol/L.<sup>20,21</sup> Collectively, these data indicated suboptimal LDL-c management in very high-risk T2DM patients.

The risk of CV events increases with higher LDL-c levels and advancing age. In a primary prevention cohort, the risk of myocardial infarction and ASCVD events increased for every 1.0 mmol/L increase in LDL-c in all age groups, with the highest increase noted in individuals aged  $\geq 70$  years.<sup>22</sup> A recent meta-analysis reported that lowering LDL-c levels by statin therapy resulted in significant reductions in major vascular events, irrespective of age, including those in patients > 75 years of age.<sup>23</sup> Therefore, the ESC/EAS guidelines for dyslipidemia provide the same recommendations for LDL-c control to older individuals with ASCVD as those for younger patients.<sup>17</sup> However, little is known about the optimal control of LDL-c in older individuals. Our study results showed that patients with T2DM at very high CV disease risk often did not achieve their LDL-c goal. This poor achievement suggests the need for efforts to improve the management of hypercholesterolemia in older patients with T2DM with a very high risk of CV disease.

#### Factors Associated with Not Achieving the LDL-c Goal in Patients with T2DM at Very High CV Disease Risk

Previous studies revealed factors associated with not achieving LDL-c goals, including obesity, female sex, high CV disease risk, no (vs. lower dose) statin therapy, lower (vs. higher) statin dose, and non-adherence to statin therapy.<sup>16,24</sup> In patients with diabetes, two studies showed that female sex was a predictor for not achiev-

ing LDL-c goals.<sup>20,25</sup> However, these studies used higher LDL-c target values and did not focus on the older population. Our study identified obesity and high-intensity statin therapy as factors associated with LDL-c goal non-achievement in patients with T2DM at very high CV disease risk.

Both obesity and high LDL-c levels are risk factors for CV in patients with T2DM.<sup>18</sup> Obesity can induce abnormal changes in lipid metabolism, leading to elevated triglyceride, small dense LDL-c, non-HDL-c, and low HDL-c levels.<sup>26</sup> In the Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) trial that enrolled high-risk patients with T2DM in 32 countries, the prevalence of obesity was 62.1% (of them, 73.2% were  $\geq 60$  years of age), and obese patients were less likely to reach defined lipid goals.<sup>27</sup> Previous studies also revealed that modest weight loss had positive effects on glycemic control, lipid profiles, and other CV risk factors.<sup>28–30</sup> Moreover, the ESC/EASD and American Diabetes Association guidelines identified obesity management as an important target for T2DM treatment.<sup>18,31</sup> However, the strategy for weight control for older patients with T2DM is complex because older individuals often present with other aging-related health issues such as frailty, impaired functional status, polypharmacy, and polymorbidity.<sup>32</sup> Further longitudinal studies are needed to clarify the optimal BMI range for older adults with T2DM and the impact of BMI on their lipid profiles.

Numerous meta-analyses of data from randomized controlled trials have demonstrated that intensive lowering of LDL-c levels with high-intensity statin therapy provides a significant benefit over low-to-moderate intensity statin therapy in terms of preventing non-fatal CV events.<sup>33–35</sup> Furthermore, reaching LDL-c goals was more prevalent in patients treated with high-dose statin thera-

py than in those treated with low-to-moderate-dose statin therapy.<sup>24,36</sup> However, in our study, only 22.4% of all patients with T2DM with very high CV disease risk received high-intensity statin therapy, which can explain the high prevalence of non-achievement of the LDL-c goal of < 1.4 mmol/L (89.2%). The difficulty in managing this very high-risk group was also reported in a recent study in South Korea, which showed that high-intensity statins were prescribed to only 9.1% of patients with very high risk, with 61% of these patients not achieving the LDL-c goal of < 1.8 mmol/L.<sup>37</sup> Suboptimal doses of statins were observed in several Asian countries in the DYSIS-II study,<sup>38</sup> mainly due to concerns about the side effects of higher statin doses satisfaction with patients' LDL-c levels.<sup>39</sup> Our findings highlight the gap between clinical practice and existing guidelines, in that statin utilization remains inadequate, thus contributing to not achieving LDL-C goals.

#### **Non-achievement of the Non-HDL-c Goal in Patients with T2DM with Very High CV Disease Risk**

Non-HDL-c reflects the full spectrum of atherogenic lipoproteins, rather than LDL-c alone. Among statin-treated patients, the association strength with the risk of major CV events was greater for non-HDL-c than for LDL-c.<sup>40</sup> Furthermore, non-HDL-c was a strong predictor of CV disease in patients with diabetes.<sup>41</sup> Thus, the ESC/EAS guidelines for dyslipidemia also define secondary goals based on non-HDL-c levels.<sup>17</sup> In our study, 87.9% of patients did not reach the non-HDL-c goal (< 2.2 mmol/L). Additionally, those participants who did not meet the LDL-c goal were more likely to also not meet the non-HDL-c goal. Our results revealed suboptimal achievements of LDL-c and non-HDL-c goals, as recommended by the ESC/EAS guidelines, in very high-risk patients and should raise physician awareness regarding the need for more aggressive control of dyslipidemia in these patients. This study has several limitations. First, our study was only performed at urban hospitals and included patients who were managed by geriatricians. Thus, the results may not entirely reflect the lipid goal achievement trend in Vietnam or the practices of cardiology physicians. Second, we could not estimate the effects of different types of statin treatment on lipid goal achievement because there were often switches between brand-name and generic statins and different types of statins. Third, we only obtained data on the intensity of statin therapy within one month before enrollment. Fourth, we did not assess the use of medications that may have influenced the achievement rate of the LDL-c goal or adherence to lipid-lowering treatment. Finally, due to the cross-sectional nature of the study design, we could not evaluate the causal relationships between lipid non-achievement and the related factors.

In conclusion, the results of this study showed that the rate of achieving an aggressive LDL-c goal was suboptimal in older patients with T2DM with a very high CV disease risk in Vietnam. Only 10.8% reached the recommended LDL-c goal (< 1.4 mmol/L). Obesity increased the probability of not achieving the LDL-c goal, whereas high-intensity statin therapy decreased this probability.

#### **SUPPLEMENTARY MATERIALS**

Supplementary materials can be found via <https://doi.org/10.4235/agmr.21.0099>.

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#### **CONFLICT OF INTEREST**

The researchers claim no conflicts of interest.

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#### **AUTHOR CONTRIBUTIONS**

Conceptualization, HTN; Data curation, AHN, TTN, HML; Investigation, HTN, AHN, T.T.N, HML; Methodology, HTN, KPTH, HML; Project administration, HTN, HML; Supervision, HTN, HML; Writing-original draft, HTN, KPTH; Writing-review & editing, HTN, AHN, TTN, HML.

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# Older Adults Used Fewer Home Care Services during the COVID-19 Pandemic: Findings from a Secondary Analysis of an Urgent Survey in Japan

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**Background:** This study aimed to identify reduced home care use among older people and its impact on user numbers and service provider revenues during the coronavirus disease 2019 (COVID-19) pandemic. **Methods:** We conducted this secondary analysis of cross-sectional data from long-term care providers in Japan and estimated the probability of client cancellations and service contraction for institutional and home care services adjusted for the service type, area, size, infection occurrence, and staff employment impacts. We then estimated the rate of change in user numbers and revenue related to reduced usage. **Results:** Seventy-two percent of home care providers experienced client cancellations and 42.1% experienced service contraction, both of which were more prevalent in home care than in institutional care (adjusted odds ratio [AOR]=11.09 and 1.60). Home-visit (AOR=0.70) and short-term stay (AOR=0.38) services were less likely to experience client cancellations compared with adult day services. Service contraction was less likely in home-visit services (AOR=0.60) but were more likely in short-stay services (AOR=1.49) compared to adult day services. The estimated reductions in user numbers and revenue related to service contraction for adult day services were 9.1% and 7.1%, respectively. Home-visiting services decreased by an estimated 3.4% owing to service contraction. **Conclusion:** The secondary effects of the COVID-19 pandemic include reduced use of home care services, especially adult day services that include social contact. These secondary effects of the COVID-19 pandemic may cause functional deterioration in non-infected clients and financially impact service providers.

**Key Words:** Adult day care centers, COVID-19, Home care services, Long-term care, Respite care

## INTRODUCTION

Older adults are vulnerable to both coronavirus disease 2019 (COVID-19) and the secondary effects of the pandemic.<sup>1)</sup> Given the lack of effective pharmacological treatment, home isolation has been recommended to prevent infection,<sup>2)</sup> which raises concerns regarding the secondary effects on older people living in the community, including reduced physical activity, social isolation, and reduced access to home care services.<sup>3-5)</sup>

Older people living in the community face additional challenges

related to reduced home care.<sup>6,7)</sup> Even in facilities in which no outbreaks have occurred, home care has been reduced or suspended because employees are required to stay home to prevent the spread of infection and thus are unable to provide care.<sup>8,9)</sup> Families are reluctant to send older people to long-term care (LTC) facilities,<sup>8)</sup> which causes confusion and stress not only to clients but also to family caregivers. The symptoms of people with dementia may also be aggravated by disruptions in their usual lifestyle and prolonged indoor living.<sup>1,10)</sup> Furthermore, a significant decrease in user numbers negatively affects home LTC provider businesses.<sup>11)</sup>

However, little is known about how reduced use affects home care.<sup>7)</sup>

In Japan, the Ministry of Health, Labour and Welfare restricted visits to clients in LTC facilities from February 24, 2020, before a steep increase in the number of cases.<sup>12)</sup> In early March, the first outbreak at an adult day service was identified, following which other LTC providers in the area were required to close.<sup>9)</sup> In late March, the number of infections increased, and on April 1, the government's expert panel recommended suspending or restricting day care services for persons with disability.<sup>13)</sup> A survey of home LTC providers conducted in April showed that 25.6% of respondents had experienced decreases of income of 20% or more in March compared to those in February.<sup>11)</sup> On April 7, a state of emergency was declared for seven prefectures, which was gradually expanded. One percent or more of the adult day services for people with disabilities were closed during this period.<sup>14)</sup> A total of 39 LTC facilities had experienced outbreaks by May 9.<sup>15)</sup>

This study investigated the reduced use of home LTC services using data from an urgent survey of LTC providers in Japan. Reduced usage in this study included both client cancellations (i.e., users voluntarily refraining from using the service) and service contraction (i.e., service providers reducing service availability). To evaluate the magnitude of the effects on home care, we compared the impact of home care services to that of institutional services and assessed which of these home care services were more likely to be affected. The research questions were as follows. (1) Were home LTC services more likely to experience reduced usage than institutional LTC services during the COVID-19 pandemic? Which home LTC services were the most affected? (2) To what extent did reduced usage affect user numbers and provider revenues for each service?

## MATERIALS AND METHODS

### Data

We conducted this secondary analysis of survey data from the Urgent Survey on the Impact of COVID-19 on Long-term Care and Support for Older Adults and Practices and Innovations in the Field. This web-based survey was conducted by members of the Long-Term Care Benefit Expense Subcommittee of the Social Security Council through 15 national associations of LTC providers in Japan. From May 12 to 22, 2020, a total of 6,130 providers responded to the survey. The survey was anonymously conducted, with participant contact information collected voluntarily only when the participants agreed to follow-up surveys. A report of the main survey has already been published.<sup>16)</sup> We obtained the anonymized data, and ethical approval was not required to obtain

these data because they are not participant-identifiable.

### Subjects

The analysis included institutional and home care services covered by public LTC insurance. The institutional care services included nursing homes, geriatric health service facilities, and group homes. The home care services included adult day, home visit, and short stay services.

### Research Question 1

Multivariate logistic regression analysis was conducted with usage reduction as the dependent variable and each service category (i.e., institutional or home care, adult day service, home visit service, or short stay service) as an independent variable. Usage reduction included two categories: client cancellations initiated by clients or their families and service contraction in which service providers reduced or stopped service availability. Client cancellations were measured by a single item asking providers whether they had experienced any cancellation by clients or families. Service contracts were measured using items such as facility closure owing to local governmental request or facility decision, provider requests that users refrain from using the facility, restriction or suspension of new users, and reduced daily service hours. Providers who experienced one or more of these situations were categorized as having experienced service contraction.

We adjusted for three types of variables: (1) service size (because a larger provider is more likely to experience reduced service); (2) service area (because organizations participating in the survey differed in the types of service offered and regional response rates); and (3) occurrence or suspicion of COVID-19 infection among clients, family members, or staff and the impact of COVID-19 on staff employment as they were strong predictors of service reduction. The service size was categorized as (1) < 10 full-time equivalent (FTE) employees, (2) 10–30 FTE, and (3) ≥ 30 FTE. Areas were categorized based on prefectural alert levels: (1) seven prefectures, including Tokyo, where a state of emergency was declared on April 7, (2) six prefectures that were added to the list of specified prefectures on April 16, and (3) another 34 prefectures where a state of emergency was declared on April 16 and where earlier categories indicated an earlier infection spread. The occurrence/suspicion of COVID-19 among clients or family was measured based on whether any client or family member had tested positive for or was suspected of having COVID-19 or had close contact with someone with COVID-19. The occurrence/suspicion of COVID-19 among staff was measured based on whether any staff member had tested positive for infection or had close contact with someone with COVID-19. The impact on staff em-

ployment included employment restrictions, absence or retirement related to infection, fear of infection, or increased childcare and housework of employees.

### Research Question 2

A multiple linear regression analysis was conducted for each service, with the change rate in the user numbers and revenue compared to the previous year as dependent variables and client cancellations and service contraction as independent variables adjusted for service size. This approach was adopted because the data did not include the number of clients with reduced usage and because a simple comparison to the previous year could not distinguish between the time trend and the effect of reduced usage. We retrospectively collected data on the numbers of users in April 2019 and April 2020 and calculated the rate of change by dividing the latter by the former. The participants directly provided their revenue rate of change in April 2020 compared to April 2019. We excluded cases with missing values for each analysis.

## RESULTS

### Participant Characteristics

A total of 6,171 responses were obtained. After excluding cases with missing variables, the analyses included 5,089 responses. The numbers of institutional care, adult day service, short stay service, and home visiting service clients were 2,569, 844, 217, and 1,459, respectively.

Table 1 shows the characteristics of the participating providers. More than half of the institutional care (63.3%) and short stay service (61.8%) providers were large scale providers, with smaller proportions of adult day service (5.2%) and home visiting service (1.6%) providers. The number of respondents from high-alert areas was larger for home visit services (46.8%) and smaller for short stay services (23.0%). Infection and suspected cases occurred more frequently in home visit services (29.3%). Less than 2.2% of providers had infection or contact with COVID-19 patients for all services. More than 50% of participants reported impacts on staff employment in all services.

### Client Cancellations and Service Contraction

Thirty-one percent of institutional care providers and 72.0% of home care providers experienced client cancellations. Table 2 shows the prevalence of reduced usage and the results of the logistic regression analysis with client cancellations and service contraction as dependent variables. Service type was significantly associated with client cancellations, with an adjusted odds ratio (AOR) of 11.09.

Service contraction occurred in 38.2% of institutional care and 42.1% of home care providers. While service contraction was significantly more likely to occur in home care, the AOR of 1.60 was lower than that for client cancellations. Among home care services, adult day service had the highest rate of client cancellation (76.7%). Short stay services were less likely to experience client cancellations (AOR=0.38) than adult day services but were more

**Table 1.** Service provider characteristics

	Institutional (n = 2,569)	Home care (n = 2,520)	Adult day (n = 844)	Short stay (n = 217)	Home visiting (n = 1,459)
Service size					
Small	217 (8.4)	1,600 (63.5)	473 (56.0)	30 (13.8)	1,097 (75.2)
Mid	650 (25.3)	719 (28.5)	327 (38.7)	53 (24.4)	339 (23.2)
Large	1,702 (66.3)	201 (8.0)	44 (5.2)	134 (61.8)	23 (1.6)
Area					
With earlier alert	748 (29.1)	1,000 (39.7)	267 (31.6)	50 (23.0)	683 (46.8)
With mid alert	389 (15.1)	361 (14.3)	130 (15.4)	33 (15.2)	198 (13.6)
With later alert	1,432 (55.7)	1,159 (46.0)	447 (53.0)	134 (61.8)	578 (39.6)
Infection/suspicion among users or family					
No	2,282 (88.8)	1,968 (78.1)	737 (87.3)	200 (92.2)	1,031 (70.7)
Yes	287 (11.2)	552 (21.9)	107 (12.7)	17 (7.8)	428 (29.3)
Infection/suspicion among staff					
No	2,512 (97.8)	2,474 (98.2)	831 (98.5)	214 (98.6)	1,429 (97.9)
Yes	57 (2.2)	46 (1.8)	13 (1.5)	3 (1.4)	30 (2.1)
Impact on staff employment					
No	937 (36.5)	1,208 (47.9)	409 (48.5)	94 (43.3)	705 (48.3)
Yes	1,632 (63.5)	1,312 (52.1)	435 (51.5)	123 (56.7)	754 (51.7)

**Table 2.** Associations between service types and usage restrictions

		Client cancellations					Service contraction				
		n (%)	OR	AOR	LLCI	ULCI	n (%)	OR	AOR	LLCI	ULCI
All services (n = 5,089)	Service type										
	Institutional	805 (31.3)	Ref	Ref			983 (38.3)	Ref	Ref		
	Home care	1,816 (72.1)	5.65*	11.09*	9.14	13.46	1,062 (42.1)	1.18*	1.60*	1.36	1.89
	Service size										
	Small	1,151 (63.3)	Ref	Ref			717 (39.5)	Ref	Ref		
	Mid	647 (47.3)	0.52*	1.08	0.91	1.30	465 (34.0)	0.79*	0.90	0.76	1.05
	Large	823 (43.2)	0.44*	2.58*	2.07	3.23	863 (45.3)	1.27*	1.74*	1.44	2.10
	Area										
	With earlier alert	1,079 (61.7)	Ref	Ref			881 (50.4)	Ref	Ref		
	With mid alert	390 (52.0)	0.67*	0.80*	0.66	0.98	312 (41.6)	0.70*	0.75*	0.63	0.89
	With later alert	1,152 (44.5)	0.50*	0.64*	0.56	0.74	852 (32.9)	0.48*	0.55*	0.48	0.63
	Infection/suspicion among users or family										
	No	2,019 (47.5)	Ref	Ref			1,595 (37.5)	Ref	Ref		
	Yes	602 (71.8)	2.81*	1.84*	1.53	2.21	450 (53.6)	1.93*	1.48*	1.26	1.73
	Infection/suspicion among staff										
	No	2,550 (51.1)	Ref	Ref			1,980 (39.7)	Ref	Ref		
	Yes	71 (68.9)	2.12*	1.39	0.87	2.21	65 (63.1)	2.60*	1.64*	1.08	2.5
Impact on staff employment											
No	959 (44.7)	Ref	Ref			656 (30.6)	Ref	Ref			
Yes	1,662 (56.5)	1.60*	1.87*	1.63	2.14	1,389 (47.2)	2.03*	1.75*	1.54	1.98	
Home care services (n = 2,520)	Service type										
	Adult day	646 (76.5)	Ref	Ref			365 (43.2)	Ref	Ref		
	Short stay	111 (51.2)	0.32*	0.38*	0.26	0.57	116 (53.5)	1.51*	1.49*	1.02	2.16
	Home-visiting (n = 1,549)	1,059 (72.6)	0.81*	0.70*	0.57	0.87	581 (39.8)	0.87	0.72*	0.6	0.87
	Service size										
	Small	1,133 (70.8)	Ref	Ref			678 (42.4)	Ref	Ref		
	Mid	571 (79.4)	1.59*	1.47*	1.17	1.84	275 (38.2)	0.84	0.70*	0.58	0.85
	Large	112 (55.7)	0.52*	0.77	0.51	1.16	109 (54.2)	1.61*	1.01	0.69	1.48
	Area										
	With earlier alert	784 (78.4)	Ref	Ref			479 (47.9)	Ref	Ref		
	With mid alert	259 (71.7)	0.70*	0.77	0.58	1.03	153 (42.4)	0.8	0.81	0.63	1.03
	With later alert	773 (66.7)	0.55*	0.67*	0.55	0.83	430 (37.1)	0.64*	0.68*	0.57	0.82
	Infection/suspicion among users or family										
	No	1,343 (68.2)	Ref	Ref			783 (39.8)	Ref	Ref		
	Yes	473 (85.7)	2.79*	2.34*	1.78	3.06	279 (50.5)	1.55*	1.47*	1.19	1.8
	Infection/suspicion among staff										
	No	1,777 (71.8)	Ref	Ref			1,034 (41.8)	Ref	Ref		
Yes	39 (84.8)	2.19*	1.13	0.48	2.64	28 (60.9)	2.17*	1.68	0.9	3.1	
Impact on staff employment											
No	785 (65.0)	Ref	Ref			421 (34.9)	Ref	Ref			
Yes	1,031 (78.6)	1.98*	1.81*	1.5	2.18	641 (48.9)	1.79*	1.67*	1.42	1.98	

Multivariate logistic regression analysis (adjusted for the service size, area, infections/suspicion among users and family, infections/suspicion among staff, and impact on staff employment).

OR, (crude) odds ratio; AOR, adjusted odds ratio; LLCI/ULCI, lower/upper limit of the 95% confidential interval.

\*p<0.05.

likely to experience service contraction (AOR= 1.49). The home visiting service was significantly less likely to have either client cancellations (AOR=0.70) and service contraction (AOR=0.72) than adult day services.

**Impact on Client Numbers and Revenue**

Table 3 shows the effects of client cancellations and service contracts on user numbers and revenue for each service. We observed no significant changes in the number of institutional care users but did observe significant revenue decreases related to client cancellations (b = -0.014) and service contraction (b = -0.019) in institutional LTC providers. Home care showed a significant decrease in the number of users (b = -0.057) and income (b = -0.049) related to service contraction.

In the adult day service, service contraction was associated with changes in user numbers (b = -0.091) and revenue (b = -0.071). We observed no significant changes in the short stay service. While the mean number of home visiting service users increased (+0.5%), service contraction was associated with a significant reduction in revenue (b = -0.034).

**DISCUSSION**

Home care was more likely to experience reduced usage than institutional care. It is difficult to suspend services for clients in an LTC facility and move them back to their homes or to another facility. In addition, clients in institutional care facilities had lower activities of daily living (ADLs) than those using home care; thus, it may have been difficult for them to postpone their admission and continue home care. This may have prevented reduced institutional usage especially that associated with client cancellation. We estimated that reduced institutional usage reduced revenues by 1.4%–1.9%. This was lower than that for home care, and reduced usage was assumed to occur in a limited number of patients.

In this study, 72% of home care providers experienced client cancellations, a rate significantly higher than that for institutional services. Although the government did not recommend avoiding the use of home-based services in general, clients may have perceived that the risk of infection from home care services exceeded the benefits of using them. In addition to health anxiety and risk to loved ones, regular media use and social media use were identified as predictors of fear related to COVID-19.<sup>17)</sup> While the media are critical for conveying information to the public and promoting

**Table 3.** Changes in the number of users and revenue depending on usage restrictions by service

Predictor		Change rate in the number of users				Change rate in revenue			
		n	Mean ± SD	b	95% CI	n	Mean ± SD	b	95% CI
Institutional	Total	2,353	-0.013 ± 0.864			2,569	-0.010 ± 0.092		
	Client cancellations	735	-0.018 ± 0.849	-0.010	-0.023, 0.003	805	-0.024 ± 0.105	-0.014*	-0.022, -0.006
	Service contraction	893	-0.012 ± 0.878	0.003	-0.008, 0.015	983	-0.025 ± 0.107	-0.019*	-0.026, -0.011
Home care	Total	2,150	-0.040 ± 0.728			2,520	-0.040 ± 0.172		
	Client cancellations	1,573	-0.045 ± 0.726	-0.011	-0.037, 0.016	1,816	-0.046 ± 0.177	-0.014	-0.029, 0.001
	Service contraction	907	-0.074 ± 0.718*	-0.057*	-0.081, -0.034	1,062	-0.068 ± 0.186	-0.049*	-0.062, -0.035
Adult day	Total	776	-0.098 ± 0.781			844	-0.094 ± 0.175		
	Client cancellations	592	-0.104 ± 0.772	-0.013	-0.049, 0.023	646	-0.101 ± 0.178	-0.025	-0.053, 0.002
	Service contraction	342	-0.149 ± 0.789	-0.091*	-0.122, -0.061	365	-0.135 ± 0.195	-0.071*	-0.095, -0.048
Short stay	Total	189	-0.089 ± 0.772			217	-0.035 ± 0.162		
	Client cancellations	99	-0.087 ± 0.793	0.002	-0.065, 0.069	111	-0.050 ± 0.195	-0.026	-0.070, 0.018
	Service contraction	99	-0.113 ± 0.751	-0.051	-0.116, 0.014	116	-0.048 ± 0.175	-0.026	-0.069, 0.018
Home visit	Total	1,185	0.005 ± 0.699			1,459	-0.009 ± 0.163		
	Client cancellations	882	0.000 ± 0.700	-0.018	-0.058, 0.022	1,059	-0.011 ± 0.165	-0.003	-0.022, 0.016
	Service contraction	466	-0.011 ± 0.682	-0.025	-0.061, 0.010	581	-0.030 ± 0.170	-0.034*	-0.052, -0.017

Multivariate linear regression analysis: clients' cancellation (=1, no=0) and service contraction (=1, no=0) as independent variables, adjusted for the service size. SD, standard deviation; CI, confidence interval.

\*p<0.05.

preventive behavior, information should be conveyed without sensationalism or disturbing images to avoid generating excessive fear.<sup>18)</sup> The World Health Organization has also recommended that individuals limit seeking information from the media to about twice a day.<sup>19)</sup> Additionally, service providers may have failed to adequately inform clients of the services' benefits and risks of service suspension. The purpose of LTC insurance is to provide health, medical, and welfare benefits for services necessary for clients to lead independent lives and maintain their dignity.<sup>20)</sup> In this study, service providers were concerned about a potential decline in ADLs (68.9% of respondents were concerned), fewer opportunities to go out and socialize (59.2%), cognitive function decline (58.1%), increased burden on family caregivers (57.3%), and physical inactivity (42.3%).<sup>16)</sup> Emerging evidence has shown that community-dwelling older adults experienced negative effects on anxiety, depression, sleep quality, and physical activity during the period of social isolation due to COVID-19.<sup>21)</sup> Insufficient communication on why home services are necessary and how they contribute to clients' health may have led to substantial underutilization. To avoid excessive client cancellations in future pandemics, it may be necessary to agree with clients and their families on the necessity and benefits of the regular use of home care services.

Among home care services, adult day services were more likely to experience reduced usage. Adult day service embeds social contact in its process.<sup>22,23)</sup> Because clients often stay in the same place and eat at the same time in adult day services, it may have been difficult to take measures to prevent infection. Furthermore, since clients of adult day services have lower care needs on an average than short stay service clients, adult day services may have been temporarily replaced by informal caregiving or perceived as less necessary. The average increase in the number of home visit service users suggests that some clients reduced their use of adult day services and replaced these services with home visit services. Service contraction was more likely to occur in short stay services; however, as they were mostly located in LTC institutions with residents at higher risks of severe illness, they adopted more stringent preventive measures.

The adult day service experienced the largest impact on user numbers and revenue following reduced usage. We estimated that service contraction caused a 12.0% decrease in user numbers and a 7.2% decrease in revenue. Since the average profit ratio is 3.1% for all LTC providers and 3.3% for adult day service,<sup>24)</sup> a revenue reduction exceeding 10% could be critical. In this study, 19.9% of respondents reported increased expenditures related to additional infection control materials/ equipment and working hours;<sup>16)</sup> thus, the impact on the profit ratio was likely greater. Home care providers are smaller enterprises than institutional care providers and

therefore are likely to have less financial capacity. Although the proportion of service contractions was lower than that of client cancellations, it was much higher than the proportion of infected cases among service providers and users, suggesting that services were contracted in a fairly precautionary manner. As the pandemic continues, there has been progress in infection control training, including standard precautions and stocking of infection prevention items in home services. These efforts should continue to ensure service continuity as much as possible during future pandemics.

This study was conducted with an emphasis on timeliness, which limited the representativeness of the sample. It was difficult to survey facilities in crisis situations or that were closed due to outbreaks. Nevertheless, the results of the survey of care managers<sup>16)</sup> also demonstrating that adult day services most commonly experienced service contraction, followed by short stay services and home-visiting services, suggests that this tendency is reliable.

The rates of change in client numbers and revenue are less reliable because the respondents were asked to retrospectively indicate the changes from the previous year. In addition, the rate of change was based on April data, while the usage restrictions were based on data at the time of the response (May 12–22); thus, there is a time gap. The results of this study should be followed up with further analyses of LTC insurance records and ongoing administrative survey data. Prolonged reduced usage may cause deterioration of physical and psychological outcomes, regardless of the COVID-19 situation. The potential long-term impact on the older population requires further investigation. In addition, the data did not include the condition of the affected clients (e.g., care level). This topic also requires further exploration as older people with higher care levels may be more vulnerable to the negative effects of service reduction.

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**CONFLICT OF INTEREST**

The researchers claim no conflicts of interest.

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**AUTHOR CONTRIBUTION**

Conceptualization, MK, SH; Data curation, HM, SH; Investigation, MK, SH; Methodology, HM; Project administration, MK, SH; Supervision, MK, SH; Writing-original draft, HM; Writing-review & editing, MK, SH, and HM.

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# Determination of an Optimal Frailty Cutoff Score of Tilburg Frailty Indicator and Frailty Associated Factors in Community-Dwelling Turkish Older Adults

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**Background:** Frailty is a multidimensional and dynamic state that has adverse physical, psychological, and social outcomes. The Tilburg Frailty Indicator (TFI) has the most robust evidence of reliability and validity for assessing frailty. However, the characteristics of TFI have not been investigated in detail. This study aimed to set a cutoff score for frailty and evaluate frailty-associated factors in community-dwelling older adults. **Methods:** This cross-sectional study assessed frailty according to both the TFI and Fried criteria. The Geriatric Depression Scale, basic and instrumental activities of daily living, and Hospital Anxiety and Depression Scale-Anxiety subscale were also implemented. **Results:** This study included 166 older adults. The area under the receiver operating characteristic curve was 0.735 (95% confidence interval, 0.648–0.823). A TFI cutoff point of 8, showed a sensitivity of 60% and specificity of 72.5% for the prediction of frailty ( $p < 0.05$ ). Frailty according to the TFI was more associated with the physical and psychological parameters, while frailty according to the Fried score was more closely related to the physical parameters ( $p < 0.05$ ). **Conclusion:** The results of this study suggested an optimal TFI cutoff score of 8 as a frailty instrument in community-dwelling older adults. Additionally, the TFI included physical, psychological, and social aspects, thereby providing a multidimensional evaluation of frailty.

**Key Words:** Aged, Frailty, Tilburg Frailty Indicator

## INTRODUCTION

Frailty is an important geriatric syndrome characterized by an age-associated decline in physiologic reserve that causes serious adverse health consequences such as hospitalization, institutionalization, and mortality.<sup>1</sup> Frail persons have increased risks of vulnerability and death due to minor external stress. Frailty is a multidimensional and dynamic state with adverse physical, psychological, and social outcomes.<sup>2</sup>

Although frailty is an important concern worldwide, no international standard definition of frailty has been established.<sup>3</sup> In recent

years, healthcare professionals and researchers have suggested the need to evaluate frailty using a multidimensional approach that includes physical, psychological, and social dimensions.<sup>4</sup> The commonly used frailty scales such as the Fried Frailty Index<sup>5</sup> and FRAIL<sup>6</sup> do not evaluate the psychosocial aspects of the patients. A systematic review demonstrated that the Tilburg Frailty Indicator (TFI) has the most robust evidence of reliability and validity for assessing frailty in older adults among 38 multi-component frailty assessment tools.<sup>7</sup> The TFI is a multidimensional, useful, and applicable instrument that assesses the physical, psychological, and social components of frailty in older adults.<sup>8</sup> The TFI has

been translated and validated in many languages.<sup>9,10</sup>

Different studies have reported different TFI cutoff scores. A previous study showed that a total score of 5 or more was the optimal cutoff for assessing frailty in Dutch persons who were aged 75 years and older,<sup>8</sup> while a TFL cutoff score of 6 was reported in Portuguese individuals (aged  $\geq 65$  years)<sup>11</sup> and a cutoff score of 5 was reported among Chinese community-dwelling older adults (aged  $\geq 60$  years).<sup>9</sup> Thus, different cutoff scores have been identified for different populations. In addition, the characteristics of the TFI have not been investigated in detail. Especially, the relationship between the TFI and sarcopenia according to the revised European Working Group on Sarcopenia in Older People (EWG-SOP-2) requires investigation and the risk factors for frailty should be determined. Therefore, this study aimed to determine a TFI cutoff value and frailty risk factors in older adults.

## MATERIALS AND METHODS

### Study Design and Participants

This cross-sectional study included 166 participants who were aged 60 years or older and admitted to the geriatric outpatient clinic in Turkey. We excluded individuals with severe illnesses that affected their general health statuses, such as congestive heart failure (Class III and IV), respiratory failure, acute coronary syndrome, acute renal failure, and cancer. Since the reliability of handgrip strength is low in older patients with dementia because of their difficulty in comprehension, which can cause them to fail to complete tasks, we also excluded patients with moderate and severe dementia.<sup>12</sup>

All procedures performed in studies involving human participants or human tissue were in accordance with the ethical standards of the Institutional Ethical Review Board of Dokuz Eylul University (No. 3282-GOA) and with the 1975 Declaration of Helsinki and its later amendments or comparable ethical standards. Informed consent was obtained from all participants included in the study.

### Data Collection

#### Participant characteristics

Participant characteristics (age, sex, years of education, comorbidities, falls in the previous year, and the number of medications) were recorded. On admission, the participants were asked whether they had fallen in the previous year. Dementia and depression were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5) criteria.<sup>13</sup> A comprehensive geriatric assessment was performed for each participant, in-

cluding the Mini-Mental State Examination (MMSE),<sup>14</sup> Clinical Dementia Rating Score (CDR), Geriatric Depression Scale (GDS),<sup>15</sup> basic and instrumental activities of daily living (BADL, IADL),<sup>16</sup> Tinetti Performance-Oriented Assessment of Mobility (POMA),<sup>17</sup> and Mini Nutritional Assessment (MNA).<sup>18</sup> Additionally, the Hospital Anxiety and Depression Scale-Anxiety subscale (HADS-A) was used to assess anxiety. The HADS-A comprises seven items, each of which is scored from 0 (not present) to 3 (considerable).<sup>19</sup>

#### Laboratory measurements

Laboratory tests, such as renal and liver functions and fasting blood glucose, hemogram, thyroid-stimulating hormone (TSH), C-reactive protein (CRP), vitamin D, vitamin B12, and folic acid levels were measured to evaluate the biochemical, metabolic, and nutritional status of the patients. These values were all obtained using an auto-analyzer diagnostic modular system (Roche E170 and P800; Roche, Basel, Switzerland). Serum 25-hydroxyvitamin D (25(OH)D) levels were measured by radioimmunoassay.

#### Frailty assessment

We assessed frailty according to the TFI and modified Fried Physical Frailty Scale. The TFI has two parts. Part A contains 10 items with different predictors of frailty based on socio-demographic data, while Part B contains 15 total items to assess physical (8 items), psychological (4 items), and social (3 items) parameters. The total score of the scale is calculated from Part B, with high scores indicating increased frailty.<sup>8</sup> Frailty was also evaluated using the modified Fried Physical Frailty Scale. According to this scale, the presence of three or more of the following five criteria indicated frailty: weight loss, exhaustion, low physical activity, slowness, and weakness.<sup>5</sup>

#### Sarcopenia assessment

We assessed sarcopenia according to the revised version of the EWGSOP, which recommends evaluating muscle strength, muscle quantity, and physical performance while considering ethnic differences.<sup>20</sup> Therefore, the cutoff points for skeletal muscle mass and strength were accepted according to those reported in a validated Turkish study.<sup>21</sup>

Handgrip strength was measured using a JAMAR hydraulic hand dynamometer (Model J00105; Lafayette Instrument, Lafayette, IN, USA). The arm was positioned at the side of the body, and the dynamometer was held with the elbow flexed to 90°. The measurements were repeated three times, with the maximum value of the dominant hand used in the analyses. Low muscle strength (MS) was defined as  $< 14$  kg and  $< 28$  kg in women and men, re-

spectively.<sup>21)</sup>

Bioelectrical impedance analysis (BIA) was performed using a TANITA device (MC-780U, multi-frequency segmental body composition analyzer; TANITA, Tokyo, Japan). Based on the muscle mass bioimpedance values, skeletal muscle (SM, in kg) was calculated as:<sup>22)</sup>

$$[(\text{height}^2 / R) \times 0.401] + (\text{gender} \times 3.825) + (\text{age} \times -0.071) + 5.102$$

The skeletal muscle mass index (SMI) was calculated by dividing the skeletal muscle mass (SMM) in kilograms by the length in square meters ( $\text{SMI} = \text{SMM} / \text{height}^2$ ). Low muscle quantity was defined as  $< 5.70 \text{ kg/m}^2$  and  $< 8.33 \text{ kg/m}^2$  in female and male, respectively.<sup>21)</sup>

We used the 4-m walking time to assess physical performance, with low physical performance defined as a rate of  $\leq 0.8 \text{ m/s}$ .<sup>20)</sup>

### Sample Size

The minimum sample size was calculated using the Power Analysis and Sample Size (PASS) software version 11 (NCSS Software, Kaysville, UT, USA).<sup>23)</sup> Assuming a prevalence of frailty of 28%,<sup>12)</sup> at least 150 patients were required (prevalence = 28%, hypothesis null = 0.6, hypothesis alternative = 0.8, power of 80%).

### Data Analysis

We performed all statistical analyses in SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY, USA). We used Shapiro–Wilk test and histograms to check for the normality of the data distributions. Mean and standard deviation (SD) values were reported for continuous variables and percentage values for categorical variables.

We assessed the areas under curves of receiver operating characteristic (ROC) analysis to test the predictive accuracy of the TFI for the identification of patients with frailty according to the Fried Frailty Index, which is considered the “gold standard” for evaluating frailty,<sup>5,24)</sup> and to set an appropriate cutoff point. We considered test values of  $< 0.7$ ,  $0.7\text{--}0.9$ , and  $> 0.9$  to indicate low moderate (useful for some purposes), and high accuracy, respectively.<sup>25)</sup>

We performed binary logistic regression analysis to identify variables that were potential risk factors (independent variables: POMA total, POMA gait, POMA balance, walking speed, BADL, HADS-A, GDS, IADL, MNA, low MS, low SM, sarcopenia) of frailty according to the TFI and the Fried Frailty Index (dependent variable: persons with  $\text{TFI} < 8$  and  $\text{Fried} < 3$  who were not frail). The regression analysis included continuous variables (total POMA gait, POMA balance, walking speed, BADL, HADS-A, GDS, IADL, and MNA) and categorical variables (low MS, low SM, and sarcopenia). The reference group notations for low MS,

low SM, and sarcopenia were 1. We expressed the results as adjusted odds ratios (ORs) with corresponding 95% confidence intervals (CIs). The level of significance was set at  $p < 0.05$ .

## RESULTS

This study included a total of 166 older adult patients. The mean ages in the frail and non-frail groups were 73.10 years and 72.89 years, respectively (Table 1). The characteristics and outcome measures of the participants are presented in Table 1. The non-frail group showed higher education level, laboratory values (hemoglobin, vitamin D, and vitamin B12 levels), POMA score (total, balance, gait), activities of daily living (IADL and BADL scores), MNA score, handgrip strength, SMM, SMI, gait speed, and BMR and lower number of medications, falls, GDS, and HADS-A scores, than the frail group ( $p < 0.05$ ) (Table 1). The Fried frailty states differed between groups ( $p < 0.05$ ) (Table 1, Fig. 1). The comorbidities were similar between the groups ( $p > 0.05$ ) (Table 1).

The area under the ROC curve was 0.735 (95% CI, 0.648–0.823). A TFI cutoff point of 8, showed a sensitivity of 60% and specificity of 72.5% for the prediction of frailty ( $p < 0.05$ ). In the assessment of the diagnostic value of the area under the curve, this value was significant ( $p < 0.05$ ) (Fig. 2).

Frailty according to the TFI was more associated with lower POMA total-balance scores, lower BADL scores, higher HADS-A scores, higher GDS scores, lower MNA scores, and low MS. Frailty according to the Fried score was more closely related to lower POMA total-balance scores, lower walking speed, lower ADL scores, lower MNA score, and low MS ( $p < 0.05$ ) (Table 2). Neither TFI nor Fried scores were associated with sarcopenia ( $p > 0.05$ ) (Table 2).

## DISCUSSION

The main finding of the study was that a total TFI score of 8 or more was the optimal cutoff for assessing frailty in older adults. Second, the Fried score was more closely related to physical parameters, while the TFI score was more associated with both psychosocial and physical parameters. Third, the measures of psychosocial and physical parameters were better in the non-frail group than those in the frail group. Additionally, neither the TFI nor the Fried scores were associated with sarcopenia.

Frailty is one of the most crucial problems associated with a high risk of adverse outcomes. Frailty is a multidimensional and dynamic state that has adverse physical, psychological, and social outcomes.<sup>2)</sup> The TFI had the most robust evidence of reliability and validity for assessing frailty in older adults among 38 multi-compo-

**Table 1.** Participant characteristics

	All participants (n = 166)	Frail group (TFI ≥ 8) (n = 57)	Non-frail group (TFI < 8) (n = 109)	p-value
<b>Demographic characteristics</b>				
Age (y)	72.96 ± 6.41	73.10 ± 6.54	72.89 ± 6.36	0.84
Sex, female	112 (67.5)	48 (84.2)	64 (58.7)	< 0.01*
BMI (kg/m <sup>2</sup> )	28.57 ± 5.22	29.54 ± 5.63	28.06 ± 4.95	0.08
Education (y)	7.42 ± 4.92	5.33 ± 4.60	8.53 ± 4.74	< 0.01*
Number of medications	5.04 ± 2.87	6.05 ± 3.13	4.51 ± 2.59	< 0.01*
Falls	54 (32.5)	25 (43.9)	29 (26.6)	0.03*
MMSE score	26.49 ± 3.69	26.13 ± 3.80	26.72 ± 3.62	0.45
<b>Laboratory values</b>				
Hemoglobin (g/dL)	12.77 ± 1.28	12.39 ± 1.17	12.97 ± 1.30	< 0.01*
CRP	4.50 ± 7.36	4.95 ± 8.67	4.19 ± 6.34	0.36
Albumin	4.14 ± 0.33	4.08 ± 0.35	4.17 ± 0.31	0.16
Folic acid	9.89 ± 4.47	9.50 ± 5.08	10.10 ± 4.11	0.12
Vitamin D (ng/mL)	24.13 ± 10.96	21.68 ± 9.33	25.48 ± 11.58	0.03*
Vitamin B12 (pg/mL)	389.32 ± 246.09	335.38 ± 190.76	418.10 ± 267.44	0.04*
Blood Glucose (mg/dL)	111.39 ± 40.26	119.14 ± 53.35	107.26 ± 30.64	0.12
TSH (mLU/L)	1.80 ± 1.54	1.96 ± 1.79	1.72 ± 1.39	0.33
<b>Comorbidities</b>				
Cerebrovascular disease	8 (4.8)	4 (7.0)	4 (3.7)	0.44
Diabetes mellitus	55 (33.1)	20 (35.1)	35 (32.1)	0.73
Hypertension	109 (65.7)	38 (66.7)	71 (65.1)	0.86
Hyperlipidemia	44 (26.5)	19 (33.3)	25 (22.9)	0.19
Congestive cardiac failure	8 (4.8)	4 (7.0)	4 (3.7)	0.44
COPD	17 (10.2)	5 (8.8)	12 (11.0)	0.79
Dementia	18 (10.8)	6 (10.5)	12 (11.0)	0.92
Sarcopenia	15 (9.0)	6 (10.5)	9 (8.3)	0.62
<b>Comprehensive geriatric assessment</b>				
Fried frailty score	1.56 ± 1.30	2.15 ± 1.41	1.24 ± 1.12	< 0.01*
Fried frailty states				0.01*
No abnormalities	37 (22.3)	7 (12.3)	30 (27.5)	
Pre-frail	94 (56.6)	29 (50.9)	65 (59.6)	
Frail	35 (21.1)	21 (36.8)	14 (12.8)	
POMA total score	25.68 ± 3.44	24.26 ± 3.96	26.42 ± 2.88	< 0.01*
POMA balance score	14.55 ± 2.15	13.61 ± 2.5	15.05 ± 1.75	< 0.01*
POMA gait score	11.13 ± 1.51	10.65 ± 1.70	11.39 ± 1.34	< 0.01*
IADL score	19.59 ± 4.59	18.42 ± 5.31	20.20 ± 4.06	0.01*
BADL score	92.78 ± 8.41	89.16 ± 10.82	94.68 ± 6.07	< 0.01*
GDS score	3.32 ± 3.63	5.91 ± 3.9	2.04 ± 2.63	< 0.01*
HADS-A score	6.66 ± 4.77	9.52 ± 4.28	5.16 ± 4.32	< 0.01*
MNA score	12.84 ± 1.56	12.16 ± 1.78	13.19 ± 1.30	< 0.01*
Handgrip strength (kg)	19.37 ± 9.46	15.37 ± 8.64	22.95 ± 9.37	< 0.01*
Low muscle strength	76 (45.8)	33 (57.9)	43 (39.4)	< 0.01*
SMM (kg)	18.69 ± 4.53	17.14 ± 3.62	19.50 ± 4.76	< 0.01*
SMI (kg/m <sup>2</sup> )	7.45 ± 1.31	7.15 ± 1.23	7.60 ± 1.32	0.03*
Low muscle quantity	27 (16.3)	9 (15.8)	18 (16.5)	0.90
Gait speed (m/s)	1.00 ± 0.34	0.85 ± 0.32	1.08 ± 0.32	< 0.01*
Low physical performance	48 (28.9)	26 (45.6)	22 (20.2)	< 0.01*
BMR (kcal)	1,408.96 ± 215.13	1,360.87 ± 210.27	1,434.11 ± 214.30	0.03*

Values are expressed as mean (standard deviation) for continuous variables and percent was reported for categorical variables.

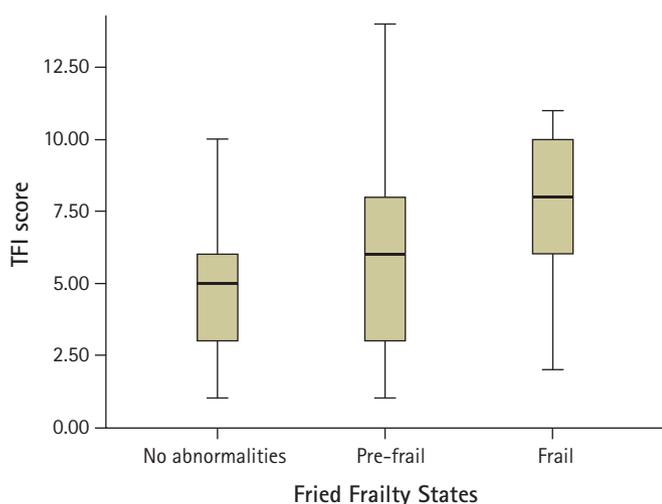
BMI, body mass index; MMSE, Mini-Mental State Examination; TSH, thyroid-stimulating hormone; COPD, chronic obstructive pulmonary disease; TFI, Tilburg Frailty Indicator; POMA, Performance-Oriented Movement Association; BADL, basic activities of daily living; IADL, instrumental activities of daily living; CDR, Clinical Dementia Rating Score; GDS, Geriatric Depression Scale; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; MNA, Mini Nutritional Assessment; SMM, skeletal muscle mass; SMI, skeletal muscle mass index; BMR, basal metabolic rate.

\*p<0.05.

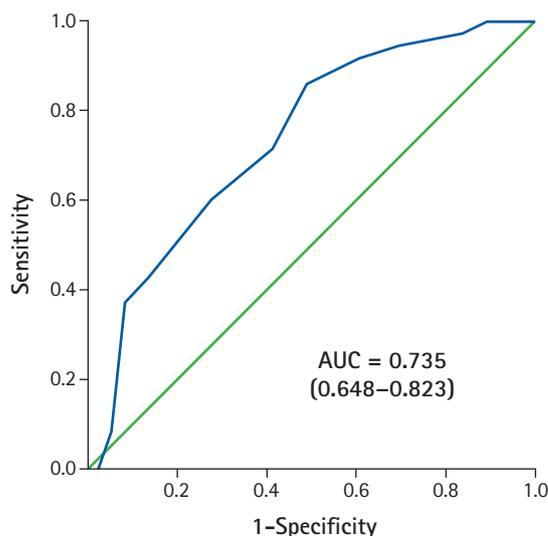
nent frailty assessment tools.<sup>7)</sup> The TFI is a multidimensional, useful, and fast instrument to assess the physical, psychological, and social components of frailty in older adults.<sup>8)</sup> Fried frailty is the most widely used scale for identifying frailty. The scale has five criteria—weight loss, exhaustion, low physical activity, slowness, and weakness. According to this scale, a score > 3 or more indicated frailty.<sup>5)</sup> A cutoff score was calculated for the TFI based on the Fried Frailty, which is considered the “gold standard” for evaluating frailty.<sup>24)</sup> We found that a TFI cutoff score of 8 showed the optimal specificity and sensitivity values. Gobbens et al.<sup>8)</sup> reported a TFI cutoff score of 5 to identify frailty. Our cutoff score was 3 points

higher than that of Gobbens’ study. Gobbens’ study included community-dwelling individuals aged ≥ 75 years, with a mean participant age of 80 years.<sup>8)</sup> Thus, the cutoff score may have differed due to the difference in mean age in these studies.<sup>8)</sup> In addition, factors such as ethnicity and comorbidities can also affect the cutoff score.<sup>9,11)</sup>

Among the many subjective and objective frailty assessment methods,<sup>26)</sup> Fried Frailty is commonly used.<sup>5,27)</sup> This instrument classifies older adults as frail, pre-frail, or non-frail, based on five criteria.<sup>5)</sup> While Fried Frailty predominantly assesses physical frail-



**Fig. 1.** Box-plot of the frailty of the Tilburg Frailty Indicator (TFI) score.



**Fig. 2.** Receiver operating characteristic curve for the Tilburg Frailty Indicator (TFI) cutoff value. AUC, area under the curve.

**Table 2.** Binary logistic regression model for frailty

Variable	TFI score ≥ 8 (frail)				Fried score ≥ 3 (frail)			
	B	SE	p-value	OR (95% CI)	B	SE	p-value	OR (95% CI)
POMA total	-0.15	0.06	0.01*	0.85 (0.75–0.96)	-0.18	0.06	< 0.01*	0.82 (0.72–0.94)
POMA gait	-0.21	0.12	0.09	0.80 (0.62–1.03)	-0.18	0.13	0.15	0.83 (0.64–1.07)
POMA balance	-0.30	0.11	< 0.01*	0.73 (0.59–0.91)	-0.41	0.11	< 0.01*	0.66 (0.52–0.83)
Walking speed	-1.41	0.73	0.05	0.24 (0.05–1.02)	-5.82	1.30	< 0.01*	0.01 (0.01–0.03)
BADL	-0.08	0.02	< 0.01*	0.91 (0.86–0.96)	-0.08	0.03	< 0.01*	0.91 (0.86–0.97)
HADS-A	0.19	0.04	< 0.01*	1.21 (1.11–1.33)	0.06	0.04	0.18	1.06 (0.97–1.16)
GDS	0.30	0.07	< 0.01*	1.35 (1.17–1.56)	0.13	0.06	0.05	1.13 (1.00–1.29)
IADL	-0.06	0.04	0.14	0.93 (0.85–1.02)	-0.15	0.05	< 0.01*	0.85 (0.77–0.95)
MNA	-0.40	0.12	< 0.01*	0.66 (0.52–0.85)	-0.34	0.13	0.01*	0.70 (0.54–0.92)
Low MS	1.10	0.41	< 0.01*	3.03 (1.35–6.78)	1.39	0.46	< 0.01*	4.03 (1.61–10.10)
Low SM	0.21	0.51	0.67	1.24 (0.45–3.42)	-0.60	0.60	0.31	0.54 (0.16–1.79)
Sarcopenia	0.34	0.64	0.58	1.41 (0.40–5.00)	0.22	0.67	0.74	1.25 (0.33–4.68)

TFI, Tilburg Frailty Indicator; GDS, Geriatric Depression Scale; POMA, Performance-Oriented Movement Association; BADL, basic activities of daily living; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; MS, muscle strength; SM, skeletal muscle; SE, standard error; OR, odds ratio; CI, confidence interval.

\*p<0.05.

ty, it also has good validity for assessing frailty.<sup>5,28,29)</sup> We found that the Fried score was more closely related to physical parameters, while the TFI score was more associated with both psychosocial and physical parameters. Thus, the TFI is multidimensional and more comprehensive in evaluating frailty. However, more studies on this subject are required.

Frailty is an important problem that affects the physical and psychological performance of older adults.<sup>2)</sup> Physical and psychological parameters decrease in frail older adults compared to non-frail ones.<sup>2,3)</sup> Consistent with the literature, we found better measures of psychosocial and physical parameters in the non-frail group compared to those in the frail group. Together, these results show the importance of holistic approaches toward frail older adults.

Frailty and sarcopenia are important age-related concerns, with overlap between the two conditions. Frailty and sarcopenia are similar, especially in terms of evaluating physical parameters.<sup>30)</sup> Sarcopenia is now formally recognized as a muscle disease that occurs in older adults but that can also occur earlier in life.<sup>20)</sup> The EWGSOP-2 recommends assessments of muscle strength, muscle quantity, and physical performance in the evaluation of sarcopenia.<sup>20)</sup> We found that neither the TFI nor the Fried scores were associated with sarcopenia, while frailty was associated with low muscle strength, which is the sub-evaluation parameter of sarcopenia. Thus, frailty and sarcopenia are different concepts, between which only physical parameters can be similar.<sup>30)</sup>

This study has some limitations. First, the cross-sectional design precluded inferences about the direction of causality among the variables. Second, BIA was used to assess muscle mass. While it is a valid tool for assessing muscle mass, it does not measure mass directly.

In conclusion, the results of this study suggested an optimal TFI cutoff score of 8 as a frailty instrument in community-dwelling older adults. Additionally, the TFI included physical, psychological, and social aspects, thereby providing a multidimensional evaluation of frailty.

## ACKNOWLEDGMENTS

### CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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None.

### AUTHOR CONTRIBUTIONS

Conceptualization, GO, EAB, BG, NI, ATI; Data curation, GO,

EAB; Funding acquisition, GO, EAB, BG, NI, ATI; Investigation, GO, EAB, BG; Methodology, GO, EAB, BG, NI, ATI; Project administration, GO, NI, ATI; Supervision, NI, ATI; Writing-original draft, GO, EAB, BG; Writing-review & editing, GO, EAB, BG, NI, ATI.

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# Effect of Communication and Education within the Rehabilitation Team: Therapists' and Nurses' Views

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## INTRODUCTION

As modern society enters super-aging status, rehabilitation medical care is important to restore the independence of older adults and individuals with disabilities. In addition, as stated in the 2020–2030 Healthy Aging Decade, hospital culture should aim to be friendly to older adults and provide integrated care. In this context, multidisciplinary care centered on hospitalized older adults and individuals with disabilities is essential.<sup>1,2)</sup>

**Background:** To improve the rehabilitation team's awareness of patient mobility and participation by enhancing communication between therapists and nurses and conducting patient education. **Methods:** This study used a non-equivalent control group with a non-synchronized design. To facilitate communication between therapists and nurses, we used a manual for mobility management to improve the sharing of information on the functional status of patients. We also implemented patient education to improve their awareness of mobility and participation. Finally, we conducted newly devised surveys related to patient functional status and awareness that were applied by therapists and nurses. **Results:** The nurses reported significantly lower functional levels of patients compared to those assessed by therapists. After the intervention, the kappa values representing the concordance between therapists and nurses improved to almost perfect agreement for transfer ability ( $\kappa=0.836$ ), mobility ( $\kappa=0.664$ ), and toileting ( $\kappa=1.000$ ). We also observed a statistically significant increase in questionnaire scores with respect to nurses' awareness ( $p<0.05$ ). **Conclusion:** Improving communication among the rehabilitation team, including nurses through the use of a continuous education program, was effective in promoting the mobility and functional level of patients in the inpatient ward.

**Key Words:** Interdisciplinary communication, Rehabilitation, Activities of daily living, Physical functional performance, Education

The goal of rehabilitation therapy is to improve the activities of daily living (ADL) and increase the participation of patients through functional recovery, which determines the time required for their return to daily life and their level of participation in the community.<sup>3,4)</sup> Among patients receiving rehabilitation therapy, the restoration of mobility and independence is essential for functional improvement.<sup>4,5)</sup> As limited time is available for receiving rehabilitation therapy in the gym and patients spend most of their time in the inpatient ward, patient mobility in the

ward is also important.<sup>6)</sup> However, inappropriate hyperactivity that does not match the patient’s functional status can cause falls, which can lead to fractures, fear of walking, disability, increased hospital stays, and additional costs, thereby inhibiting more effective rehabilitation treatment.<sup>4,7)</sup> Therefore, to promote independence and prevent falls, individualized programs that consider patient function are needed to promote the mobility of patients in the ward.

However, unlike a therapist whose primary goal is to improve mobility and function, nurses in an inpatient rehabilitation ward tend to create dependency and immobility issues due to a lack of knowledge and experience regarding rehabilitation to improve mobility.<sup>5,8-11)</sup> Thus, patient mobility and participation levels differ between the gym and the ward. The insufficient education of nurses regarding rehabilitation leads to their lack of knowledge regarding the importance of rehabilitation for improving mobility. This prevents nurses from facilitating therapy continuation and integration, which play important roles in multidisciplinary rehabilitation team.<sup>12-15)</sup> In this context, the present study aimed to improve the mobility and participation of patients in an inpatient ward by enhancing communication between therapists and nurses and implementing an educational program.

## MATERIALS AND METHODS

### Study Design and Participants

This study was performed between August and November 2019 at

the rehabilitation unit of a community-based hospital in Korea. The participants comprised 45 patients admitted to the rehabilitation department, three therapists in charge, and 32 nurses dedicated to the inpatient rehabilitation ward. This study included all admitted patients receiving rehabilitation therapy, regardless of the diagnosis. The pre-intervention group included 30 patients hospitalized before the intervention period who participated in the survey without intervention, while the intervention group included 27 patients who participated in the survey after the intervention. The intervention group also included 12 patients in the pre-intervention group who were continuously hospitalized during the intervention period. We excluded patients who could not answer the survey questions or who did not agree to participate. We conducted the pre-intervention survey between August 1 and September 30, 2019. The intervention commenced on October 1, 2019 and we conducted the post-intervention survey after 2 weeks (Fig. 1). The surveys were administered on paper, and patients who were unable to complete the questionnaire due to cognitive problems were assisted by a caregiver. The nurses enrolled in this study were not familiar with rehabilitation to improve mobility because they had not received detailed rehabilitation education. Three therapists had extensive experience in rehabilitation for mobility. This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (No. B-2102-664-116).

### Interventions

We conducted two kinds of interventions: efficient communica-

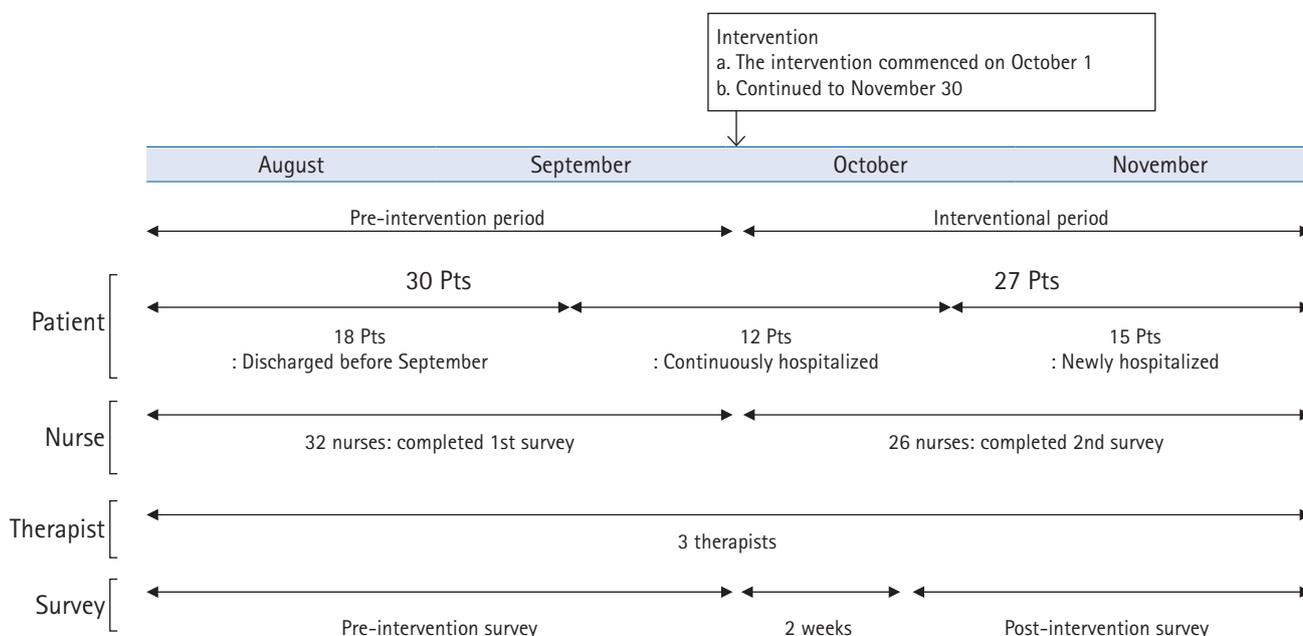


Fig. 1. The process of the study including the data collection timeline and the instrument used. Pts, patients.

tion among rehabilitation staff and promoting awareness of mobility and functional status among nurses and patients (Fig. 2). To do so, the research team produced a manual called “My Rehabilitation Story.” This manual contained useful information about using devices for mobility, such as wheelchairs and walkers, and skills for improving transfer, walking, and toileting. In particular, it contained information about the functional status according to individual patient evaluation. It describes the functional level, such as rolling, sitting up, transitioning from sitting to standing, sitting balance, standing balance, transfer, and performing ADL. The functional level was categorized into four levels according to the degree of help required (independent, supervision, help, and impossible) and recorded, which allowed clear communication of the patient’s functional level by sharing the manual.

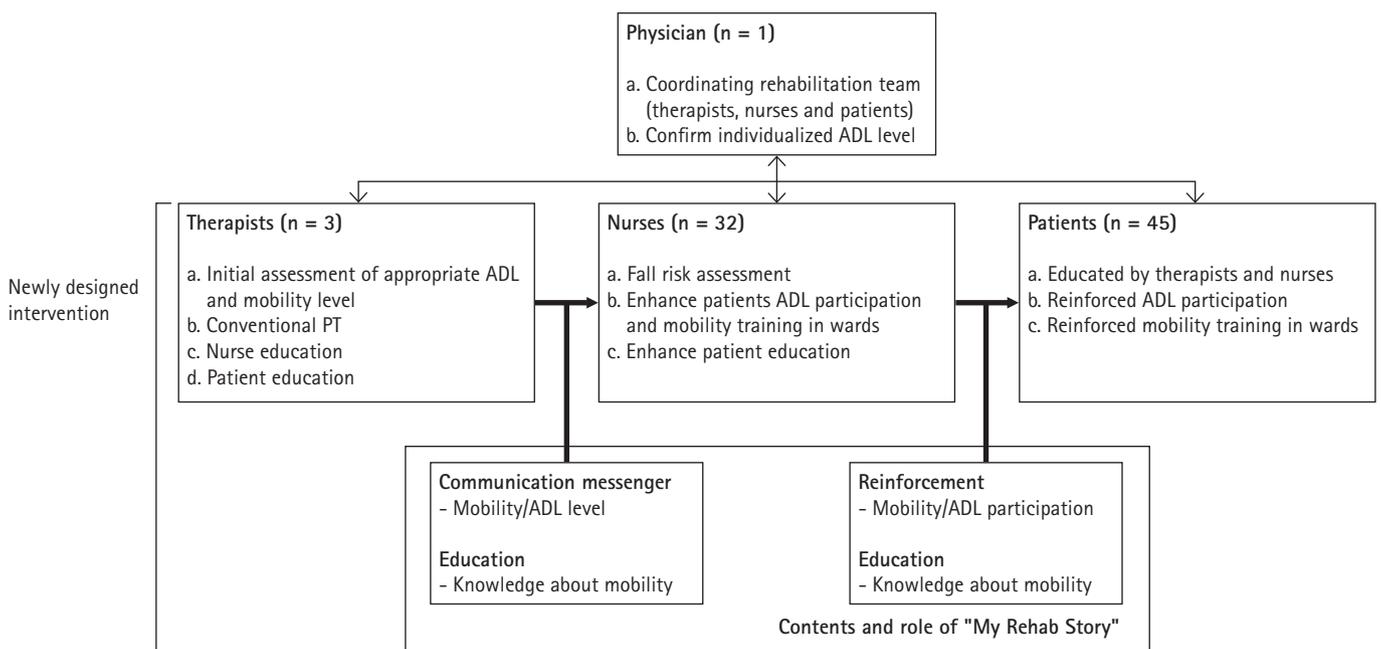
First, the manual was used as a tool for communication between nurses and therapists to share information about each patient’s functional status. The patients’ safe mobility, transfer ability, and toileting level based on the results of the functional evaluation were marked by the therapists on the lists of activities in the manual, which was then delivered to the nurses in the ward as a form of communication. The manuals were kept in the ward to continuously monitor each patient’s level of activity and provide feedback to the patients, with all nurses checking the patient if necessary. In addition, to maximize communication, the rehabilitation team held a 30-minute team meeting once weekly. Second, the manual was used for patient education by therapists and nurses. At the

same time, the nurses could also use the manual for self-directed learning.

### Survey Methodology

This study applied two survey questionnaires devised by the research team. The first questionnaire was related to the patients’ functional status and was administered by the therapists and nurses after the initial functional assessment. The purpose of this survey was to determine the differences in each patient’s functional level, as assessed by therapists and nurses. The survey consisted of multiple-choice questions about transfer ability (Question 1), mobility (Question 2), and toileting (Question 3). The respondents were asked to choose the answer that best suited the patient’s functional level (Supplementary Table S1). Through these questions, we analyzed the agreement on the functional status of each patient between therapists and nurses before and after the intervention.

The second questionnaire was related to the awareness of mobility management. We applied this survey to nurses and patients before and after the intervention and assessed their overall understanding of mobility (Questions 1–2), understanding of patient mobility and function (Questions 3–9), and activity recommendation performance (Question 10). The nurses’ questionnaire consisted of 10 questions, while the patients’ questionnaire consisted of nine questions, as it excluded the question on functional ambulation categories (Question 2). We used a 4-point Likert scale to analyze and interpret the results of the survey (Table 1).



**Fig. 2.** The study was designed to enable efficient communication between physicians, therapists, and nurses and improve activity-related education. We used an activity manual called “My Rehabilitation Story.” ADL, activities of daily living; PT, physical therapy.

### Statistical Analysis

Frequency analysis was performed using descriptive statistics to analyze the general characteristics of the participants.  $\chi^2$  and Fisher exact tests were used to identify differences in participant characteristics between the two time points. Concordance between the therapists and nurses at the functional level was determined using Cohen's kappa ( $\kappa$ ). Response options 1 and 2 were combined into one category, "totally dependent," whereas 3–6 were combined into the category "partially dependent or independent." Agreement was defined as poor ( $< 0.20$ ), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80), or excellent (0.81–1).<sup>16)</sup> The analysis of the nurses' and patients' questionnaires used an ordinal 4-point Likert-type scale with possible responses of "fully disagree," "partly disagree," "partly agree," and "fully agree." Wilcoxon signed-rank tests were used to evaluate the significance of the differences in the responses to these questions. All analyses were performed using SPSS Statistics for Windows, version 22.0 (IBM SPSS, Armonk, NY, USA). In all analyses, statistical significance was set at  $p < 0.05$ .

## RESULTS

### Patient Demographics

Table 2 summarizes the general demographic characteristics of the

patients included in this study. The pre-intervention group included 13 men (43.3%) and 17 women (56.7%) with a mean age of  $71.7 \pm 12.8$  years, while the intervention group included 14 men (48.2%) and 13 women (48.2%) with a mean age of  $67.2 \pm 14.0$  years. The most common diagnosis was stroke in both groups—pre-intervention group, 17 patients (56.7%); intervention group, 15 patients (55.6%). In the pre-intervention group, the Functional Ambulation Category score was  $2.54 \pm 1.50$ , the modified Barthel Index score was  $54.95 \pm 24.25$ , the Mini-Mental State Examination-Dementia Screening score was  $20.33 \pm 7.58$ , and the Global Deterioration Scale score was  $3.44 \pm 1.54$ . In the intervention group, these scores were  $2.44 \pm 1.72$ ,  $57.94 \pm 24.23$ ,  $20.46 \pm 7.04$ , and  $3.54 \pm 1.45$ , respectively. We observed no significant differences in the characteristics or scores between the two groups ( $p > 0.05$ ).

### Agreements on Patient Functional Levels between Therapists and Nurses

We analyzed the views of the therapists and nurses on each patient's functional level. We compared the proportions of patients that therapists and nurses classified as immobile or totally dependent. Regarding transfer ability, nurses and therapists classified 33.3% and 16.7% of patients, respectively, as totally dependent. This difference decreased from 16.6% to 3.7% after the interven-

**Table 1.** Results of surveys assessing the awareness of mobility management among nurses and patients

Questions	Nurses			Patients		
	Non-intervention survey (n = 32)	Post-intervention survey (n = 26)	p-value	Non-intervention period (n = 30)	Post-intervention survey (n = 27)	p-value
Q1 I know how to use a wheelchair and walking aid (walker, cane, crutch, etc.).	3.1 ± 0.6	3.3 ± 0.5	0.27	3.0 ± 0.8	3.2 ± 0.9	0.17
Q2 I know about Functional Ambulation Categories (FAC).	1.7 ± 0.6	2.7 ± 0.7	< 0.01*	†	-	-
Q3 I share the patient's (or my) functional level with the therapist.	1.9 ± 0.6	2.9 ± 0.7	< 0.01*	3.2 ± 0.8	3.3 ± 0.8	0.75
Q4 I know the patient's (or my) strength and level of ambulation in the therapy room.	2.0 ± 0.7	3.2 ± 0.5	< 0.01*	3.1 ± 0.7	3.2 ± 0.8	0.31
Q5 I know how to transfer my patient (or myself). (e.g., wheelchair to bed, wheelchair to toilet)	2.8 ± 0.8	3.4 ± 0.5	0.01*	2.8 ± 0.7	3.4 ± 0.6	< 0.01*
Q6 I know the patient's (or my) safe ambulation level (e.g., walker, cane, wheelchair, self-ambulation).	2.9 ± 0.8	3.2 ± 0.6	0.08	3.0 ± 0.6	3.2 ± 0.9	0.26
Q7 I know the patient's (or my) safe voiding and defecation level (e.g., catheter use, diaper, toilet use).	2.8 ± 0.8	3.3 ± 0.6	0.02*	3.0 ± 0.9	3.3 ± 0.8	0.14
Q8 I know the level of exercise that my patient (or I) can do himself or herself (or myself) in the ward.	2.4 ± 0.6	3.0 ± 0.6	0.01*	3.1 ± 0.7	3.0 ± 0.8	0.94
Q9 I know the fall risk associated with the patient (or myself) (e.g., drugs, catheter, mental condition).	3.1 ± 0.6	3.3 ± 0.6	0.16	2.9 ± 0.7	3.2 ± 0.8	0.10
Q10 I encouraged patients to participate in mobility training in the wards/I exercise on my own initiative in the ward.	2.4 ± 0.7	3.2 ± 0.6	< 0.01*	2.8 ± 0.9	3.0 ± 0.9	0.27

Questions were answered on a 4-point Likert scale (1=fully disagree, 2=partly disagree, 3=partly agree, 4=fully agree).

†, Question 2 was not included for the patients and caregivers.

\* $p < 0.05$ .

**Table 2.** Patient demographic data and clinical characteristics

	Non-intervention period (n = 30)	Intervention period (n = 27)	p-value
Sex			0.60
Male	13 (43.3)	14 (51.9)	
Female	17 (56.7)	13 (48.2)	
Age (y)	71.7 ± 12.8	67.15 ± 13.9	0.25
Diagnosis			0.92
Stroke	17 (56.7)	15 (55.6)	
Hip fracture	7 (23.3)	7 (25.9)	
TKRA	3 (10.0)	1 (3.7)	
Other	3 (10.0)	4 (14.8)	
Pain			0.15
Yes	23 (76.7)	25 (92.6)	
No	7 (23.3)	2 (7.4)	
FAC	2.54 ± 1.50	2.44 ± 1.72	0.94
MBI	55.0 ± 24.3	57.9 ± 24.2	0.65
MMSE-DS	20.3 ± 7.58	20.5 ± 7.04	0.95
GDS	3.44 ± 1.54	3.54 ± 1.45	0.87

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

TKRA, total knee replacement arthroplasty; FAC, Functional Ambulation Categories; MBI, Modified Barthel Index; MMSE-DS, Mini-Mental State Examination-Dementia Screening; GDS, Global Deterioration Scale.

tion (Fig. 3). Regarding mobility, nurses and therapists classified 53.3% and 30% of patients, respectively, as immobile. This difference of 23.3% ( $p = 0.037$ ) decreased to 11.1% ( $p = 0.311$ ) after the intervention. Regarding toileting, nurses and therapists classified 40% and 16.7% of patients, respectively, as totally dependent, with a difference of 23.3% ( $p = 0.045$ ). However, there was no difference between the two groups after the intervention ( $p = 1.000$ ) (Fig. 3). The inter-rater agreement ( $\kappa$ ) rates between therapists and nurses on patient functional level was moderate before the intervention as follows: transfer ability,  $\kappa = 0.571$  ( $p < 0.01$ ); mobility,  $\kappa = 0.494$  ( $p < 0.01$ ); and toileting,  $\kappa = 0.462$  ( $p < 0.01$ ). However, the rates improved substantially to almost perfect agreement after the intervention as follows: transfer ability,  $\kappa = 0.836$  ( $p < 0.01$ ); mobility,  $\kappa = 0.664$  ( $p < 0.01$ ); and toileting,  $\kappa = 1.000$  ( $p < 0.01$ ) (Table 3, Fig. 4).

### Results of Surveys Assessing Awareness of Nurses about Mobility Management

Analysis of the survey of nurses showed increased mean scores for all questions after the intervention. The score increases were significant ( $p < 0.05$ ) for all questions except for those on the use of aids (Question 1), identifying patient mobility level (Question 6), and fall risk assessment (Question 9). The three items that did not exhibit significantly different scores post-intervention had higher scores in the pre-intervention survey than the other items. The rate of disagreement in responses decreased from 42.5% before the in-

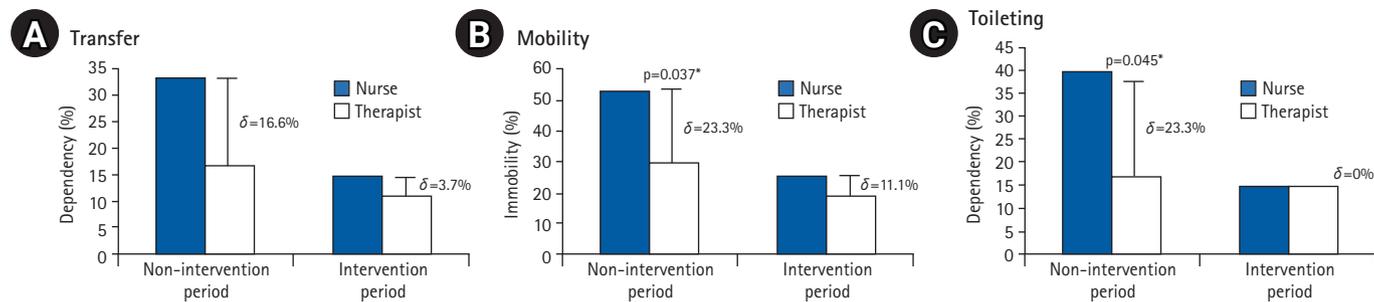
tervention to 10.4% after the intervention (Table 1).

### Results of Surveys Assessing Patient Awareness of Mobility Management

As with the results of the survey for nurses, the intervention group had higher average scores for all items. However, we observed no significant differences between the non-intervention and intervention groups, except for the question about transfer ability (Question 5,  $p < 0.01$ ) (Table 1). In addition, we compared the results of the surveys for nurses and patients conducted during the non-intervention period, as the questionnaire included the same questions except for Question 2. The mean score of the patient group was higher for all questions except for those about the use of aids (Question 1) and fall risk assessment (Question 9).

## DISCUSSION

This study was conducted to improve the rehabilitation team's awareness of patient mobility and participation by enhancing communication between therapists and nurses and conducting patient education. Our intervention yielded several findings. First, after the intervention, the nurses showed significant improvements in their awareness of patient mobility and safety. The survey conducted before the intervention indicated that the nurses lacked awareness of patient fall risk, mobility, and functional levels. However, these improved within a short time through communication and



**Fig. 3.** The proportion of patients determined to be immobile or totally dependent for activities of daily living by nurses and therapists. For all questions, the difference between nurses and therapists was reduced after the intervention, with decreases of 16.6% to 3.7%, 23.3% to 11.1%, and 23.3% to 0% observed for questions related to (A) transfer ability, (B) mobility, and (C) toileting, respectively. \* $p < 0.05$ .

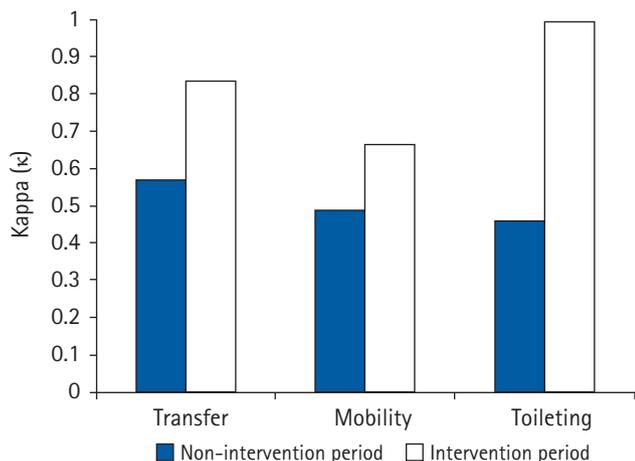
**Table 3.** Descriptive statistics, Cohen’s kappa coefficient ( $\kappa$ ), and measures of the strength of agreement for each item

	Non-intervention period				Intervention period			
	Crude agreement <sup>a)</sup> (%)	Cohen’s $\kappa$	SE of $\kappa$	Strength of agreement <sup>b)</sup>	Crude agreement <sup>a)</sup> (%)	Cohen’s $\kappa$	SE of $\kappa$	Strength of agreement <sup>b)</sup>
Transfer ability	83.3	0.571	0.571	Moderate	96.3	0.836	0.158	Almost perfect
Mobility	73.3	0.494	0.132	Moderate	88.8	0.664	0.172	Substantial
Toileting	76.7	0.462	0.150	Moderate	100	1.000	0.000	Almost perfect

SE, standard error.

<sup>a)</sup>Percentage of therapists and nurses who placed the patient in the same category.

<sup>b)</sup>Strength of agreement based on Landis and Koch:<sup>16)</sup> poor,  $\kappa < 0.20$ ; fair,  $\kappa = 0.21 - 0.40$ ; moderate,  $\kappa = 0.41 - 0.60$ ; good,  $\kappa = 0.61 - 0.80$ ; excellent,  $\kappa = 0.81 - 1.00$ .



**Fig. 4.** The inter-rater agreement ( $\kappa$ ) between therapists and nurses regarding patient functional level. Moderate agreement was observed before the intervention, with agreement values of  $\kappa = 0.571$ ,  $\kappa = 0.494$ , and  $\kappa = 0.462$  for questions related to transfer ability, mobility, and toileting, respectively. Agreement levels improved substantially to almost 100% after the intervention, with agreement values of  $\kappa = 0.836$ ,  $\kappa = 0.664$ , and  $\kappa = 1.000$ , respectively.

educational sessions. These results supported those of previous reports suggesting that a lack of awareness prevents nurses from promoting patient mobility.<sup>5,17,18)</sup> Our observations also underscored the need to emphasize patient mobility and functional levels in education programs for nurses.

Second, the different perceptions of patient functional levels between therapists and nurses confirmed the need for communication within the rehabilitation team.<sup>19)</sup> We observed moderate agreement between therapists and nurses before the intervention ( $\kappa = 0.41 - 0.60$ ). In particular, compared to therapists, nurses had a greater tendency to limit active participation in daily activities. A previous study reported differences in the perceptions of roles between nurses and therapists. According to Dalley and Sim,<sup>12)</sup> nurses tended to limit therapists’ roles in facilitating mobility and functioning. They also tended to consider therapists as having distinct and different roles in the rehabilitation team.<sup>12)</sup> Doherty et al.<sup>20)</sup> also reported that it was difficult for nurses to set an acceptable patient functional level. In contrast, Long et al.<sup>13)</sup> emphasized coordination and communication among nurses’ roles in a multi-professional rehabilitation team. They reported that nurses play a role in integrating rehabilitation care through ongoing communication with therapists.

The manual developed by our team, “My Rehabilitation Story,” improved the sharing of information related to the patient’s functional level. This written medium allowed both formal and informal communication, which helped to set appropriate patient mobility participation levels in the ward. Previous studies have demonstrated the effectiveness of communication processes in multidisciplinary teams. Papadimitriou and Cott<sup>21)</sup> reported that interprofessional communication allowed effective team perfor-

mance and enhanced client-centered practice. Tyson et al.<sup>22)</sup> also reported that the use of objective measurement tools was effective in avoiding communication conflicts in a multidisciplinary team approach. However, all previous studies were qualitative, with case report designs. Therefore, they were insufficient to clarify the effects of communication. However, it is meaningful to analyze the effect of communication based on an objective and quantitative index; namely, inter-rater agreement ( $\kappa$ ). To our knowledge, this study is the first to report a quantitative analysis of the effect of communication between therapists and nurses in a rehabilitation setting.

Third, education on mobility and participation improved patient awareness. This finding was consistent with those of previous studies showing that patient education prevented immobility and improved functional status, independence, and mobility.<sup>23-26)</sup> However, despite the overall improvement, we observed no statistically significant improvements in any of the question scores, except for Question 5 ( $p < 0.01$ ). This might have been due to the high survey scores by the pre-intervention group. Interestingly, the patients had a greater awareness of their mobility than their nurses. This was because, even during the non-intervention period, therapists provided education on mobility as part of the patients' rehabilitation program.

Patients participating in rehabilitation therapy experience more falls due to the promotion of mobility and participation.<sup>4,27)</sup> Moreover, if they experience a serious fall, patients tend to passively participate in ADL.<sup>28)</sup> In this study, the number of falls did not increase, even though we promoted mobility. Only one fall occurred during both the non-intervention (907 person-days) and intervention (958 person-days) periods. Therefore, the intervention conducted in this study was suitable for promoting mobility without increasing fall accidents. Previous studies have highlighted this as an important element of mobility promotion programs.<sup>29)</sup>

The contribution of nurses to rehabilitation for improving mobility is important for maximizing patient functional outcomes.<sup>30-32)</sup> Nurses who promote patient ADL participation while communicating with therapists can speed patient recovery and reduce rehabilitation time.<sup>13)</sup> Burton<sup>33)</sup> reported that nurses also wanted to help patients to use the skills in their ADL that they had learned from therapists in the gym. The improvement in communication between therapists and nurses with the continuous educational program proposed in this study is consistent with the ideal nursing practice for promoting patient mobility advocated by King et al.<sup>34)</sup>

This study had some limitations. We included only a single site and a small sample size, which could potentially limit the generalizability of our findings. In addition, this was not a randomized

controlled trial, which might have led to bias. Finally, due to the lack of clinical outcomes to assess the effectiveness of interventions, further studies are needed to determine whether mobility facilitation in an inpatient ward can, in turn, facilitate functional improvement.

The results of this study confirmed that improving communication among healthcare professionals from multiple disciplines, including nurses and therapists, through continuous educational programs promoted patient mobility and ADL participation in the inpatient ward. Therefore, our findings provide evidence of the benefits of a ward culture that facilitates a team approach to promote and recommend appropriate mobility for patients.

## SUPPLEMENTARY MATERIALS

Supplementary materials can be found via <https://doi.org/10.4235/agmr.21.0085>.

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### CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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### AUTHOR CONTRIBUTION

Conceptualization, KJY, JJH, KJY, KCH; Data curation, JJH; Investigation, KJY, KCH; Methodology, JJH, KJY; Project administration, LJY; Supervision, KJY, LJY; Writing-original draft, JJH; Writing-review & editing, KJY, LJY.

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# Health Literacy among Older Adults during COVID-19 Pandemic: A Cross-Sectional Study in an Urban Community in Thailand

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**Background:** This study assessed health literacy (HL) and its associated factors among older adults during the coronavirus disease 2019 (COVID-19) pandemic. **Methods:** This cross-sectional study included older adults in urban communities in Thailand. We randomly selected a total of 421 older adults and performed multiple logistic regression analyses. **Results:** The average age of the respondents was 70.0±7.1 years. Most respondents were female, married, had a low education level (primary school or lower), were unemployed, and had sufficient income. We observed nonproficient and proficient HL levels in 56.1% and 43.9% of respondents, respectively. The factors influencing HL included attending healthcare services at a tertiary hospital, good accessibility to COVID-19 prevention materials and health information, and provision of a high level of social support from neighbors and health personnel. **Conclusion:** The results of our study provide important information on the outcome of accessibility and social support among older adults in an urban community during the COVID-19 pandemic. In addition, access to health services, prevention equipment, and information was important for people at risk of HL and helped promote good behaviors.

**Key Words:** Health literacy, COVID-19, Frail elderly, Health promotion

## INTRODUCTION

The coronavirus disease 2019 (COVID-19) global pandemic began at the end of 2019.<sup>1,2</sup> Within 1 year, 208 million individuals worldwide were infected by this virus and 4.38 million individuals died.<sup>3</sup> In Thailand, 948,442 cases of COVID-19 have been confirmed, with 730,437 cured and 7,973 deaths.<sup>3</sup> The pandemic affected all age groups, causing economic deterioration and ensuing health problems.<sup>4</sup> More than 50% of fatalities occurred among older adults owing to increased complications and longer lengths of hospital admission compared to those in other populations.<sup>5</sup> As a result, treatment costs and numbers of lost family members were high.<sup>6</sup> COVID-19 prevention behaviors were extremely important in reducing viral spread and casualties in populations at risk.<sup>7</sup>

As COVID-19 is transmitted by droplets,<sup>8</sup> health authorities in

several countries, including Thailand, promoted frequent hand washing with soap and water, use of masks, and social distancing to reduce exposure, in addition to strict citywide lockdowns to control the spreads of the epidemic.<sup>9</sup> Moreover, accessing fundamental health information, obtaining a genuine understanding of the principles of disease prevention, and managing public health remained crucial, especially for at-risk populations.<sup>10,11</sup> Making decisions about how to follow health advice was one of the processes necessary for COVID-19 prevention behaviors.<sup>12</sup>

Health literacy (HL) is a concept addressed in healthcare systems and research on health promotion.<sup>13</sup> It constitutes the process by which individuals acquire knowledge and motivation and how they understand and access information, express opinions, and make decisions about promoting and maintaining health.<sup>14,15</sup>

A recent study applied HL to promote health among chronically ill

patients.<sup>16,17</sup> Previously, older adults with poor education or limited access to health information (AHI) received health information from healthcare workers and community health volunteers.<sup>18,19</sup> Because physical deterioration affects the ability to learn new knowledge, HL regarding health problems faced by older adults have gradually been learned over longer periods compared to other population groups. Related studies have demonstrated inadequate HL among older adults, especially those with cognitive impairment and poor vision and hearing.<sup>19</sup> Individuals with low education levels also have low HL scores and tend to have worse communication skills and lack critical HL.<sup>18,19</sup> However, healthcare communication is extremely important for maintaining and promoting health and well-being.

In the context of Thai communities, families are characterized by nuclear and extended families, meaning that family members, relatives, and neighbors can provide interaction and support regarding the physical and psychological well-being of older adults.<sup>20</sup> However, during the COVID-19 pandemic, relatives, neighbors, and public health workers were educated and built an understanding of protection measures using mass media, including online networks, to provide information designed for older adults.<sup>21</sup> HL on managing common health problems differs from that in critical or epidemic situations as it constitutes a new epidemic, in which unclear knowledge related to COVID-19 prevention behaviors and HL were lacking among older adults.<sup>18</sup>

A literature review on HL in the COVID-19 context revealed that few studies have assessed factors associated with HL among older adults in Thailand. Studies on the general public, university students, and factors related to the COVID-19 pandemic have all been conducted.<sup>22,23</sup> However, during COVID-19, older adults are in triple jeopardy, especially if they reside in crowded areas, such as urban communities. Furthermore, although many older adults were advised to self-quarantine and avoid direct contact with those who may infect them, their social connections in the community were one of the most important supportive resources available.

As mentioned above, the prevention of COVID-19 among older adults in crisis areas such as urban communities required their increased HL in addition to efforts to assess and explore factors influencing HL in this population. This information can be used for developing and implementing interventions and policies. When developing the conceptual framework for the present study, we applied the ecological assessment of the PRECEDE-PROCEED model<sup>24</sup> to determine the predisposing, reinforcing, and enabling factors that influenced HL among older adults in an urban community. The model explained the predisposing factor as the basis on which individuals increased their

motivation to perform a behavior, the reinforcing factor as that which encouraged individuals to perform a particular behavior, and enabling factor as the environmental influencing factor that directly affected the behavior to support or prevent the degradation of behavior among individuals. This study assessed and determined factors influencing HL among older adults living in urban communities during the pandemic.

## MATERIALS AND METHODS

### Research Design and Sampling

This cross-sectional community-based survey was conducted in Ubon Ratchathani Province, Thailand, which has the highest proportion of older adults at a risk of COVID-19. The selection criteria of the subjects were male and female sex, age 60 years and older, residence in the study area over 2 years, and ability to participate while collecting data. We excluded older adults who could not speak the Thai language and were unable to communicate or diagnose cognitive impairments.

We applied a multistage sample technique. First, one district in each district health zone was chosen for sampling from among the three district health zones in Ubon Ratchathani Province, Thailand. Second, in each district, one urban community, also known as a municipal area, was chosen. Finally, we selected a target population at random using a community name list from four districts in Northeast Thailand. We calculated the sample size using G\*Power.<sup>25</sup> The effect size was 0.30, with an alpha level of 0.05 and a power of 0.80. The resulting calculated sample size was 384. To prevent data loss, an additional 10% of subjects were included. Thus, this study included a total of 421 subjects. Based on sample size, we randomly selected 105–106 individuals from each urban community.

The protocol for this study was reviewed and approved by the Ethics Review Committee (IRB) of the Faculty of Public Health, Mahidol University (MUPH 2020-156). An informed consent statement was obtained before commencement of the data collecting.

### Research Instrument

Data were collected using self-reported questionnaires that were conducted in the respondents' homes and communities. A panel of three experts rated the overall content validity of all instruments at 1.00 and the index of item objective congruence was over 0.5. We assessed the interrater reliability of the self-reported questionnaire between the principal and co-principal investigators in all settings in a pilot test of 30 participants, which showed acceptable values of 0.71–0.93, with structured questionnaires comprising the

six parts described below.

(1) Access to health services (AHS) was developed based on literature reviews. AHS included two questions. First, where the respondents accessed their healthcare services. The healthcare services in the study area comprised a subdistrict health-promoting hospital (primary healthcare unit), a community hospital, and a regional hospital (tertiary hospital). Second, the assessment of the ease of accessing healthcare services involved three individual items: “was the hospital far from your home?” “was the cost of travel expensive,” and “were you able to pay the extra treatment costs?” The Cronbach’s alpha was 0.77.

(2) Access to COVID-19 preventive materials was developed based on literature reviews. It comprised five items: access to alcohol-based hand rub, access to free alcohol-based hand rub or soap, access to masks, access to free masks, and access to face shields. Respondents who always had access to these preventive measures earned one point, with scores ranging from 0 to 5 points. Good access to COVID-19 preventive material was defined as individuals who were able to access all materials (five points). The Cronbach’s alpha was 0.77.

(3) AHI comprised nine items related to AHI from health personnel, health volunteers, neighbors, village headman, TV, radio, internet, family members, and documents. For example, one question asked, “did you regularly access health information from public health officials?” A positive response was scored one point. The scores ranged from 0 to 9 points. Good access health to information was defined as scores of 7–9. The Cronbach’s alpha was 0.71.

(4) Social support was developed by applying the social support theory described by Cobb,<sup>26)</sup> which comprises eight items. Each item involved four rating scales (never, rarely, sometimes, and always), and each was scored from 1 to 4 points. The total score ranged from 8 to 32 points. A high level of received social support from family members was defined as total scores of 25–32 points. The Cronbach’s alpha was 0.79.

Social support from neighbors was developed by applying the social support theory proposed by Cobb<sup>26)</sup> and comprised seven items. Each item involved four rating scales (never, rarely, sometimes, and always), and each was scored from 1 to 4 points. The total score ranged from 7 to 28 points. A high level of social support was defined as a total score of 22–28. The Cronbach’s alpha was 0.88.

Social support from health personnel was developed similar to others.<sup>26)</sup> It comprised seven items with four rating scales as described above. The total score ranged from 7 to 28 points. A high level of received social support was defined as a total score of 22–28. The Cronbach’s alpha was 0.93.

(5) HL was developed by the Health Education Department of

the Ministry of Public Health, Thailand.<sup>27)</sup> It comprises 24 items in the following six elements: AHI, understanding, interaction to change, decision-making, modification, and discussion of health. The responses used a five-point Likert scale: strongly disagree = 1, disagree = 2, neither agree nor disagree = 3, agree = 4, and strongly agree = 5. Total scores of 96–120 points indicated proficient HL, in which individuals had adequate HL. The Cronbach’s alpha was 0.93.

(6) The sociodemographic variables of the study population consisted of four items with open-ended questions with multiple-choice responses, including age, sex, marital status, and current work.

### Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences version 18.0 (SPSS Inc., Chicago, IL, USA). Frequency, percentage, mean, and standard deviation were used to describe respondent characteristics. To explore factors associated with HL, we performed multiple logistic regression analysis, with the results presented as odds ratios (ORs) and 95% confidence intervals (CIs). Statistical significance was set at  $p < 0.05$ .

## RESULTS

### Characteristics of the Study Population

The average age of the respondents was  $70.0 \pm 7.1$  years; most respondents (53.4%) were aged 60–69 years, followed by 70–79 years (36.1%) and 80 years and over (10.5%). Overall, 62.7% of respondents were female and 37.3% were male. Over 60% of respondents were married, 30.4% were separated/divorced/widowed, and 5.5% were single. Almost 40% of respondents were employed, 43.5% were farmers, 28.5% were business owners, and 28.0% were temporary employees (Table 1).

### Study Variables

The predisposing factors included education level, income sufficiency, and chronic illness. Most subjects had graduated at the primary school level or lower (63.4%), possessed sufficient income (69.6%), and experienced chronic illness (61.5%). Among reinforcing factors, 83.4%, 76.9%, and 70.1% of respondents received sufficiently high levels of social support from family members, neighbors, and health personnel, respectively.

Among enabling factors, most of the respondents accessed healthcare services at district (53.4%), regional (23.8%), and sub-district health-promoting (22.8%) hospitals. Moreover, 76.7% reported that receiving healthcare services in these hospitals was convenient. Regarding accessing COVID-19 prevention materials,

**Table 1.** Factors associated with HL among older adults by binary logistic regression analysis

Factor	HL			OR (95% CI)	p-value
	Total	Proficiency	Non-proficiency		
<b>Clinical factors</b>					
Age (y)	70.0±7.1	-	-		
60–69	225 (53.4)	97 (43.1)	128 (56.9)	0.93 (0.63–1.37)	0.713
≥ 70	196 (56.6)	88(44.9)	108 (55.1)	Ref.	
Sex					
Female	264 (62.7)	153 (58.0)	111 (42.0)	Ref.	
Male	157 (37.3)	83 (52.9)	74 (47.1)	1.23 (0.83–1.83)	0.31
Marital status					
Non-married	151 (35.9)	58 (38.4)	93(61.6)	Ref.	
Married	270 (64.1)	127 (47.0)	143 (53.0)	1.42 (0.95–2.14)	0.09
<b>Predisposing factors</b>					
Education					
Primary school	267 (63.4)	111 (41.6)	156 (58.4)	Ref.	
Higher	154 (36.6)	74 (48.1)	80 (51.9)	1.55 (0.90–2.64)	0.11
Working status					
Unemployed	186 (44.2)	76 (40.9)	110 (59.1)	Ref.	
Employee	235 (55.8)	109 (46.4)	126 (53.6)	1.25 (0.85–1.85)	0.26
Sufficiency income					
Insufficiency	128 (30.4)	54 (42.2)	74 (57.8)	Ref.	
Sufficiency	293 (69.6)	131 (44.7)	162 (55.3)	1.11 (0.73–1.69)	0.63
Chronic illness					
No	162 (38.5)	72 (44.4)	90 (55.6)	Ref.	
Yes	259 (61.5)	113 (43.6)	146 (56.4)	0.97 (0.65–1.44)	0.87
<b>Enabling factors</b>					
Access to health services					
Other	321 (76.2)	190 (59.2)	131 (40.8)	Ref.	
Regional hospital	100 (23.8)	54 (54.0)	46 (46.0)	1.70 (1.08–2.68)	0.02*
Easy to access health services					
No	98 (23.3)	34 (34.7)	64 (65.3)	Ref.	
Yes	323 (76.7)	151 (46.8)	172 (53.2)	1.65 (1.03–2.64)	0.03*
Access to preventive material					
Poor	265 (62.9)	89 (33.6)	176 (66.4)	Ref.	
Good	156 (37.1)	96 (61.5)	69 (38.5)	3.16 (2.10–4.77)	<0.001**
Access to health information					
Poor	176 (41.8)	47 (26.7)	129 (73.3)	Ref.	
Good	245 (58.2)	138 (56.3)	107 (43.7)	3.16 (2.01–4.77)	<0.001**
<b>Reinforcing factors</b>					
Family support					
Poor	70 (16.6)	17 (24.3)	53 (75.7)	Ref.	
Good	351 (83.4)	168 (47.9)	183 (52.1)	2.86 (1.59–5.14)	<0.001**
Social support by neighbor					
Poor	135 (32.1)	32 (23.7)	103 (76.3)	Ref.	
Good	286 (76.9)	153 (53.5)	133 (46.5)	3.70 (2.34–5.86)	<0.001**
Social support by health person					
Poor	126 (29.9)	29 (23.0)	97 (77.0)	Ref.	
Good	295 (70.1)	156 (52.9)	139 (47.1)	3.75 (2.34–6.03)	<0.001**

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

HL, health literacy; OR, odds ratio; CI, confidence interval.

\*p<0.05, \*\*p<0.01.

most respondents (62.9%) replied that they did not access them; however, 58.2% reported good AHI (Table 1).

### HL in the study population

We observed nonproficient and proficient HL in 56.1% and 43.9% of Thai older adults, respectively, during the COVID-19 pandemic in this study.

### Factors associated with proficient HL among older adults

Table 1 indicates that no predisposing factors, such as education level, sufficient income, and chronic illness, were associated with proficient HL ( $p > 0.05$ ). Regarding enabling factors, AHS, convenient AHS, access to preventive materials, and AHI were associated with proficient HL. Our findings indicated that older adults accessing healthcare services at regional hospitals were 1.7 times more likely to have proficient HL (OR = 1.70; 95% CI, 1.08–2.68;  $p = 0.02$ ). Respondents with convenient access to healthcare services were 1.65 times more likely to have proficient HL (OR = 1.65; 95% CI, 1.03–2.64;  $p = 0.03$ ). Regarding access to preventive materials, participants who could access all materials were 3.16 times more likely to have proficient HL (OR = 3.16; 95% CI, 2.10–4.77;  $p < 0.001$ ). Lastly, participants with high levels of AHI were 3.16 times more likely to have proficient HL (OR = 3.16; 95% CI, 2.10–4.77;  $p < 0.001$ ) (Table 1).

Regarding reinforcing factors, older adults receiving high-level

social support from family members were 2.86 times more likely to have proficient HL (OR = 2.86; 95% CI, 1.59–5.14;  $p < 0.001$ ). In addition, older adults receiving high levels of social support from neighbors were 3.7 times more likely to have proficient HL (OR = 3.70; 95% CI, 2.34–5.86;  $p < 0.001$ ). Finally, those receiving high levels of social support from health personnel were 3.7 times more likely to have proficient HL (OR = 3.75; 95% CI, 2.34–6.03;  $p < 0.001$ ) (Table 1).

Multiple logistic regression analysis of reinforcing factors showed that high levels of social support from neighbors and health personnel significantly predicted proficient HL in older adults. Participants receiving high levels of social support from their neighbors were more than twice as likely to have proficient HL compared to those receiving low levels of support (OR = 2.02; 95% CI, 1.16–3.53;  $p < 0.01$ ). Additionally, those who received high levels of social support from health personnel were more than twice as likely to have proficient HL compared to those who had low levels (OR = 2.55; 95% CI, 1.47–4.41;  $p < 0.01$ ). However, while high levels of social support from family members were more likely to predict HL, HL did not differ from those receiving low levels of support ( $p > 0.05$ ) (Table 2).

The enabling factors predicted significantly proficient HL ( $p < 0.05$ ). Older adults accessing health services at regional hospitals had adequate HL (OR = 2.53; 95% CI, 1.47–4.34;  $p < 0.01$ ), and older adults with convenient access to healthcare services were

**Table 2.** Factors associated with HL in older adults by multiple logistic regression analysis

Variable	OR (95% CI)	p-value
Predisposing factors		
Young older adults (< 70 y)	1.240 (0.78–1.96)	0.358
Male	1.158 (0.72–1.86)	0.544
Married	1.618 (0.99–2.63)	0.052
Higher education	1.321 (0.80–2.17)	0.274
Current working	0.988 (0.62–1.59)	0.961
Sufficient income	0.790 (0.47–1.32)	0.365
Chronic illness	1.042 (0.66–1.65)	0.862
Reinforcing factors		
Received high level of social support from family members	1.150 (0.56–2.36)	0.709
Received high level of social support from neighbors	2.030 (1.15–3.59)	< 0.01**
Received high level of social support from health personnel	2.860 (1.62–5.06)	< 0.01**
Enabling factors		
Accessed health services at regional hospital	2.250 (1.27–3.97)	< 0.01**
Convenient to access health services in hospitals	1.890 (1.09–3.29)	0.02*
High level of access to health information	1.920 (1.18–3.12)	< 0.01**
Accessed COVID-19 prevention material	2.760 (1.72–4.41)	< 0.01**

HL, health literacy; OR, odds ratio; CI, confidence interval; COVID-19, coronavirus disease 2019.

\* $p < 0.05$ , \*\* $p < 0.01$ .

1.76 times more likely to have adequate HL compared to those without convenient AHS in hospitals (OR = 1.76; 95% CI, 1.02–3.02;  $p = 0.04$ ). Concerning access to materials for COVID-19 prevention, participants with good access were twice as likely to have adequate and proficient HL compared to those without such access (OR = 2.62; 95% CI, 1.66–4.13;  $p < 0.01$ ). Participants with good AHI were 1.95 times more likely to have adequate HL compared to those without AHI (OR = 1.95; 95% CI, 1.21–3.13;  $p < 0.01$ ) (Table 2).

## DISCUSSION

Our study explored factors influencing HL among older adults. The results showed that their HL was proficient and associated with better accessibility and social support. Individuals with proficient HL can experience healthy lives free from infectious diseases. HL not only affects a person's awareness of disease prevention but also has a greater effect on the earlier management of health problems. Proficient HL predicted good preventive behaviors at rates almost twice those of the other groups. Gautam et al.<sup>28)</sup> suggested that HL affected perceptions and behaviors related to individual protection from COVID-19 and followed the pharmacologic management of their health problems. A high proportion of HL is linked to prevention behaviors and low rates of COVID-19 nationwide.

The urgency for professionals to act and promote behavioral changes in the population is high during a pandemic. HL is a leading factor in improving awareness of risk issues and decision-making regarding changing health behaviors and lifestyles.<sup>17,29,30)</sup> Proficient HL led to ideal health behaviors and a new normal lifestyle to reduce the incidence of COVID-19 transmission.<sup>9)</sup> The older adults in urban communities in our study demonstrated adequate health knowledge and competencies very similar to those reported by related studies.<sup>18,19)</sup> We observed non-proficient and proficient HL in 56.1% and 43.9% of respondents, respectively. Previously, over half of the older adults had insufficient HL or nonproficiency. The sample population's residence in urban or semiurban settings may have resulted in a better quality of life related to education level, living conditions, and access to information.<sup>31)</sup> Although older adults in rural communities receive more support, many areas were locked down and activities canceled.<sup>32)</sup> However, women were one of the most vulnerable populations during the pandemic and often had less access to information compared to men.<sup>33)</sup> Therefore, their lifestyles may differ.<sup>31)</sup>

Moreover, our study indicated that social support was a reinforcing factor for HL among older adults, similar to other studies. Social support from neighbors is important to older adults, particu-

larly those in Asian countries.<sup>18,34,35)</sup> Neighbors are also important for communicating health information.<sup>36)</sup> Even when they are living with children, most individuals spend their free time with neighbors in the community.<sup>36)</sup> Moreover, neighbors serve as role models of behavior change and can be useful in promoting health.<sup>37,38)</sup> Thus, the HL of older adults is delivered through neighbors.<sup>39,40)</sup> When a neighbor has good HL, the older adults will also have good HL.<sup>40)</sup> In addition, when the society is strong, vulnerable individuals will be protected and enjoy good health and well-being, leading to equal AHS.<sup>37)</sup>

Unsurprisingly, we found that older adults supported by good health professionals also experienced good HL. In addition, AHS and health information were related to HL. This likely occurred because HL arises from health promotion by health personnel.<sup>18)</sup> As mentioned above, the enabling factors include environmental factors that directly influence behavior and prevent illnesses stemming from such behaviors.<sup>37)</sup> Therefore, the ability to access health services is a fundamental variable correlating to HL and health behavior. However, we found that the experience of accessing health services in tertiary hospitals was significantly associated with HL. Tertiary hospitals are large specialized hospitals providing health services that secondary and primary hospitals cannot.<sup>41)</sup> They have both talent and expertise in providing healthcare services. Although the level of hospital expertise was related to health knowledge among older adults in this study, the number of subjects was small and insufficient to understand the process of establishing health knowledge. Additional studies are needed to explore health promotion and communication skills in tertiary hospitals to promote healthful decisions and healthcare.<sup>42)</sup>

However, we found that education levels, adequate income, and chronic illnesses such as hypertension, diabetes, and cardiovascular disease were not associated with HL in older adults. To explain this, most of the older adults in our study experienced chronic illness; they also know each other well in their community and participated and share health information, which may have influenced their HL and the stability of their health behaviors. Thus, older adults with chronic diseases showed no associations with HL in our study, contrary to the findings of related studies.<sup>29,43)</sup> The literature on health knowledge arising from the learning process has demonstrated improved health knowledge following educational interventions in individuals with low education levels.<sup>26)</sup> In contrast, while highly educated people better can learn health information and understand health, their HL is directly influenced by the academic level obtained.<sup>44)</sup> Thus, our results differed from those of related studies.<sup>29,43)</sup>

Our study had several limitations. First, the sample was not statistically representative of older adults because we included only

urban communities in Northeast Thailand. Future studies should compare HL in older adults in urban, suburban, and rural communities in several settings. Second, this was the first study to use the AHS, concerning access to COVID-19 preventive materials, AHI, social support, social support from neighbors, social support from health personnel, and HL questionnaires, which was on only one aspect of its validity (content validity). Future studies should use the whole aspect of validity (content and reliability) based on reliable and valid questionnaires. Finally, because of the cross-sectional design, this study could not determine causal relationships, but only associations and correlations. However, our results demonstrated that HL among older adults after the COVID-19 pandemic could limit its transmission and permit social activities necessary for the health of older adults. Indeed, we observed higher levels of HL among older adults who accessed health services at regional hospitals compared to the levels in those who accessed other healthcare facilities. Based on our results, further studies should focus on the spread of fake news or incorrect information (e.g., vaccination) that might be associated with HL, as well as the use of health service models aimed at HL among older adults. Policymakers should also consider ways to reduce gaps and disparities in health services in vulnerable populations.

In conclusion, the results of this study demonstrated high levels of HL among older adults residing in urban communities. We also found that AHS, easily accessed preventive material, and AHI predicted HL in older adults. Promoting proficient HL among older adults is important. Additionally, social support from family, neighbors, and health personnel was associated with HL in older adults. Strong social support can encourage high levels of HL and healthy behaviors in this population. Family, neighbors, and health personnel are important, and policymakers should consider effective channels of communication and health promotion. Lastly, good access to health care services, preventive material, and health information predicted high levels of HL. AHS, prevention equipment, and convenient information are important for people at risk of HL and to promote good behaviors.

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## CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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## AUTHOR CONTRIBUTIONS

Conceptualization, KP, KY, WK, PC, WS. Data curation, KP, KY, WS. Writing-original draft, KP, KY, WK, PC. Writing-review & editing, KP, KY, WK, PC.

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# Association between Health Literacy, Self-care Behavior, and Blood Sugar Level among Older Patients with Type 2 Diabetes in Rural Thai Communities

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**Background:** Diabetes mellitus is a major problem worldwide. Moreover, older patients with significantly limited health literacy (HL) tend to have worse self-care behaviors and health outcomes. This study aimed to describe the associations of HL, self-care behavior, and blood sugar levels among older patients with type 2 diabetes in rural Thai communities. **Methods:** This cross-sectional study included 415 patients with diabetes who were purposively selected from rural Thai communities. Data were collected using questionnaires and analyzed using descriptive statistics, Pearson correlation, Spearman rho, and stepwise multiple linear regression. **Results:** The results revealed that most participants were women (66.50%). The respondents had moderate overall HL ( $2.68 \pm 0.64$ ). On average, the respondents had fair overall self-care behavior ( $4.0 \pm 0.33$ ). We discovered that HL was significantly positively correlated with self-care behavior ( $r=0.90$ ) but not with blood sugar level. In addition, self-care behavior was significantly negatively correlated with blood sugar level ( $r=-0.50$ ). Self-care behaviors and blood sugar levels were significant predictors of HL in patients with type 2 diabetes (total variance, 28.4%). **Conclusion:** The results suggested increased HL in patients with diabetes would improve self-care behavior and, consequently, decrease their blood sugar level. Our findings indicate the need to involve nurses and multidisciplinary healthcare teams when developing health promotion programs to encourage blood sugar control.

**Key Words:** Health literacy, Type 2 diabetes mellitus, Blood glucose, Health behavior, Nurses

## INTRODUCTION

Diabetes mellitus is a chronic condition that affects millions of people globally. According to the International Federation of Diabetes, approximately 415 million individuals worldwide had diabetes in 2015, a number that is expected to reach 642 million by 2040.<sup>1)</sup> In Thailand, the prevalence of diabetes increased from 7.7% in 2004 to 7.8% in 2009 and 9.9% in 2014,<sup>2)</sup> making it the second-ranking non-communicable disease, following high blood sugar levels.<sup>3,4)</sup> Patients with long-term diabetes and inadequate blood glucose management are prone to develop complications that result in mortality and increased disease severity,<sup>5,6)</sup> as well as

acute respiratory distress syndrome in coronavirus disease 2019 (COVID-19),<sup>7)</sup> mainly due to a higher incidence of diabetes-specific complications (e.g., coronary heart disease, stroke, kidney failure, and peripheral vascular disease).<sup>8)</sup> Diabetic treatment aims to maintain blood sugar levels as close to standard as feasible. Thus, after 8–12 hours of fasting, blood glucose readings must be 90–130 mg/dL or the glycated hemoglobin (HbA1c) level < 7%.<sup>9)</sup>

Effective communication between patients and healthcare providers is necessary to ensure that patients correctly comprehend and follow healthcare providers' advice. The language used in communication and one's perspective on the subject under discussion are critical components of reciprocal and improved under-

standing. Patients with a low degree of health literacy (HL) will not follow doctors' directives since they are unable to comprehend health information. Low HL is a barrier to good health, as it leads to patients' disregard for healthcare providers' advice or instructions. Additionally, a previous study reported a link between HL and self-care behavior in patients with type 2 diabetes.<sup>10)</sup>

HL or health skills were first recognized in the United States, where individuals with diverse ethnic backgrounds, languages, and cultures coexist. These individuals frequently lack an understanding of health issues and information as well as methods for better self-care management.<sup>11)</sup> People with low HL were more likely to be careless with their health; they had high blood sugar levels, more diabetes problems, and were frequently admitted to the hospital.<sup>12)</sup> People with diabetes who lacked functional HL were also more likely to have difficulty controlling their blood glucose levels.<sup>13)</sup> This may result from an inability to comprehend health information recommended by healthcare specialists. Patients with a high HL may better understand the recommendations of healthcare practitioner and maintain more stable blood sugar levels.

Self-care behavior is a principal concept in health promotion that refers to decision-making and health behaviors that an individual could make to address a health issue or maintain their current level of health.<sup>14)</sup> Self-care encompasses four dimensions: the physical, averting complications, treatment, and psychosocial dimensions.<sup>15)</sup> Additionally, patients must learn to motivate themselves and gain social support to sustain their efforts.<sup>16)</sup> On the other hand, social support, particularly from peers, friends, and families, is also a barrier to treatment adherence and self-care, although high levels of support are connected with greater long-term self-care management. As such, this study aimed to improve the understanding of the relationships between HL and self-care behaviors and blood sugar levels in patients with type 2 diabetes living in rural Thai communities.

## MATERIALS AND METHODS

### Research Design and Sampling

The sample in this cross-sectional survey consisted of 60- to 80-year-old male and female adults living in Samut Songkram Province in southern central Thailand, which comprises three districts: Samut, Amphawa, and Bangkhonthi. This province is an important economic area in the central part of Thailand, where most residents produce palm sugar as a household industry. Bangkhonthi District has 13 sub-district health promotion hospitals, three of which—Jormploug, Bang Prom, and Bang Yeerong—are primary care centers. Each center serves three to five sub-district health promotion hospitals. In this study, we selected a sample of 415 pa-

tients with diabetes living in rural Thai communities.

### Research Instruments

The survey questionnaires used in the current study were divided into the following four research instruments.

#### *Self-care behavior assessment (SBA)*

The SBA is based on the concept of self-care behavior theory first described by Orem.<sup>15)</sup> We applied a questionnaire developed by Suksatan and Prabsangob.<sup>10)</sup> The self-care behavior questionnaire included four dimensions (physical, prevention of complications, treatment, and psychosocial), each of which comprised five questions. The participants answered each question by rating their response from 1 (never) to 5 (always). The total score for self-care behaviors was 100 points, with higher scores indicating better self-care behavior.

#### *Blood sugar control assessment (BSCA)*

We used Dextrostix (DTX), which is the preferred method for diabetes screening and diagnosis. DTX was used to assess blood glucose levels after fasting for at least 6–8 hours. We used the latest DTX results from patients' health records at the health promotion hospitals, which were assessed by technicians the sub-district health promotion hospitals.

#### *Health literacy scale (HLS)*

We applied the three-level HLS developed by Ishikawa et al.,<sup>17)</sup> to assess the HL level. The test is used to measure functional, communicative, and critical HL and consists of three groups of questions based on three different levels of HL: basic (composed five questions), interactive (five questions), and critical (four questions). The participants were asked to read the questions or to have them read to them. The patients answered each question by rating their responses from 1 (never) to 4 (regular). Then, the scores of each group of questions were collected and divided by the number of questions. The score results ranged between 1 and 4, with higher scores indicating higher HL, except for the score result of basic HL, in which a higher score indicated a lower HL. We used the total HL score in this study (56 points: 14 multiplied by 4) by defining percentage scores of < 60%, 60%–69.99%, 70%–79.99%, and > 79.99%, indicating poor, fair, good, and very good HL, respectively.

#### *Sociodemographic variables*

We assessed the general information of the participants using an instrument with five items: sex, age, education level, monthly income, and diabetes duration.

### Data Analysis

We used IBM SPSS Statistics for Windows version 21.0 (IBM, Armonk, NY, USA) to analyze the data. The frequencies, percentages, means, and standard deviations of the data were presented. Pearson correlation coefficient and Spearman rho were used to examine the relationships between the participants' sociodemographic factors, self-care behaviors, and blood sugar levels and their HL. We used a stepwise multiple linear regression analysis to test the factors predicting these variables. The significance level was set at  $p < 0.05$ .

### Ethical Considerations

The current study was carried out according to the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all the participants. Ethical approval was attained from the Suan Sunandha Rajabhat University Institutional Review Board on human rights prior to commencing the study (No. COA.1-037/2018).

## RESULTS

We purposively selected a total of 415 participants receiving health services at sub-district health promotion hospitals in rural Thai communities as a sample group. The demographic data and clinical characteristics of the participants were as follows: 66.50% female ( $n = 276$ ) and a mean age of 64.1 years. Most participants had graduated from primary school (71.30%,  $n = 29$ ) and 65% of participants had a monthly income of  $< 5,001$  Thai Baht ( $n = 164$ ). Furthermore, most participants had had diabetes for 5–9 years (39.80%,  $n = 165$ ) and most had blood sugar levels of 126–154 mL/dL (51.45%,  $n = 214$ ) (Table 1).

### Participant HL

The participants had fair overall HL (mean, 2.68), with a mean total score of 36.89. The mean scores for functional, interactive, and critical HL were 3.11, 2.32, and 2.61, respectively (Table 2).

### Participant Self-care Behaviors

The participants had a mean score of overall self-care behavior of 4.00. The mean score was highest for the treatment dimension (4.34), followed by the physical (4.00), prevention of complications (3.89), and psychosocial (3.75) dimensions (Table 3).

### Relationships of Participants' Sociodemographic Characteristics, HL, Self-care Behaviors, and Blood Sugar Levels

Pearson correlation coefficient analysis showed that HL was significantly positively correlated with self-care behavior ( $r = 0.90$ ,

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

Characteristic	Value
Sex	
Male	139 (33.50)
Female	276 (66.50)
Age (y)	64.1 ± 8.1 (50–80)
50–59	148 (35.70)
60–69	175 (42.20)
70–80	92 (22.10)
Education levels	
Lower than primary school	36 (8.70)
Primary school	296 (71.30)
Secondary/Vocational school	64 (15.40)
Bachelor's degree and above	19 (4.60)
Monthly income (Thai Baht)	
< 5,001	164 (39.51)
5,001–10,000	139 (33.49)
10,001–15,000	80 (19.30)
15,001–20,000	16 (3.85)
> 20,000	16 (3.85)
Duration of diabetes (y)	
< 5	105 (25.20)
5–9	165 (39.80)
> 10	145 (35.00)
Blood sugar, DTX (mL/dL)	
< 126	125 (30.10)
126–154	214 (51.45)
155–182	60 (14.56)
> 182	16 (3.89)

Values are presented as number (%) or mean ± standard deviation (min–max). DTX, Dextrostix.

**Table 2.** Health literacy of the participants

Health literacy	Mean ± SD	Interpretation
Functional	3.11 ± 0.86	High
Interactive	2.32 ± 0.86	Fair
Critical	2.61 ± 0.96	Fair
Total (range 1–4)	2.68 ± 0.64	Fair
Total score (range 14–56)	36.89 ± 7.11	Fair

SD, standard deviation.

**Table 3.** Self-care behavior of the participants

Self-care behavior	Mean ± SD
Physical dimension	4.00 ± 0.71
Prevented complication dimension	3.89 ± 0.53
Treatment dimension	4.36 ± 0.40
Psychosocial dimension	3.75 ± 0.72
Total self-care behavior	4.00 ± 0.33

SD, standard deviation.

$p < 0.001$ ) but not blood sugar levels ( $r = -0.023, p = 0.638$ ). In addition, self-care behavior was significantly negatively correlated with blood sugar levels ( $r = -0.50, p < 0.001$ ). Positive correlations were observed between patient education and self-care behaviors ( $r = 0.36, p < 0.05$ ) and HL ( $r = 0.38, p < 0.05$ ). We also observed significant positive correlation between patient age and blood sugar levels ( $r = 0.28, p < 0.05$ ), self-care behavior ( $r = 0.22, p < 0.05$ ), and HL ( $r = 0.30, p < 0.05$ ) (Table 4).

**Factors Predicting HL**

Stepwise multiple regression analysis to identify factors that could predict HL identified self-care behaviors and blood sugar levels ( $\beta = 0.419$  and  $0.230$ , respectively). Combined, these factors predicted HL with 28.4% accuracy (Table 5).

**DISCUSSION**

The low HL levels among older adults with type 2 diabetes in rural Thai communities could be explained by their advanced age, lack of education, and low income. Our findings are consistent with those of Schillinger et al.<sup>18)</sup> and Manganello<sup>19)</sup> who established the prevalence of inadequate HL among low-income and undereducated older adult patients with diabetes. Our examination of each facet of HL revealed the lowest mean score for interactive HL compared to functional and critical HL. Interactive HL refers to being literate in basic health and cognitive and social skills used to participate in social activities and select updated information to improve health behaviors.<sup>20,21)</sup> Low interactive HL indicates that patients with diabetes have less communication with others regarding their health and diabetes.<sup>10)</sup>

Our results also revealed interesting relationships between patient age, blood sugar levels, self-care behaviors, and HL. Patient age was associated with HL in Spearman rho tests, although the association disappeared when communicative HL was included in the model. Previous studies have also reported an association be-

tween patient age and blood sugar levels,<sup>2,21)</sup> self-care behaviors,<sup>21,22)</sup> and HL.<sup>2,21,23)</sup> Contrary to previous findings, patient age was not associated with HL in older adults in urban communities in Thailand.<sup>14,24)</sup>

The current study’s findings indicated that HL was associated with positive self-care behaviors, whereas self-care behaviors were negatively associated with blood sugar levels. Thus, increasing HL in patients with diabetes results in improved self-care behavior and, as a result, lower blood sugar levels.<sup>23)</sup> This finding is consistent with those of a previous study reporting a relationship between low HL and failure to control blood glucose levels in patients with type 2 diabetes.<sup>18)</sup> This occurred because diabetic patients with low HL frequently had difficulty reading medicine labels or comprehending blood sugar levels results and healthcare provider’s prescriptions.<sup>22)</sup> Thus, patients were unable to practice effective self-care. Additionally, patients with low HL frequently did not know or recall the names of medications or how to use them<sup>25)</sup> and were unaware of their health condition and how to manage it.<sup>26)</sup> Patients with low HL demonstrated difficulties in remembering and comprehending medical information. This prevented them from gathering or searching for additional information, as they could not comprehend or recall the details received from hospitals due to ineffective communication.<sup>25)</sup> Furthermore, in their comparisons of communication levels between healthcare providers and patients with adequate and low HL, Schillinger et al.<sup>18)</sup> reported that healthcare providers rarely explained health conditions and treatment steps to the low HL group in a way that the patients

**Table 5.** Results of the stepwise multiple regression analysis between predictors and health literacy among the study participants

Predicting factors	B	SE	Beta	t	p-value
Constant	2.340	0.561		-4.172	<0.001
Self-care behaviors	0.240	0.060	0.419	4.029	<0.001
Blood sugar levels	0.126	0.054	0.230	2.336	0.002

$R^2=0.299$ , adjusted  $R^2=0.284$ .

**Table 4.** Correlations between participant sociodemographic characteristics, health literacy, self-care behavior, and blood sugar level

Variable	Mean ± SD	Age	Education	Monthly income	Duration of diabetes	Blood sugar levels	Self-care behavior	Health literacy
Age	64.11 ± 8.10							
Education	3.04 ± 0.62	0.34 <sup>a)</sup>						
Monthly income	6,232.5 ± 984.3	-0.52 <sup>b)</sup>	0.93 <sup>a)</sup>					
Duration of diabetes	6.42 ± 2.53	0.37 <sup>b)</sup>	0.06 <sup>a)</sup>	0.20 <sup>b)</sup>				
Blood sugar levels	134.60 ± 32.47	0.28 <sup>b)*</sup>	0.62 <sup>a)</sup>	0.28 <sup>b)</sup>	0.46 <sup>b)</sup>			
Self-care behavior	4.00 ± 0.33	0.22 <sup>b)*</sup>	0.36 <sup>a)*</sup>	0.08 <sup>a)</sup>	0.38 <sup>b)</sup>	-0.50 <sup>b)**</sup>		
Health literacy	147.46 ± 41.91	0.30 <sup>b)*</sup>	0.38 <sup>a)*</sup>	0.09 <sup>b)*</sup>	0.44 <sup>b)</sup>	-0.23 <sup>b)</sup>	0.90 <sup>b)*</sup>	

SD, standard deviation.

<sup>a)</sup>Spearman rho, <sup>b)</sup>Pearson correlation.

\* $p < 0.05$  (two-tailed), \*\* $p < 0.01$  (two-tailed).

could understand and apply. That study also reported that HL was not significantly associated with blood sugar levels.

Despite receiving education from health providers about diabetes, patient blood sugar control did not improve because the patients did not apply the knowledge. Healthcare service providers must have knowledge and understanding of patients' thoughts and points of view regarding meeting with healthcare providers. While many patients understand and remember the health information and behavior changes provided by healthcare providers, many do not practice these recommendations; rather, the patients' attitudes or views about diabetes are contrary to those of the healthcare providers.

Finally, we found that self-care behaviors and blood sugar levels were predictors of HL in Thai patients with type 2 diabetes. The results of the current study are consistent with those of Yodmai et al.<sup>14</sup> and Caruso et al.<sup>23</sup> demonstrating the importance of self-care behaviors and maintaining blood glucose levels to improving the physical and mental health behaviors of patients with type 2 diabetes, which are associated with HL.

The present study has some limitations. First, the participants were patients with type 2 diabetes who received care in only one province in Thailand. This may limit the generalizability of our findings to other patients with type 2 diabetes in different contexts (e.g., urban communities, nursing homes). Second, the sample was obtained using a purposive selection method. The lack of random sampling may have resulted in sample selection bias, limiting the generalizability of the findings. Third, we used only the DTX method to assess blood glucose levels after fasting for at least 6–8 hours. However, this method shows potential for mass screening programs for patients with type 2 diabetes, as it accurately classified patients and provided rapid results. Future studies should use other methods to evaluate blood glucose levels that are standard and accurate for patients with type 2 diabetes, such as fasting plasma glucose or HbA1c levels. Fourth, we examined the relationship between HL, self-care behaviors, and blood sugar levels among older patients with type 2 diabetes using only a self-reported questionnaire. Future interventional or longitudinal studies are needed to clarify the long-term outcomes of patients with diabetes. Fifth, we did not examine the severity of type 2 diabetes. Therefore, additional studies are needed to examine the relationship between HL and disease severity in type 2 diabetes, such as emergency room visits, treatment intensity, and time off work due to diabetes. Finally, we assessed HL, self-care behavior, and blood sugar levels among older patients with type 2 diabetes. Our findings would be more informative if social support, family support, access to healthcare information, and perceived self-efficacy were included, which might have also significantly affected patient HL.

In conclusion, the results of the current study demonstrated moderate HL in most older adult patients with type 2 diabetes in Thai communities. Increased HL among these patients was associated with better self-care behavior and, consequently, decreased blood sugar levels. Nurses and healthcare providers should be involved when developing health promotion programs to encourage blood sugar control and improve patient quality of life, particularly in older adults with diabetes.

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### CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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### AUTHOR CONTRIBUTION

Conceptualization, WS, KP, BP; Data curation, WS, KP; Funding acquisition, WS, KP, BC; Investigation, WS, KP; Methodology, WS, BC; Project administration, WS, KP; Supervision, WS; Writing-original draft, WS, KP; Writing-review & editing, WS, KP, BP.

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## Health Literacy among Older Adults during COVID-19 Pandemic

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Dear Editor,

We would like to share our ideas regarding “Health literacy (HL) among older adults during the coronavirus disease 2019 pandemic: a cross-sectional study in an urban community in Thailand.”<sup>1)</sup> Pechrapa et al.<sup>1)</sup> presented a case and concluded that “The results of our study provide important information . . . community during the COVID-19 pandemic.” In this report, the authors conducted a small questionnaire-based survey in a rural district of a country in Indochina.<sup>1)</sup> They assessed demographic parameters to draw conclusions regarding HL. However, they did not include the complete original questionnaire, and their classification of HL level is unclear.

A recent report from Australia observed a relationship between HL and anti-COVID-19 practices.<sup>2)</sup> In general, HL among older adults depends on several factors. Older adults in different age groups might have differing abilities to comply with HL assessments. Since it is unclear how HL was classified in the present report, it is difficult to interpret the relationship between observed HL and practice. Therefore, the further implications on local public health policies might be limited. Additionally, a recent study from Thailand also showed a significant disparity between knowledge, determined by HL, and practice regarding COVID-19.<sup>3)</sup> That study also demonstrated that the knowledge of local Thai older adults was not associated with preventive behaviors against COVID-19,<sup>3)</sup> contrary to reports from Australia,<sup>2)</sup> and the United States.<sup>4)</sup>

These findings might indirectly imply that information from the HL survey might not be useful for preventive management for COVID-19 in this setting. In many poor communities, local people might not be able to afford resources for prevention. In addition, insufficient use of preventive equipment, such as facemasks, remains a challenge in many areas.<sup>5)</sup>

Moreover, while knowledge levels may be good, other factors, such as a lack of facilities, may challenge good practices by older

adults during pandemics. Developing communities in Indochina face many barriers, including policy barriers and limited local resources, to allow local people to have good health practices despite a good background HL.<sup>6)</sup> In conclusion, HL assessment is a useful tool for assessing basic health knowledge of older adults, but confounding contexts must be considered regarding their implications in real practice.

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### CONFLICT OF INTEREST

The authors claim no conflicts of interest.

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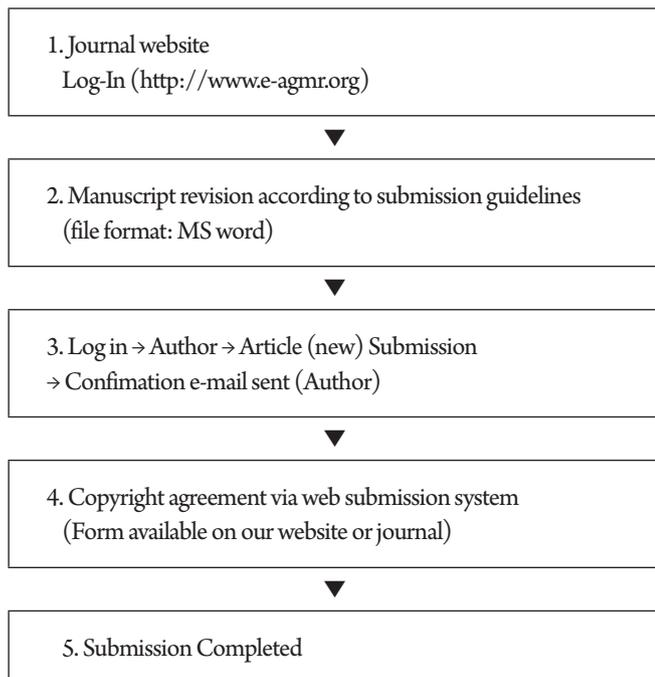
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- Page numbers must be indicated in Arabic numerals in the middle of the bottom margin, starting from the abstract page.
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The manuscript sections should be presented in the following order: Cover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

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

Type of article	Abstract (word)	Text (word) <sup>a)</sup>	Reference	Table & figure
Original article	Structured <sup>b)</sup> , 250	3,500	50	7
Review	150	6,000	unlimited	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.

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

<sup>b)</sup>Background, methods, results, and conclusion.

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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.

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- **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).

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### **Reference Style**

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

- 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>.

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### Other Manuscript Formats

General guidelines are same as for original articles.

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- Case Reports
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# Annals of Geriatric Medicine and Research

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AGMR 2021

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