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Aims and Scope

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

General Information

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

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Appreciation to Our Peer Reviewers in 2019

Jae-Young Lim

Editor-in-Chief of Annals of Geriatric Medicine and Research, Seoul National University Bundang Hospital, Seongnam Korea

As we begin the first issue of 2020, the Editorial Board, Associate Editors, and Editor-in-Chief of *Annals of Geriatric Medicine and Research* (AGMR) would like to thank our reviewers for their ongoing service and commitment to AGMR. We rely on the clinical and research expertise of peer reviewers to ensure that the manuscripts submitted to the journal undergo a thorough, fair, and timely review.

Over the last year, AGMR has continued to move forward as a growing platform for the academic needs of geriatrics and gerontology professionals and researchers. In November 2019, AGMR was accepted for inclusion in Scopus, an abstract and citation database from Elsevier. As a fast-growing journal in the multidisciplinary aging research field, our success in entering the scholarly universe of Scopus will improve the visibility of our scientific literature to researchers working in relevant fields. This achievement would not have been possible without the voluntary contributions of our reviewers to improve the scientific quality of our journal.

AGMR invited 62 experts to peer review manuscripts in 2019, some of whom received multiple invitations. With deep gratitude, I would like to particularly acknowledge the dedication of two of these peer reviewers, Drs. Jongkyoung Choi and Sun-Wook Kim, who were selected to receive Best Reviewer awards. Once again, we appreciate the rigorous and conscientious efforts of all of our reviewers and humbly request their ongoing interest and support in 2020.

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Motoric Cognitive Risk Syndrome: A Risk Factor for Cognitive Impairment and Dementia in Different Populations

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Changes in gait, especially decreased gait velocity, may be a harbinger of cognitive decline in aging. Motoric cognitive risk syndrome (MCR), a pre-dementia syndrome combining slow gait and cognitive complaints, is a powerful clinical tool used to identify older adults at a high risk of developing dementia. The mean prevalence of MCR worldwide, including in a Korean cohort, was around 10%. The reported risk factors for incident MCR include older age, low education, cardiovascular disease, obesity, physical inactivity, and depression. In addition to dementia, MCR is also a risk factor for other age-related adverse conditions such as falls, disability, frailty, and mortality. The use of MCR has advantages over other pre-dementia syndromes in being much simpler to implement and requires fewer resources. Identification of mechanisms responsible for MCR may help in developing interventions to reduce the growing burden of dementia and disability worldwide.

Key Words: Motoric cognitive risk syndrome, Gait, Cognitive impairment, Dementia

INTRODUCTION

The population worldwide is aging rapidly. The percentage of people above 65 years of age is the most rapidly growing segment of the population and is estimated to nearly double between 2019 and 2050.[1] Therefore, age-related diseases are becoming an important burden on people's lives and countries' economies. Dementia and cognitive disorders are common among the aging population and play an important role in increasing morbidity and reducing the quality of life of older adults.[2] Over 50 million people were estimated to be living with dementia globally in 2019 and this number is expected to increase to 152 million by 2050. The current estimated annual cost of dementia is US $1 trillion globally, a figure set to double by 2030. Gait disturbances are also common with aging and are associated with increased morbidity and mortality.[3]

Given this global burden associated with aging, there is a pressing need to identify older adults at risk for dementia to institute preventive interventions, make healthcare decisions, and consider advanced planning decisions. Cognitive decline and dementia have been implicated in gait dysfunction through disturbances in top-down brain control mechanisms.[4] Emerging evidence supports gait dysfunction as a harbinger of dementia; this association could be a novel method to assess dementia risk.[5] Motoric cognitive risk syndrome (MCR) is a pre-dementia condition combining motor signs (slow gait) and cognitive symptoms (self-reported cognitive complaints).[6] Studies across the globe have shown that the presence of MCR increases the risk of dementia as well as other age-related adverse outcomes. More recent studies have also uncovered links between MCR and genetic, metabolic, and imaging factors.[7]

This review discusses the epidemiology of MCR, its role in increasing the risks of dementia and other geriatric outcomes, and recent biological discoveries regarding its pathophysiology. A sys-

tematic search was conducted using the Medical Subject Heading terms "slow gait", "subjective cognitive impairment", "subjective cognitive decline", and "motoric cognitive risk syndrome".

GAIT SPEED AND COGNITIVE DECLINE IN GENERAL

Gait is a complex and multifactorial process in terms of its underlying central and peripheral neural control mechanisms. Similar brain regions control both gait and cognitive functions, particularly frontal and prefrontal lobe-related networks.[8] These brain areas are responsible for mediating executive functions (EFs), a variety of higher cognitive processes that integrate information from many cortical sensory systems and modulate and produce effective and goal-directed actions and behavior.[9,10] The aging process is accompanied by atrophy of many of these brain regions, causing both cognitive and gait decline.[11-13] Changes in the aging brain include atrophy of the frontal and temporal areas and the occurrence of periventricular white matter lesions. Abnormal gait is a prominent feature in neurodegenerative diseases, especially those that affect mainly the frontal lobes.[14,15] Pilot intervention trials to enhance EF either by cognitive training or brain stimulation have shown improvements in gait velocity.[16,17]

Slow gait speed may be the first sign of degenerative or non-degenerative brain pathologies and may manifest before other cognitive symptoms. Clinical gait disturbances in older adults may be due to neurological, muscular, or arthritic etiologies as well as combinations of these factors. Neurological gait abnormalities were reported to predict the incidence of non-Alzheimer's dementia in the Bronx Aging Study.[18] Velocity is the most widely used quantitative performance index of gait; however, other gait variables such as stride length, cadence, swing and stance time, and symmetry obtained from quantitative gait assessments are also used to evaluate gait quality.[19] Growing evidence suggests that not only a decline in gait speed predicts dementia but also that a decline in gait speed may precede the decline in cognitive performance in dementia.[7,20] These observations suggest that clinical or quantitative gait disturbances may be used to identify people at risk to develop dementia.

MCR DIAGNOSIS ACROSS POPULATIONS

In 2013, Verghese et al.[21] introduced the concept of MCR to describe people who are still cognitively intact but with cognitive complaints and slowing of gait, who are at higher risk of developing dementia. The criteria for MCR in this initial study were built on those for mild cognitive impairment syndrome (MCI),[22] and included the presence of subjective (self-reported) cognitive complaints measured by a structured questionnaire or clinicians' interview, slowness of gait defined as one standard deviation (SD) below age- and sex-specific gait speed mean values established in the same population, independence in activities of daily living, and absence of dementia. The main criterion distinguishing MCR from MCI was substituting a slow gait criterion for objective impairment on a cognitive test in MCI. Out of the 997 community-residing individuals aged 70 years and older participating in the Bronx-based Einstein Aging Study, 7% met this operational definition of MCR. Over a follow-up period of 36.9 months, those diagnosed with MCR at their baseline visit had a higher risk of developing dementia, especially vascular dementia, compared to those without MCR at baseline.[19] Since then, the prevalence of MCR has been examined in many other cohorts and populations worldwide and found to vary between 2% and 27% (Table 1).[21,23-43] These studies differed in the way MCR and the reported MCR risk factors in different populations. The differences in estimated MCR prevalence may be attributed to the way MCR criteria are operationalized in studies as well as the different populations recruited in previous studies. Cognitive tests are not required to diagnose MCR, which increases its clinical utility. The assessment for subjective cognitive complaints was performed using different methods in different cohorts, such as the 15-item Consortium to Establish a Registry for Alzheimer's Disease (CERAD) questionnaire,[44] one or two incorrect responses on the Short Portable Mental Status Questionnaire (SPMSQ),[45] the memory item from the 15-item Geriatric Depression Scale,[46] the eight-item informant interview (AD8),[47] or the Clinical Dementia Rating scale.[48] In other studies, positive responses from participants to questions such as "Do you have trouble remembering?" or "Is your memory worse than 10 years ago?" were sufficient. Even a referral to a memory clinic has been used to assess for the MCR subjective cognitive complaint criterion.[41,42] This heterogeneity in subjective cognitive complaint ascertainment may lead to differences in prevalence estimates of MCR as well as variability between studies in the cognitive impairment of individuals diagnosed with MCR. Subjective cognitive complaints related to the early stages of dementia may also be expressed differently in different cultures and parts of the world. As subjective cognitive complaints are key criteria to diagnose MCI and dementia, issues regarding the specificity of this criterion are not unique to MCRs.

All MCR studies have used normal walking gait velocity to evaluate gait slowness; however, methods have varied across studies with assessments done either by instrumented walkways such as the GAITRite system[49] (CIR Systems Inc., Sparta, NJ, USA) or by timing participants' walk at normal pace using a stopwatch over a fixed distance. The distances used have also varied from 2.44 m (8 feet) to 9.70 m (20 feet), which may also influence slow gait deter-

Table 1. Motoric cognitive risk syndromes (MCRs) prevalence and characteristics in 16 different studies

No.	Study	Year	Country/ Cohort	Number of patients	Sex, women (%)	Education (y)	High school (%)	Mean age (y)	Mean follow-up (y)	Mean gait speed (cm/s)		MCR prevalence (%)	MCR risk factors	Dementia conversion rate (aHR)
										With MCR	Without MCR			
1	Verghese et al.[21]	2013	USA/EAS	767	60	14	-	79.8 (≥70)	3.6	59.5	96.9	6	Black ethnicity, less education, hypertension, diabetes, arthritis	All: 3.27 Vascular: 12.81
2	Verghese et al.[23,24]	2014	17 countries/22 cohorts	26802	55.7	7	-	71.6 (≥60)	5.1–9.3	47.8	95.8	9.7	Age, CVD, Hypertension, diabetes, stroke, depression, arthritis	All: 1.93
3	Doi et al.[25]	2015	Japan/NCGG-SGS	9683	52	9	11.8	73.6 (≥65)	NA	80	117	6.4	Age, less education, diabetes, obesity, sedentariness, depression	NA
4	Kumai et al.[26]	2016	Japan/Kurihara Project	513	61	9	-	79.8 (≥75)	2020-03-05	80	120	11.1	Low education	All: 1.38
5	Wang et al.[27]	2016	India/KES	139	33.1	8.9	-	66.6 (≥60)	NA	61.9	91	27.3	None	NA
6	Allali et al.[29]	2016	USA/CCMA	314	56	14.2	-	76.9 (≥65)	NA	66.1	103.8	8	Obesity, sedentariness	NA
7	Doi et al.[30]	2017	Japan/OSHPE	4235	50	11.4	-	72.0 (≥65)	2.6	87	123	6.3	Less education, diabetes, obesity, sedentariness, depression, CVD	All: 2.49
8	Beauchet et al.[28] Sekhon et al.[31] Beauchet et al.[32]	2016 2017 2018	France/GAIT	238	37.4	-	40	71.4 (≥65)	NA	80.2	114.7	16.8	Waist-Hip ratio, hypertension, diabetes	NA
9	Maguire et al.[33]	2018	Ireland/TILDA	2151	55.6	-	79	67.8 (≥60)	NA	99.9	132.8	2.56	Hypertension, poor vision, obesity, diabetes, CVD, stroke	NA
10	Chhetri et al.[33]	2020	China/BLSA II	4632	61	-	61	75.4 (≥55)	NA	41	NA	9.6	Age, CVD, stroke, diabetes, depression, smoking	NA
11	Aguilar-Navarro et al.[35]	2019	Mexico/MHAS	726	54	5.35	-	69.8 (≥60)	2.9	NA	NA	14.3	Age, less education, multiple comorbidities, diabetes, depression	Cognitive impairment: 2.46
12	Lau et al.[36]	2019	Malaysia/TUA	1366	51	5.04	-	68.5 (≥60)	NA	NA	NA	3.4	Age, women, rural areas, obesity, diabetes, CVD, cancer	NA
13	Beauchet et al.[37,39] Beauchet et al.[38]	2019 2020	France/EPIDOS	5958	100	-	70	80.2 (≥75)	7	60	90	9.9	Age, less education, BMI, diabetes, hypertension, CVD, stroke depression, sedentariness	All: 2.18 AD: 2.23
14	Sekhon et al.[40,41]	2019	Canada/CLSA	29569	50.9	-	95.7	62.9 (≥45)	NA	NA	NA	7	Younger age, women in some age groups, hypertension, obesity[a], diabetes, CVD, depression, anxiety	NA
15	Verghese et al.[42]	2019	USA/EAS, MAP, ROS	4597	70	14.8	-	62.9–98.7 (≥60) EAS ≥70	2.9	42.4	NA	13.3	NA	NA
16	Shim et al.[43]	2020	Korea/KFACS	2881	52	-	56.3	75.9 (≥70)	NA	75	114	8.02	less education, sedentariness, hypertension, diabetes	NA

EAS, Einstein Aging Study; NCGG-SGS, National Center for Geriatrics and Gerontology – Study of Geriatric Syndromes; KES, Kerala-Einstein study; CCMA, Central Control of Mobility in Aging; OSHPE, Obu Study of Health Promotion for the Elderly; GAIT, Gait and Alzheimer Interactions Tracking; TILDA, The Irish Longitudinal Study on Aging; BLSA-II, Beijing Longitudinal Study of Ageing II; MHAS, Mexican Health and Aging Study; TUA, Towards Useful Aging; EPIDOS, Epidemiologie de l'Osteoporose; CLSA, Canadian Longitudinal Study on Aging; MAP, Rush Memory and Aging project; ROS, Religious Order Study; KFACS, The Korean Frailty and Aging Cohort Study; CVD, cardiovascular disease; NA, not applicable; AD, Alzheimer's disease; BMI, body mass index; aHR, adjusted hazard ratio.
[a]BMI ≥ 25 kg/m^2.

mination. Differences in measuring methods and in population characteristics explain why the cutoff velocity for the diagnosis of MCR is so different between studies (Table 1). Although all studies defined slow gait as walking speed 1 SD below age- and sex-specific means individualized to each cohort, the mean velocity for each cohort varies significantly. The mean velocity for the diagnosis of MCR varies between 41 cm/s[34] and 99.9 cm/s.[33] Age and sex are important factors in determining gait velocity; therefore, many studies calculated specific means for different age groups to reduce heterogeneity. Although a universal single cutoff velocity for determining slow gait criterion may add clinical utility to the MCR definition, it may not be practical given the variability in gait velocity across age groups, sexes, and populations.[50] Other motoric tests such as the Five-Times-Sit-to-Stand Test (FSTT) were less specific to diagnose MCR when used as a substitute for gait velocity.[51,52] Other quantitative gait variables have been used to diagnose MCR subtypes and were shown to identify older adults with different cognitive trajectories[29] and risk factors[52] than the classical MCR definition. However, assessment for these subtypes requires access to an instrumented walkway, which limits its use in many clinical settings.

The third component of MCR is independence in activities of daily living. This component was examined in published studies using either a structured questionnaire developed to assess function in community-residing older adults[53] or by study clinician interviews. The multi-country MCR prevalence study used mobility disability for this criterion as information on activities of daily living were not available in all of the 22 included cohorts.[23] The fourth component of the syndrome is the absence of dementia. This was assessed either using known clinical criteria for dementia, such as those in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV),[54] and diagnosed at consensus case conferences, through participant or informant report of physician-diagnosed dementia, or by applying established cut-off scores on cognitive tests such as the Mini-Mental State Examination (MMSE).[55] These criteria vary considerably across studies and may result in the inclusion of individuals with different levels of cognitive disturbance.

Study populations have varied across MCR studies. While most studies were restricted to older populations, some also included younger people. Most studies used an entry age of 60, 65, or 70 years. Two studies included only adults 75 years and above,[26,37] while two other studies used an entry criterion of 45 years.[34,40] This difference in the age of entry affects the determination of slow gait and other parameters related to MCR prevalence and risk factors. The prevalence of women in the studies varies between 33% and 70%, with one study including only women.[37] Recruitment methods also increased the variability of study populations in previous reports. A multi-country prevalence study included data from 22 cohorts,[23] 16 of which were community-based, 4 were recruited participants from memory clinics, and 2 were recruited from both clinics and the community. The highest prevalence of MCR was reported in the Indian and French cohorts, which were memory clinic-based populations.[23] MCR studies have included data from cohorts from different countries and ethnic groups. In one US-based study that included both African American and Caucasian populations, the prevalence of MCR was higher among

African American participant.[21] MCR studies have also been conducted in individuals with low income and low education levels.[23,28,35,36] The MCR definition has shown relatively stable prevalence estimates in studies with various populations and variable education and socioeconomic levels, supporting its role as a practical and reliable clinical assay for dementia risk worldwide.

MCR Risk Factors across Populations

The risk factors for MCR include age, sex, level of education, obesity, physical inactivity and sedentariness, depressive mood, and cardiovascular disease. Most studies reported that advanced age increased the risk of MCR,[23,25,34-37] similar to dementia. For instance, in a multi-country MCR study that included over 26,000 participants,[23] the MCR prevalence was 10.6% in the group aged 75 years and older as compared to 8.9% in the group aged 60–74 years. However, MCR studies from Ireland and Korea reported that the prevalence of MCR did not increase with advancing age and was similar across age groups.[33,43] In one study from Canada,[37] the risk of MCR was higher in the younger age groups (45–55 years) compared to that in more advanced age groups. However, this was the only community-based study to include such a young age group. The next-highest prevalence of MCR in this study was that in the older group of 75 years and above. This finding of increased MCR prevalence with age is consistent with the reported higher prevalence of cognitive complaints and dementia with increasing age.

Most studies did not find any difference in MCR prevalence between sexes. However, some studies reported a higher rate of MCR among women. In a prevalence study from Malaysia that included 1,366 participants, the prevalence rate of MCR was 5% among women and 1.8% among men.[36] The authors attributed this finding to the higher prevalence of frailty among older Malaysian women compared to that in men. A Canadian study[37] reported a higher MCR prevalence in women aged 45–54 and 65–74 years but with opposite results in the other age groups, a finding with unclear interpretation.

Most, but not all MCR studies found that lower levels of educa-

tion are a risk factor for MCR.[23,25,30,35,37,43] Most studies used years of schooling to measure education, which may not be a perfect measure. In a Canadian study with 29,569 participants, lower education level was a risk factor for MCR only in the 55–64 and 65–74 years age groups and not in the youngest or the oldest groups.[40] In a multi-country study including more than 26,000 participants, a higher level of education (> 12 school years) was associated with a lower prevalence of MCR.[23] The best explanation is that, similar to MCI and dementia, higher levels of education are also a protective factor for MCR, perhaps by increasing brain cognitive reserves.[56]

Similar to studies of MCI and dementia,[57,58] most studies reported sedentary lifestyle to be a risk factor for MCR.[25,29,30,37,43] The methods used to determine levels of physical activity varied between studies, with some studies adopting a structured questionnaire and others using a simple question regarding regular participation in a sport or leisure physical activity (i.e., at least 1 hour a week for the past month). Sedentariness was also examined by self-reported difficulty in walking less than a quarter mile or negotiating stairs.[59] The TILDA study based in Ireland[33] reported no significant correlation between physical activity level and MCR prevalence; however, participants in this study were more likely to be cognitively healthy and with high physical functioning. The protective effect of physical activity in MCR, like in MCI and dementia, can be explained by several mechanisms such as the positive effects of physical exercise on cardiovascular risk factors including hypertension, insulin resistance, and high cholesterol levels as well as other biological mechanisms such as enhanced immune system function, anti-inflammatory properties, and increased neurotrophic factors.[60]

One notable risk factor of MCR was obesity, defined either by body mass index (BMI) or waist-to-hip ratio.[25,29,30,33,36,37,40] Most MCR studies did not evaluate body composition. In two studies from China and Korea, obesity was not correlated with MCR, suggesting possible ethnic differences in this MCR risk factor.[34,43]

Cardiovascular diseases and cardiovascular risk factors such as hypertension and diabetes increase MCR risk, similar to the increased risk reported for these risk factors with dementia and MCI.[61-63] Diabetes was a risk factor in almost all studies.[34] Hypertension was a risk factor in most, but not all, studies.[25,34,36] Ischemic heart disease was also a risk factor in the majority of studies.[23,30,33,34,36,37,40] Smoking was identified as a risk factor for MCR in one study from China[32] but not in other studies in which it was documented.[25,30,36] Alcohol consumption was not found to be a risk factor for MCR in any of the studies.

Polypharmacy is a known risk factor for frailty and cognitive decline in old age.[64] Several studies have examined the relationship between the number of medications prescribed and the occurrence of MCR;[25,30,33,37-39,42] most studies reported that increased numbers of medications were associated with MCR. The mean number of medications taken by participants with MCR varied between 2.3 and 6.6. Using a widely accepted definition of polypharmacy as five or more medications daily, two studies showed that polypharmacy was a risk factor for MCR.[33,37,38]

Depression and anxiety are strongly associated with MCR. This association was found in large-scale studies including a multi-country study and the Canadian CLSA study.[23,40] The latter study observed this association in all age groups. The use of anti-depressive medications was also associated with MCR.[33] Depression in old age is related to cognitive decline and dementia and may be an early manifestation of dementia due to neurodegenerative or vascular brain diseases.[65] Other significant risk factors for MCR examined in individual studies were arthritis,[21,23] poor vision,[33] and living in rural areas.[36]

MCR as a Risk Factor for Cognitive Decline and Dementia

A recent meta-analysis by Sekhon et al.[66] including seven studies evaluated the relationship between MCR and the development of cognitive impairment and dementia and examined the relationship between MCR and the development of either dementia or cognitive impairment. In general, MCR was associated with increased risks of incident cognitive impairment (adjusted hazard ratio [aHR] = 1.70) and dementia (aHR = 2.50). This meta-analysis included four studies that examined the association between MCR and the incidence of dementia.[21,23,26,30] Since then, another study from France reported an association between MCR and dementia.[38] MCR has been shown to have incremental predictive validity for dementia over its cognitive (cognitive complaints) and motoric (slow gait) components.[21]

There is heterogeneity in terms of study populations, follow-up time, and criteria employed for the diagnosis of MCR and cognitive disorders among studies that have examined the predictive validity of MCR for cognitive decline. In a homogenous cohort from the US,[21] the aHR to develop dementia overall in participants with MCR was 3.27; however, MCR did not predict Alzheimer disease (AD) but did strongly predict vascular dementia (aHR = 12.81). This finding was consistent with that of a previous study that showed slow gait to be a predictor of vascular dementia and not AD.[21] In contrast, a combined analysis of four cohorts that included 4,812 participants with longitudinal data reported MCR to be a risk factor for dementia overall including AD (aHR = 1.93).[23] In a study from Japan including 4,235 participants,[30] over a mean follow-up of 2.6 years, the aHR to develop dementia overall in participants with MCR at baseline was 2.49; however, the de-

mentia subtypes were not specified. In another small study from Japan including 299 participants with a follow-up of 3–5 years, the odds ratio of conversion to dementia overall was 1.38 in the MCR group compared to the non-MCR group. A recent study of 651 French women followed up to 7 years[38] reported a nearly two-fold increased risk of incident dementia in the MCR group than that in the non-MCR group (41.9% vs. 23.3%). MCR was positively associated with the incidence of overall dementia and AD but not with non-AD dementia incidence. This study included only women; therefore, the results may not apply to the general older population.

A recent multicenter study including 610 older adults with MCR from three US-based cohorts followed over a mean of 2.9 years investigated which components of the MCR syndrome predicted transition to dementia.[42] The cognitive components — measured by a cognitive complaint severity index, logical memory test,[67] and MMSE[55]—predicted the transition from MCR to dementia, whereas the motoric component of MCR (gait velocity) did not. This finding may be attributed to the fact that the cognitive complaints and tests in MCR patients may better correlate with the worsening of dementia-related pathology or spread of pathology into brain areas responsible for other non-motor behaviors and cognitive impairments associated with dementia. An alternative explanation might be that, since this study included only individuals with MCR with a restricted range of gait velocities, slower gait was not a predictor of dementia. Finally, since memory-related questions were used for the diagnosis of MCR and the incident dementia cases included a high proportion of AD patients, cognitive complaints but not gait velocity predicted dementia in this analysis.

Several studies evaluated the association between MCR and other pre-dementia syndromes such as MCI.[21,23,31] MCI diagnosis is based on subjective cognitive complaints (as in MCR), objective cognitive impairment in the memory or non-memory domains assessed by neuropsychological tests, and without impairment of activities of daily living or dementia.[68] The co-occurrence of MCI among MCR was 54%, 47%, or 39% in different studies, respectively.[21,23,31] The combination of MCR and MCI was associated with lower cognitive performance compared to that in individuals with MCR but without MCI.[31] While there is overlap between MCR and MCI cases, MCR syndrome still statistically predicted the risk of dementia in previous studies after accounting for MCI cases or excluding individuals who met criteria before or simultaneously with MCR. These observations emphasize the importance of diagnosing both pre-dementia syndromes to identify all individuals at risk. MCR should be seen as a complementary rather than an alternative approach to MCI.

Six studies evaluated the association between MCR and cognitive performance, with mixed results.[23,26,29,31,33,43] These studies assessed several domains of cognitive function, including global cognitive functions, memory, EF, processing speed, attention, visuospatial abilities, and language. In most studies, MCR was negatively associated with global cognitive performance and EF, supporting the hypothesis that frontal lobe dysfunction is involved in both gait and EF control.[9] However, one study did not show an association with EF but found that the MCR group performed worse on measures of global cognition, memory, and sustained attention.[33] The authors attributed this finding to the larger size of their sample and the specific characteristics of the population in this cohort (TILDA). The relationship between memory functions and MCR is conflicting, with several studies reporting lower performance in memory tests in MCR,[23,31,33] while others did not find such a correlation.[29,43] One study reported an association between language difficulties and MCR;[29] however, other studies did not test this domain.

MCR as a Risk Factor for Other Geriatric Outcomes

MCR is reportedly a risk factor not only for dementia but also for other adverse conditions in older adults such as falls, disability, frailty, and mortality.[69] Falls are an important medical problem in the older population. An estimated 32%–42% of all people above 70 years of age will fall every year.[70] Falls in older adults are associated with complications including fractures, surgery, and hospitalization and are related to increased disability and mortality.[71] Maintaining balance and preventing falls is a complicated function that requires efficient integration of motoric, cognitive, and psychological functions. Individuals with MCR have a combination of cognitive impairment, mainly in EF, and motor disturbances that place them at high risk for falls. Several studies have investigated this association. Callisaya et al.[72] examined 6,204 participants from five large cohorts across three countries and revealed that 33.9% of subjects with MCR reported a fall over follow-up of 12 months, resulting in a pooled relative risk (RR) of MCR for any falls of 1.44; this association reduced in strength but persisted after adjusting for previous falls (RR = 1.37). As for dementia outcomes,[73] MCR had incremental predictive validity for falls over its cognitive and motoric components. In a study of 2,569 French women, MCR increased the risk for any fall (aHR = 1,22), recurrent falls (aHR = 1.46), and falls complicated by hip fracture (aHR = 2.54).[37]

Few studies have examined the association between MCR and disability and frailty among older adults. In a study of 4,235 Japanese older adults (mean age, 72 years), MCR was associated with an increased risk of disability, defined as certification by long-term care insurance, with an aHR of 1.69.[30] Frailty is a multidimension-

al construct associated with low physiologic reserves and increased vulnerability to adverse outcomes such as disability and death.[74] In a study of 641 adults aged 65 years and above, higher frailty at baseline, as assessed using a cumulative deficit index, increased the risk of developing incident MCR even after accounting for several confounders, suggesting shared mechanisms between these two syndromes.[75]

Two studies investigated the relationship between mortality and MCR. Among 11,867 participants from three different cohorts over a median follow-up of 28 months, MCR at baseline was associated with increased mortality overall (aHR = 1.69) and 2-year mortality (aHR = 1.89) even after adjusting for gait speed and memory test scores.[76] In a study of 3,778 French women followed up for 19 years, MCR was associated with mortality at 10 years (aHR = 1.27), 15 years (aHR = 1.22), and 19 years (aHR = 1.41).[39]

MCR Studies in Korea

Two studies examined the epidemiology of MCR in Korea. The MCR multi-country prevalence study included a sample of 549 individuals aged 65 to 102 years (63.8% women) from the Korean Longitudinal Study on Health and Aging (KLoSHA).[23] The prevalence of MCR in this cohort was 10.0%, compared to 8.02% in the nationwide Korean Frailty and Aging Cohort Study (KFACS) that included 2,881 community-dwelling older adults aged 70–84 years (52% women; mean age, 75.9 years).[43] The prevalence of MCR did not increase with age (70–74 years, 8.90%; 75–79 years, 7.06%; and 80–84 years, 8.04%). Similar to previous studies, the MCR group had lower education levels and reduced physical activity, higher prevalence of hypertension and diabetes, and higher numbers of comorbidities and medications as compared to those in the non-MCR group. Participants with MCR had greater difficulty with respect to mobility and were more likely to report a history of falls. In addition, participants with MCR rated their health poorer compared to that in those without MCR.[43] In contrast, participants with MCR did not show significant differences in BMI or depressive symptoms. MCR in the KFACS cohort was associated with a decline in global cognitive function, attention, processing speed, and EF.

While these two cohort studies are not fully representative of the entire population of older Korean adults, the MCR estimates are consistent with the MCR prevalence reported in developed countries.

BIOLOGY OF MCR

Four studies reported on the relationships between brain imaging and MCR including white matter and gray matter abnormalities and brain volume and atrophy.[66] A study of 358 participants from two cohorts in France and India reported white matter hyperintensities (WMH) on magnetic resonance imaging (MRI) in 72.9% of the participants. WMH in the frontal, parieto-occipital, temporal, basal ganglia, cerebellum, or brainstem were not associated with MCR in either of the two cohorts.[77] WMH are ubiquitous in aging populations and have often been regarded as non-specific. Another study of 139 participants from the Kerala-Einstein Study in India investigated the relationship between MCR and brain WMH as well as the presence of lacunar infarctions and microbleeds.[27] In this study, only the presence of lacunar infarctions in the frontal lobe was correlated with the presence of MCR at cross-section. All other parameters including WMH, other stroke, lacunar infarctions in other areas, and microbleeds were not associated with MCR. The authors assumed that vascular mechanisms other than WMH may contribute to the pathophysiology of MCR; however, they emphasized that the evaluation of WMH was based solely on manual quantification and not on automatic measurements that could provide a more objective measure and metric information such as volume. The correlation between global and regional brain volumes with MCR syndrome was evaluated in 171 participants from France.[28] Multiple logistic regression models showed that smaller volumes of total gray matter, total cortical gray matter, premotor cortex, prefrontal cortex, and dorsolateral segment of prefrontal cortex were associated with MCR. Similar to previous studies, WMH and total white matter volume were not correlated with MCR. Negative results were also found for hippocampus and subcortical gray matter volumes. Similar results were reported in a larger study that included 267 participants from three cohorts.[78] The significant gray matter volume covariance pattern associated with MCR even after adjusting for demographic characteristics was primarily composed of the supplementary motor, insular, and prefrontal cortex regions (Fig. 1). In contrast, relatively less atrophied regions as a function of MCR included the cerebellum as well as the inferior and middle temporal, para-hippocampal, and precuneus regions. The authors[79] concluded that MCR was primarily associated with gray matter atrophy in brain regions previously linked to the control aspects of gait such as motor planning and modulation.

The underlying biological and genetic mechanisms for MCR have not yet been established and few studies have been published to date. A study of 530 community-dwelling Ashkenazi Jewish adults age 65 years and older reported that single nucleotide polymorphisms in the transcriptional regulatory regions of cytokine interleukin 10 (IL10) were associated with the incidence of MCR over a median follow-up of 2.99 years.[80] Inflammation may play a

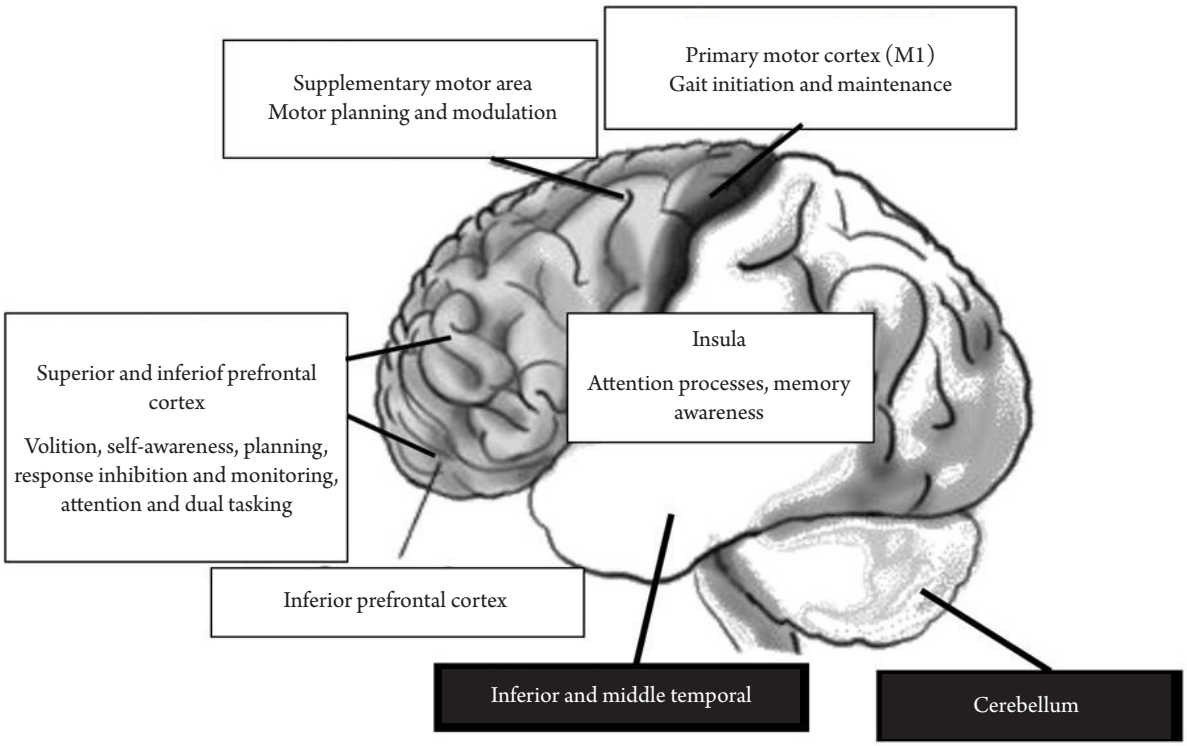

Fig. 1. Brain areas involved in motoric cognitive risk syndrome (MCR) and related cognitive mechanisms responsible for gait control (white boxes, more atrophied regions as a function of MCR; black boxes, less atrophied regions as a function of MCR).

significant role in the pathogenesis of dementia and cognitive decline;[81] this finding also suggests a role for inflammation in MCR pathogenesis. A preliminary study of the polygenic effects of selected clinical phenotypes on MCR was conducted in 4,915 individuals, age 65 years and above from the Health and Retirement Study.[79] Higher polygenic scores (PGS) for BMI and waist circumference were associated with MCR and PGS of AD showed a suggestive association, while higher PGS for higher well-being was protective. The authors suggested that obesity-related genetic traits may play an important role in the development of MCR and may serve as potential therapeutic targets in dementia prevention. Fig. 2 provides a graphical representation of the suggested biological mechanisms involved in the pathogenesis of MCR and MCI that may contribute to the increased risk of dementia in these pre-dementia syndromes.

POSSIBLE INTERVENTIONS TO IMPROVE FUNCTION AND PREVENT DETERIORATION IN MCR

No studies have reported therapeutic measures such as physical exercise or cognitive training in MCR populations to improve gait and cognition and prevent deterioration to dementia. Although epidemiological studies have shown the positive effect of mainly aerobic exercise on cognitive functions in normal or demented older adults, several meta-analyses failed to confirm the cognitive protective effect of exercise in clinical trials.[82,83] In contrast, small studies have shown cognitive training programs to improve gait functions.[84] A recent meta-analysis including 10 randomized clinical trials and a total of 351 participants showed that cognitive training interventions provided a small effect on complex walking conditions requiring higher-order EFs.[17] There is a need for large-scale randomized clinical trials, perhaps using multi-modal interventions, combining physical activity with cognitive stimulation or training, in MCR to improve cognitive function and mobility and prevent further deterioration towards dementia.

CONCLUSION

With the increasing aging population worldwide, the burden of cognitive disorders such as dementia is escalating. The coexistence of physical limitations and cognitive decline are common in aging adults, leading to many detrimental effects. MCR is a pre-dementia

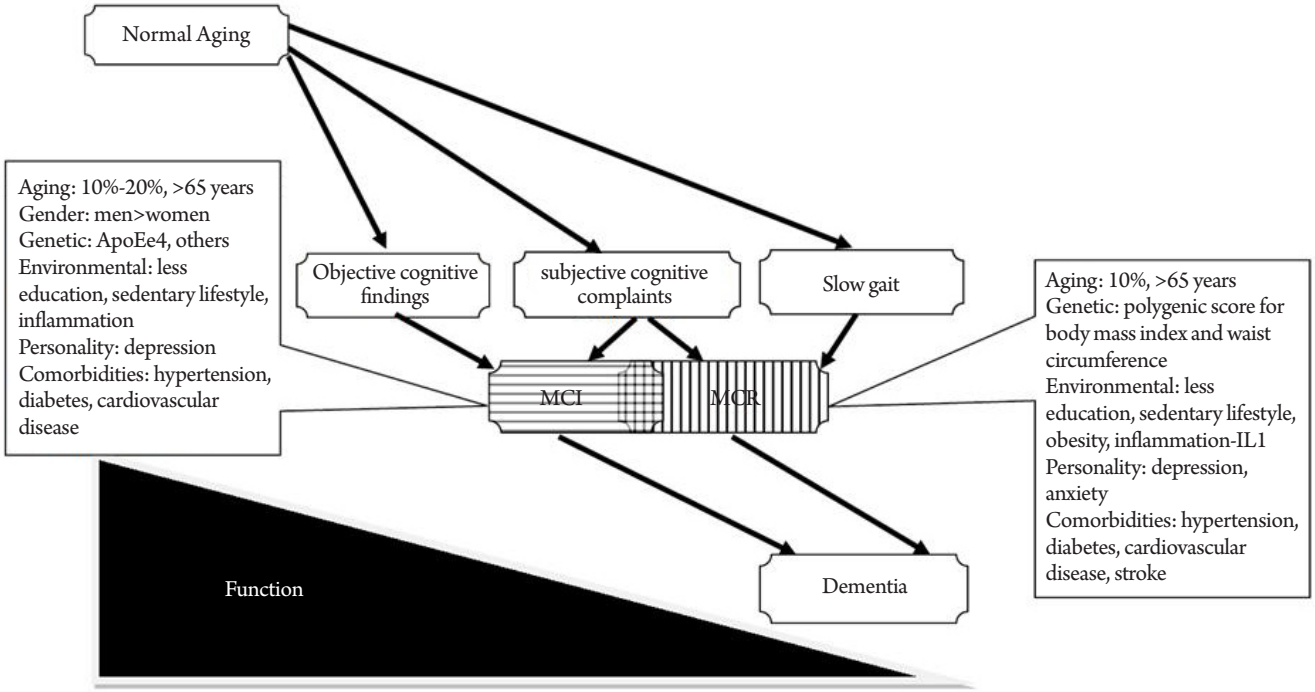

Fig. 2. Potential biological mechanisms in mild cognitive impairment (MCI) and motoric cognitive risk syndrome (MCR).

syndrome combining cognitive and motor components that increases the risk for cognitive decline and dementia as well as other age-related negative geriatric outcomes. In contrast to MCI, the diagnosis of MCR does not rely on formal neuropsychological assessments; thus, it requires fewer resources and is independent of language and level of education. The biology of MCR remains obscure, and further studies are needed to investigate the relationship between physical and cognitive domains in older adults. The results of such studies could facilitate the design of more effective preventive intervention strategies against dementia and other deleterious effects of aging. Recent studies suggest that one in 10–12 community-residing Korean seniors may have MCR. The MCR concept is of particular importance in Korea as it is one of the most rapidly aging nations worldwide.[85,86]

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CONFLICT OF INTEREST DISCLOSURES

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, JV, ZM; Methodology, JV, EA; Data curation, ZM, EA; Project administration, EA; Writing original draft, ZM; Writing, review & editing, JV, EA.

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Impact of Hypertension on Cognitive Decline and Dementia

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Dementia reduces a person's ability to perform their activities of daily living and is the leading cause of morbidity worldwide. While most preventive measures are ineffective in reducing dementia risk, active treatment of hypertension in middle-aged and older adults without dementia may reduce the incidence of dementia. Hypertension is associated with vascular dementia but may also affect the manifestations of Alzheimer disease. Observational studies support the association between hypertension and white matter lesions, hippocampal atrophy, and cognitive decline. Both increased and decreased blood pressure were related to the development of white matter lesions. Cohort studies showed that hypertension treatment and treatment duration were associated with lower cognitive decline. This review describes findings from randomized controlled studies on the effects of antihypertensives on cognitive decline. Only the Systolic Hypertension in Europe (Syst-Eur) trial using calcium-channel blockers demonstrated a significant reduction in dementia incidence. Further studies are required to evaluate the long-term benefits of antihypertensive treatment in dementia.

Key Words: Hypertension, Dementia, Prevention, White matter, Alzheimer disease

INTRODUCTION

Dementia is a disease resulting from acquired cognitive and functional impairments that reduce a person's ability to perform everyday activities and live independently.[1)] Dementia significantly affects individuals and their caregivers, families, communities, and societies.[2)] Dementia is currently the leading cause of morbidity worldwide, with an estimated annual global cost of US $818 billion.[2,3)]

The increasing longevity and number of older people worldwide are associated with a growing number of people living with dementia, particularly in lower and middle-income countries. Although most preventive measures are ineffective, active treatment of hypertension in middle-aged and older adults without dementia may reduce the incidence of dementia.[2)]

This paper provides an overview of hypertension and dementia, including recent evidence regarding hypertension treatment for dementia prevention.

HYPERTENSION AND ITS ASSOCIATION WITH COGNITIVE DECLINE

Several hypotheses purport to explain the relationship between hypertension and cognitive decline. The conventional theory is that hypertension is associated with cerebrovascular disease, leading to vascular or multi-infarct dementia. The International Workshop of the National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) criteria for vascular dementia (VaD) require the presence of cerebrovascular disease based on the detection of focal signs on neurologic examination, or evidence of cerebrovascular disease on brain imaging including large vessel infarcts, a strategically placed infarct multiple basal ganglia and white matter lacunes, extensive periventricular white matter lesions, or a combination of these radiological findings.[4)] VaD is likely if a person presents such evidence of cerebrovascular disease and manifests dementia symptoms, particularly if

there is a stepwise progression of cognitive deficits.

Long-term hypertension affects cerebral blood flow and metabolism as vessel injury causes thickening of the vessel walls and luminal narrowing via medial hyalinosis, resulting in stiffness and tortuous elongation.[5] The resulting endothelial dysfunction and blood-brain barrier alterations cause plasma protein leakage, oxidative stress, inflammation, and edema. These further compress brain tissue, contributing to hypoperfusion and demyelination.[6] Impaired cerebral autoregulation results in the loss of protective mechanisms, leading to a vicious cycle of neuronal injury. These disturbances in the blood-brain barrier cause diffuse white matter damage or leukoaraiosis. This is most evident in the periventricular white matter located at the boundary between different arterial territories, as these are the areas of the brain most susceptible to hypoperfusion.[7]

Although hypertension was traditionally considered to be associated with vascular dementia, it may also affect the manifestations of Alzheimer disease (AD). There is an overlap between markers of vascular injury and the hallmark pathology of AD. For example, blood-brain barrier dysfunction affects amyloid transport between the brain and periphery, leading to parenchymal and neurovascular amyloid deposition. AD pathology also causes vascular injury by damaging the blood vessel endothelium via Aβ-induced inflammation.[8]

Increasing evidence also suggests that sporadic AD is a vascular disorder caused by impaired cerebral perfusion rather than simply a neurodegenerative disorder.[9] Several epidemiological studies reported stroke, cardiac disease, and atherosclerosis to be the three most important risk factors for AD; these factors are also classic vascular risk factors.[10-12] Regional cerebral hypoperfusion is also a potential early marker of AD symptoms. Regional cerebral blood flow measurement by single-photon emission computed tomography (SPECT) showed that patients with mild cognitive impairment with significant hypoperfusion of the hippocampal-amygdala complex converted to AD within 3 years, while those with normal cerebral perfusion did not.[9,13]

Relationships among diabetes mellitus, AD, and vascular risk factors have also been reported. Insulin influences memory through receptors present in the hippocampus and medial temporal cortex. Insulin resistance and hyperinsulinemia lead to reduced brain insulin signaling, increased tau phosphorylation, and increased intracellular Aβ. Thus, diabetes increases the risk of both AD and VaD, regardless of the age at which diabetes occurs. The risk-enhancing mechanisms include the effects of insulin resistance described above; hyperglycemia-related increases in advanced glycation end products; and oxidative stress, inflammation, and macrovascular and microvascular injury. Interactions among lipids, lipoproteins, and Aβ play a critical role in Aβ production and clearance, whereas midlife obesity, hypercholesterolemia, and high systolic blood pressure additively increase the risk of dementia.[14]

In short, the vascular changes induced by hypertension increase brain susceptibility to ischemic-hypoxic damage in vulnerable white matter regions and may also promote AD neuropathology. Vascular changes and risk factors, especially diabetes, may be provoking and additive risk factors, while genetic factors such as apolipoprotein E (APOE) ε4 allele contribute to plaque formation.[15]

HYPERTENSION AND ITS ASSOCIATIONS WITH VASCULAR BURDEN ON NEUROIMAGING

There is a move towards routine structural neuroimaging with magnetic resonance imaging (MRI) for dementia evaluation owing to its greater sensitivity and ability to differentiate among dementia subtypes as compared with computed tomography.[4] Vascular burden is defined as the presence of many lacunae, strategic infarcts, substantial burden (> 25%) of white matter lesions, or combination of these findings. White matter lesions caused by long-standing hypertension are associated with cognitive impairment.[16]

The risk of severe white matter lesions is higher in people with poorly controlled hypertension than in those without or with treated hypertension. Increased systolic blood pressure is also associated with more severe periventricular and subcortical white matter lesions.[6] The Investigating Silent Strokes in Hypertensives: a Magnetic Resonance Imaging Study (ISSYS) cohort study of individuals with hypertension found that those with progression of periventricular white matter hyperintensities had a higher odds of cognitive decline compared to the odds for individuals with incident infarcts or microbleeds.[17] Diastolic hypertension was also associated with hippocampal atrophy compared to systolic hypertension, with hippocampal atrophy predictive of cognitive decline.[18] These observations support the association between hypertension and white matter lesions, hippocampal atrophy, and cognitive decline.

However, it is difficult to accurately determine the relative contributions of AD and cerebrovascular disease to a person's cognitive decline based on imaging findings alone.[2] For example, periventricular hyperintensities were correlated with age and were more severe in all dementia subtypes but were higher in patients with VaD than in those with dementia with Lewy bodies or AD.[19]

HYPERTENSION TREATMENT AND REDUCTION IN WHITE MATTER LESIONS OR DEMENTIA

An observational study of the efficacy of long-term hypertension

treatment observed an increased risk of late-life cognitive impairment and white matter lesions among individuals with hypertension at midlife.[20] Each year of hypertension treatment reduced the risk of dementia by 5%, with a lower cognitive decline observed for treatment durations of more than 5 years. However, studies on hypertension treatment efficacy have yielded conflicting results. The findings from randomized controlled studies of the effects of antihypertensives on the risk of cognitive decline are summarized in Table 1.

The Systolic Hypertension in Europe (Syst-Eur) trial compared the use of nitrendipine (with the possible addition of enalapril or hydrochlorothiazide) to reduce systolic blood pressure below 150 mmHg to placebo in terms of stroke and dementia outcomes. The trial was stopped prematurely after 2 years owing to a 42% decrease in fatal and non-fatal stroke and a 55% reduction in incident dementia.[16,21] Although the results of this trial showed great promise, subsequent studies have shown less positive results.

The SPRINT-MIND study randomized patients to receive intensive hypertension (systolic blood pressure < 120 mmHg) or standard (< 140 mmHg) treatments. The intensive control group had a significantly reduced risk of mild cognitive impairment but no reduction in the risk of dementia.[22]

In the treatment arm of the Hypertension in the Very Elderly Trial Cognitive Function Assessment (HYVET-COG), patients received indapamide with the possible addition of perindopril to target systolic and diastolic blood pressures of 150 and 80 mmHg, respectively. While the trial was stopped after 2-year follow-up due to a significant reduction in stroke and mortality incidence, there was no significant difference in the rate of cognitive decline or dementia between groups.[16] Similarly, while the Systolic Hypertension in the Elderly Programme (SHEP) trial used chlorthalidone (with the possible addition of atenolol and reserpine) to reduce systolic blood pressure to below 160 mmHg, active treatment reduced the incidence of cardiovascular events, but not those of dementia and disability.[23]

The Study on Cognition and Prognosis in the Elderly (SCOPE) randomized patients to receive candesartan or placebo and evaluated cardiovascular endpoints and cognitive function. No significant reduction in cardiovascular mortality, myocardial infarction, stroke or cognitive decline was observed between the treatment and placebo groups.[16,24] Finally, the Intensive Versus Standard Ambulatory Blood Pressure Lowering to Lessen Functional Decline in the Elderly (INFINITY) study randomized patients to receive intensive blood pressure-lowering (systolic < 130 mmHg) or standard treatment (target 145 mmHg). While intensive blood pressure lowering for 3 years significantly reduced the accumulation of subcortical white matter disease, it was not associated with differences in cognitive function.[25]

Overall, while these studies on antihypertensive treatment showed benefits in terms of cardiovascular risk, the effect on cognitive decline was less impressive. The choice of antihypertensive may be important, as the only study to convincingly show a cognitive benefit was the Syst-Eur study,[21] which utilized nitrendipine. As impaired intracellular calcium regulation contributes to brain

Table 1. Randomized controlled trials of hypertension treatment and its effect on the risk of cognitive decline

Trials (studies)	Follow-up duration (y)	Treatment vs. control	Blood pressure difference between treatment and control groups (mmHg)		Dementia incidences in treatment vs. control groups (per 1,000 patient-years)	Effectiveness of antihypertensive treatment in reducing dementia incidence and/or cognitive decline
			Systolic	Diastolic		
SYST-EUR[21]	2	Nitrendipine vs. placebo	-8.3	-3.6	7.7 vs. 3.8 (95% CI, 0–76)	Yes
SPRINT-MIND[22]	5.11	All classes but recommended thiazide-type diuretics as a first-line agent, loop diuretics in chronic kidney disease, and β-adrenergic blockers in coronary artery disease	-13.3	-	7.2 vs. 8.6 (HR = 0.83; 95% CI, 0.67–1.04)	Yes
HYVET-COG[16]	2	Indapamide +/- perindopril vs. placebo	-15	-5.9	33 vs. 38 (HR = 0.86, 95% CI, 0.67–1.09)	No
SHEP[23]	5	Chlorthalidone +/- atenolol +/- reserpine vs. placebo or reserpine	-11 to -14	-	No negative impact of blood pressure lowering on cognitive function (dementia incidence not measured)	No
SCOPE[24]	4.5	Candesartan vs. placebo	-3.2	-1.6	Dementia incidence not measured (95% CI, 0.08–0.38)	No
INFINITY[25]	3	ACEI or ARB, diuretics, CCBs, MRAs, beta-blockers vs. placebo	-15	-	No difference in cognitive endpoints (dementia incidence not measured)	No

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin-receptor blocker; CCB, calcium channel blocker; MRA, mineralocorticoid receptor antagonist; HR, hazard ratio; CI, confidence interval.

aging and AD neuropathology, the benefit observed in this study may be due to the central nervous action of dihydropyridines.[3] The duration of these trials may also have been too short to observe any cognitive benefits.[16] Further studies may need to utilize other measures such as white matter lesions as a marker of cognitive decline or perform longer-term follow-up.

CONCLUSION

Hypertension is associated with cognitive decline and dementia and is a potential target for interventions to reduce dementia risk. While the treatment of hypertension shows great promise in reducing cardiovascular risk only the Syst-Eur trial using nitrendipine, a dihydropyridine calcium-channel blocker, demonstrated a significant reduction in dementia incidence. Further studies are required to evaluate the long-term benefits of antihypertensive treatment in dementia prevention.

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CONFLICT OF INTEREST DISCLOSURES

The researchers claim no conflicts of interest.

AUTHOR CONTRIBUTIONS

Conceptualization, HLN, SPT; Data curation, HLN, SPT; Writing_original draft, HLN, SPT; Writing_review & editing, HLN, SPT.

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Anticholinergic Cognitive Burden as a Predictive Factor for In-hospital Mortality in Older Patients in Korea

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Background: With the increasing prevalence of chronic disease due to aging, many older adults experience multimorbidity and polypharmacy. Medications with anticholinergic properties are particularly associated with adverse cognitive outcomes, including functional decline and mortality. We assessed the clinical impact of anticholinergic cognitive burden (ACB) on clinical outcomes of older patients acutely admitted to a single, hospitalist-operated medical unit of a tertiary hospital in Korea. **Methods:** This retrospective study reviewed electronic medical records of 318 patients aged 65 years or older admitted to the hospitalist-operated medical unit through the emergency department of Seoul National University Hospital. The analyzed clinical outcomes were the length of hospital stay, in-hospital mortality, unplanned intensive care unit admission, and unexpected readmission within 30 days. **Results:** The clinical outcomes did not differ between patients who took five or more drugs and those who did not. Patients with an ACB score of 3 or higher had a higher in-hospital mortality rate and longer hospital stay than those who did not. After adjusting for confounding factors, an ACB score of 3 or higher was an independent predictive factor for in-hospital mortality (odds ratio=3.09; 95% confidence interval, 1.18–8.06). **Conclusion:** ACB rather than the number of medications was associated with in-hospital mortality in acutely ill older patients. Further analytic and interventional studies are required to assess potentially inappropriate medication use and ACB in older inpatients.

Key Words: Geriatrics, Multimorbidity, Polypharmacy, Mortality, Length of stay

INTRODUCTION

With the increasing prevalence of chronic disease with aging, many older adults are treated concurrently for two or more diseases, a condition commonly referred to as a state of multimorbidity.[1,2] A recent report indicated that the prevalence of multimorbidity in Korea is up to 73%,[3] predominantly due to common diseases such as hypertension, osteoarthritis, and hyperlipidemia. Since medical management for these conditions requires medications for specific diseases, older adults with multimorbidity are likely to take multiple medications simultaneously. Consequently, polypharmacy, a geriatric condition defined as taking multiple medications (usually five or more per day) is a frequently encountered clinical condition in medical care for older adults.[4,5]

Medical care for older patients, especially those with polypharmacy, should consider factors such as prescribing cascade, drug-drug interactions, drug-disease interactions, and potentially inappropriate medications (PIMs) for older adults.[6-9] Among these factors, the presence of PIMs is reportedly associated with increased adverse outcomes, including delirium, falls, functional decline, and mortality. Therefore, guidelines have recommended to reduce the use of or to replace PIMs with safer alternatives.[8-10] Moreover, the concept of deprescribing, an individualized therapeutic strategy that considers the risks and benefits of medications according to patient functional and comorbid status, has emerged with efforts to minimize adverse outcomes with polypharmacy.[11]

PIMs include a wide range of medications with anticholinergic properties affecting the cognitive states of older patients.[8,12] Clinical evidence has shown associations between these medications and adverse cognitive outcomes,[13] backed by evident scientific knowledge of the importance of acetylcholine signaling in cognitive performance.[14,15] Accordingly, varying clinical measures to quantify anticholinergic cognitive burden (ACB) have been developed and validated.[13,16,17]

Older patients admitted through the emergency department in tertiary hospitals tend to have multimorbidity and polypharmacy, suggesting high exposure to anticholinergic medications in this population that may lead to adverse outcomes.[18,19] However, to our knowledge, no study has focused on ACB in acutely admitted older patients in Korea. Therefore, we assessed the clinical impact of ACB on clinical outcomes of older patients admitted via the emergency department of a single, hospitalist-operated medical unit of a tertiary hospital in Korea.

MATERIALS AND METHODS

Clinical Setting and Study Design

This retrospective study reviewed the electronic medical records at Seoul National University Hospital. We first searched for patients discharged from the hospitalist-operated medical unit at Seoul National University Hospital between February 2018 and October 2019. Among these patients, we included those 65 years of age and older admitted through the emergency department. To focus on acutely ill patients, we excluded patients admitted from the outpatient department and who were transferred from other wards, including the intensive care unit (ICU).

This study was carried out in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Seoul National University Hospital (No. H-1911-089-1079), which waived informed consent due to the retrospective nature of the study.

Measurement of ACB

Regular medications were assumed to be all the drugs regularly taken by each patient before hospitalization. We collected data on regular medications from each patient to check for polypharmacy and assessed the ACB by reviewing the patients' regular medications and those prescribed during hospitalization. Each patient's ACB score was calculated by summing the score according to the anticholinergic cognitive burden scale.[17]

Data Collections and Outcome Measures

Demographic data such as sex and age and data on medical history were collected to calculate the Charlson Comorbidity Index (CCI). To assess the condition severity at the time of admission, vital signs and laboratory test results were also collected. Length of stay (LOS), in-hospital mortality, unplanned ICU admission, and unexpected readmission within 30 days were analyzed as clinical outcomes.

Statistical Analysis

Data are expressed as mean ± standard deviation (SD) or numbers (percentage) unless stated otherwise. Chi-square or Fisher exact tests were used to compare categorical variables, while continuous variables were compared by Student t-tests. Univariate logistic regression was used to identify factors significantly influencing clinical outcomes. Multivariate logistic regression was performed with those factors to determine the independent predictive factors of ward mortality and delirium. Two-tailed p-values less than 0.05 were considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Baseline Characteristics and Clinical Outcomes in the Study Population

This study included 318 patients. Among them, the mean age was 74.9 ± 6.8 years and 205 patients (64.5%) were men. A total of 240 patients (75.5%) were taking five or more drugs and the mean ACB score was 3.1 points. The proportions of patients with hypertension, diabetes, and malignancy were 47.5%, 38.7%, and 71.1%, respectively. Multimorbidity, defined as the co-existence of two or more chronic illnesses, was present in 208 patients (65.4%) and mean the CCI was 7.5 ± 2.6 points. Regarding clinical outcomes, the in-hospital mortality and readmission rates within 30 days were 9.1% (29 patients) and 7.2% (23 patients), respectively. The mean LOS in the study population was 13.6 ± 10.3 days. Finally, 8 patients entered the ICU unexpectedly (Table 1).

Comparisons of Patients according to the Number of Concurrent Regular Medications

Patients taking five or more regular medications were categorized into the polypharmacy group. Age did not differ between the two groups. The proportion of men was higher in the polypharmacy group than that in the non-polypharmacy group (68.3 vs. 52.6%; p = 0.011). Mean ACB and CCI score were higher in the polypharmacy group than those in the non-polypharmacy group (3.2 ± 2.7 vs. 2.5 ± 2.1 and 7.7 ± 2.6 vs. 7.0 ± 2.[6,] respectively). More patients in the polypharmacy group had hypertension, diabetes, angina, and chronic kidney disease. Admission vital signs except for respi-

Table 1. Study population baseline characteristics and clinical outcomes (n=318)

Variable	Value
Age (y)	74.9 ± 6.8
Men	205 (64.5)
Polypharmacy[a)]	240 (75.5)
Non-polypharmacy	78 (24.5)
Number of regular medications	8.4 ± 5.0
ACB score	3.1 ± 2.5
CCI score	7.5 ± 2.6
Multimorbidity	208 (65.4)
Underlying illness	
Hypertension	151 (47.5)
Diabetes	123 (38.7)
Malignancy	226 (71.1)
Chronic lung disease	38 (11.9)
History of myocardial infarction	9 (2.8)
Heart failure	31 (9.7)
Angina	30 (9.4)
Asthma	13 (4.1)
Arthritis	30 (9.4)
Stroke	25 (7.9)
Chronic kidney disease	47 (14.8)
Vital signs upon admission	
Systolic blood pressure (mmHg)	126.0 ± 22.0
Diastolic blood pressure (mmHg)	73.2 ± 12.4
Pulse rate (per minute)	88.2 ± 16.6
Respiratory rate (per minute)	21.4 ± 3.2
Body temperature (°C)	36.9 ± 0.6
Initial laboratory results upon admission	
Hemoglobin (g/dL)	10.3 ± 2.3
Serum albumin (g/dL)	3.0 ± 0.6
Serum BUN (mg/dL)	26.3 ± 19.9
Serum creatinine (mg/dL)	1.3 ± 1.3
eGFR[b)] (mL/min/1.73 m^2)	75.1 ± 39.0
Serum sodium (mmol/L)	135.8 ± 9.7
Clinical outcomes	
Length of stay (day)	13.6 ± 10.3
In-hospital mortality	29 (9.1)
Readmission within 30 days	23 (7.2)
Unplanned ICU admission	8 (2.5)

Values are presented as mean±standard deviation or number (%).
ACB, anticholinergic cognitive burden; CCI, Charlson Comorbidity Index; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; ICU, intensive care unit.
[a)]Patients taking five or more concurrent regular medications.
[b)]Based on the original Modification of Diet in Renal Disease (MDRD) equation.

ratory rate were similar between groups. Serum creatinine level on admission was higher in the polypharmacy group, although blood urea nitrogen (BUN) level and estimated glomerular filtration rate (eGFR) did not significantly differ between the two groups. No significant differences in clinical outcomes were observed between the two groups for in-hospital mortality, readmission rate, mean LOS, and unexpected ICU admission (Table 2).

Comparisons of Patients according to ACB

High ACB, defined as an ACB score of 3 or higher, was observed in 156 patients (49.1%). Patients with high ACB scores were taking more concurrent regular medications than patients without high ACB scores (mean number of medications, 9.0 ± 5.0 vs. 7.8 ± 5.0; $p = 0.028$). Chronic kidney disease as an underlying illness was more common in patients with high ACB score. There were no differences in age, sex, CCI score, or admission vital signs between groups. Patients with high ACB score had lower serum albumin levels. Patients with an ACB score of 3 or higher also showed a higher in-hospital mortality rate (14.1 vs. 4.3%; $p = 0.002$) and longer hospital stays (mean LOS, 16.2 ± 11.6 vs. 11.2 ± 8.2 days; $p < 0.001$) than those who did not. No differences in the proportions of readmission within 30 days or unplanned ICU admissions were observed between groups (Table 3).

Anticholinergic Burden as an Independent Predictive Factor for In-hospital Mortality

Univariate regression analyses for all variables revealed factors such as CCI score, high ACB, admission pulse rate, and serum albumin and BUN level on admission to be associated with in-hospital mortality. Age, sex, or five or more regular medications did not predict in-hospital mortality. After adjusting for confounding factors, an ACB score of 3 or higher remained an independent predictive factor for in-hospital mortality (odds ratio [OR] = 3.09; 95% confidence interval [CI], 1.18–8.06). Moreover, one-point increment in CCI score (OR = 1.35; 95% CI, 1.12–1.63), one beat per minute increment in pulse rate (OR = 1.04; 95% CI, 1.01–1.07), and 1-g/dL increment in serum albumin level (OR = 0.36; 95% CI, 0.16–0.83) were also associated with in-hospital mortality (Table 4).

DISCUSSION

In this study, we found that older patients admitted via the emergency department had a high prevalence of polypharmacy and were also heavily exposed to medications with anticholinergic properties. Both univariate and multivariate analyses revealed that ACB and not polypharmacy, per se, was associated with in-hospital mortality. To our knowledge, this is the first study to report the association between ACB and in-hospital mortality in acutely ill patients in Korea.

Table 2. Comparisons of patients according to the numbers of concurrent regular medications

Variable	Polypharmacy[a] (n = 240)	Non-polypharmacy (n = 78)	p-value
Age (y)	75.0 ± 6.6	74.8 ± 7.3	0.798
Men	164 (68.3)	41 (52.6)	0.011
ACB score	3.2 ± 2.7	2.5 ± 2.1	0.037
CCI score	7.7 ± 2.6	7.0 ± 2.6	0.037
Underlying illness			
Hypertension	123 (51.3)	28 (35.9)	0.018
Diabetes	108 (45.0)	15 (19.2)	< 0.001
Malignancy	168 (70.0)	58 (74.4)	0.461
Chronic lung disease	31 (12.9)	7 (9.0)	0.351
History of myocardial infarction	9 (3.8)	0	0.119
Heart failure	27 (11.3)	4 (5.1)	0.129
Angina	30 (12.5)	0	0.001
Asthma	10 (4.2)	3 (3.8)	> 0.999
Arthritis	26 (10.8)	4 (5.1)	0.181
Stroke	21 (8.8)	4 (5.1)	0.467
Chronic kidney disease	43 (17.9)	4 (5.1)	0.005
Vital signs upon admission			
Systolic blood pressure (mmHg)	127.1 ± 22.7	122.7 ± 19.6	0.123
Diastolic blood pressure (mmHg)	73.5 ± 12.3	72.1 ± 12.8	0.380
Pulse rate (per minute)	88.6 ± 16.2	86.6 ± 17.8	0.358
Respiratory rate (per minute)	21.6 ± 3.5	20.8 ± 2.0	0.013
Body temperature (°C)	36.9 ± 0.6	36.9 ± 0.7	0.673
Initial laboratory results upon admission			
Hemoglobin (g/dL)	10.4 ± 2.3	10.3 ± 2.4	0.915
Serum albumin (g/dL)	3.0 ± 0.6	3.0 ± 0.6	0.909
Serum BUN (mg/dL)	27.6 ± 20.3	23.1 ± 18.7	0.107
Serum creatinine (mg/dL)	1.4 ± 1.4	1.1 ± 0.9	0.017
eGFR[b] (mL/min/1.73 m^2)	73.0 ± 40.3	81.5 ± 34.5	0.097
Serum sodium (mmol/L)	135.4 ± 10.7	137.3 ± 5.6	0.120
Clinical outcomes			
Length of stay (day)	13.5 ± 9.3	14.0 ± 13.0	0.734
In-hospital mortality	24 (10.0)	5 (6.4)	0.497
Readmission within 30 days	20 (8.3)	3 (3.8)	0.218
Unplanned ICU admission	8 (3.3)	0 (0)	0.207

Values are presented as mean±standard deviation or number (%).
ACB, anticholinergic cognitive burden; CCI, Charlson Comorbidity Index; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; ICU, intensive care unit.
[a]Patients taking five or more concurrent regular medications.
[b]Based on the original Modification of Diet in Renal Disease (MDRD) equation.

As the vast majority of commonly prescribed medications retain anticholinergic properties and also have biologic effects on cognitive performance, studies have evaluated the associations between anticholinergic exposure and clinical outcomes in older patients. Although long-term anticholinergic exposure and cognitive decline have been reported, controversies remain regarding the relevance of the short-term outcomes of ACB. Although a large-scale study showed an association between anticholinergic exposure and 2-year mortality,[20] studies on in-hospital mortality indicated no definite adverse effect of anticholinergic exposure.[21,22] In our study, ACB remained a significant predictor of mortality even after adjusting for comorbidity burden and polypharmacy.

Several possible mechanisms may explain the relationship between ACB and in-hospital mortality. Delirium, an important and

Table 3. Comparisons of patients according to ACB scores

Variable	High ACB[a)] (n = 156)	Low ACB (n = 162)	p-value
Age (y)	75.3 ± 6.4	74.5 ± 7.2	0.289
Men	108 (69.2)	97 (59.9)	0.081
Number of regular medications	9.0 ± 5.0	7.8 ± 5.0	0.028
CCI score	7.8 ± 2.6	7.3 ± 2.6	0.091
Underlying illness			
Hypertension	74 (47.4)	77 (47.5)	0.986
Diabetes	63 (40.4)	60 (37.0)	0.540
Malignancy	109 (69.9)	117 (72.2)	0.644
Chronic lung disease	17 (10.9)	21 (13.0)	0.570
History of myocardial infarction	5 (3.2)	4 (2.5)	0.746
Heart failure	20 (12.8)	11 (6.8)	0.070
Angina	16 (10.3)	14 (8.6)	0.622
Asthma	6 (3.8)	7 (4.3)	0.831
Arthritis	13 (8.3)	17 (10.5)	0.510
Stroke	15 (9.6)	10 (6.2)	0.254
Chronic kidney disease	31 (19.9)	16 (9.9)	0.012
Vital signs upon admission			
Systolic blood pressure (mmHg)	126.0 ± 21.8	126.0 ± 22.3	0.982
Diastolic blood pressure (mmHg)	72.5 ± 12.1	73.8 ± 12.8	0.350
Pulse rate (per minute)	87.6 ± 15.8	88.6 ± 17.3	0.590
Respiratory rate (per minute)	21.6 ± 3.8	21.3 ± 2.4	0.364
Body temperature (°C)	36.9 ± 0.6	36.9 ± 0.6	0.574
Initial laboratory results upon admission			
Hemoglobin (g/dL)	10.1 ± 2.2	10.6 ± 2.4	0.084
Serum albumin (g/dL)	2.9 ± 0.6	3.1 ± 0.6	0.001
Serum BUN (mg/dL)	27.6 ± 21.7	25.0 ± 18.0	0.252
Serum creatinine (mg/dL)	1.4 ± 1.3	1.3 ± 1.3	0.532
eGFR[b)] (mL/min/1.73 m^2)	74.8 ± 43.4	75.4 ± 34.4	0.900
Serum sodium (mmol/L)	135.5 ± 12.1	136.1 ± 6.7	0.581
Clinical outcomes			
Length of stay (day)	16.2 ± 11.6	11.2 ± 8.2	< 0.001
In-hospital mortality	22 (14.1)	7 (4.3)	0.002
Readmission within 30 days	14 (9.0)	9 (5.6)	0.239
Unplanned ICU admission	4 (2.6)	4 (2.5)	> 0.999

Values are presented as mean±standard deviation or number (%).
ACB, anticholinergic cognitive burden; CCI, Charlson Comorbidity Index; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; ICU, intensive care unit.
[a)]Patients with an ACB score of 3 or higher.
[b)]Based on the original Modification of Diet in Renal Disease (MDRD) equation.

Table 4. Predictive factors of in-hospital mortality

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Age (1-year increment)	1.03	0.98–1.09	0.275	1.03	0.97–1.10	0.373
Men	1.82	0.75–4.40	0.184	0.83	0.31–2.25	0.717
Five or more regular medications	1.62	0.60–4.41	0.343	1.17	0.38–3.56	0.788
ACB score of 3 or higher	3.64	1.51–8.78	0.004	3.09	1.18–8.06	0.021
CCI (1-point increment)	1.38	1.17–1.62	< 0.001	1.35	1.12–1.63	0.001
Pulse rate (increment by 1 bpm)	1.03	1.01–1.06	0.006	1.04	1.01–1.07	0.006
Serum albumin (1-g/dL increment)	0.24	0.11–0.51	< 0.001	0.36	0.16–0.83	0.018
BUN (1-mg/dL increment)	1.02	1.00–1.03	0.037	1.01	1.00–1.03	0.118

ACB, anticholinergic cognitive burden; CCI, Charlson Comorbidity Index; bpm, beats per minute; BUN, blood urea nitrogen; OR, odds ratio; CI, confidence interval.

preventable geriatric condition in hospitalized older adults, might be a mediator, as shown in studies on anticholinergic exposure, delirium, and mortality. For instance, a study from an acute care hospital in Canada reported delirium severity to be associated with a clinical-rated anticholinergic score.[23] Another study from the United States including patients receiving palliative care showed a similar association between anticholinergic exposure according to an anticholinergic risk scale and delirium incidence.[24] Both short-term and long-term time associations between delirium and mortality risk have been demonstrated.[25,26] Unfortunately, as a retrospective study, we did not include delirium as a study variable because medical record review may fail to capture hypoactive delirium, which is reportedly worse in terms of clinical outcome.

The population in the present study had a relatively higher prevalence of polypharmacy with substantial ACB compared to those in previous studies in other countries on older acute patients.[22,27,28] There may be several explanations for this difference. Firstly, the study population in the present study was inpatients admitted to an acute unit of a top-tier hospital in Korea, with a predictably high comorbidity burden. Secondly, the concepts of anticholinergic medications and PIMs are relatively unrecognized in Korea. Although Korea is experiencing an extreme pace of population aging, the concept of geriatric medicine is rarely taught in medical schools.[29] Thirdly, specialized or fragmented care for older multimorbid patients might contribute to the occurrence of prescribing cascades that often involve PIMs.[30] While our retrospective, descriptive study cannot address the contributions of these factors that may affect PIM and ACB in older patients with multimorbidities, our findings underscore the need for further research on the current nationwide status of medication usage in older adults.

As a retrospective observation performed by medical record review, our study has several limitations. Since our observations were based on the medical records of patients admitted to a single, hospitalist-run medical unit in a tertiary hospital, the characteristics of the patients in our study are not generalizable to the older population nationwide in Korea. Furthermore, our study lacks important geriatric baseline parameters including frailty, cognitive function, and daily functioning, and relevant outcome variables of ACB such as delirium and falls. Similarly, the functional outcomes of patients after discharge were unavailable in this study. Based on the results of this hypothesis-generating study, our upcoming prospective study with an interventional arm deprescribing PIMs and minimizing anticholinergic burden will provide better answers on the mediating mechanisms between ACB and clinical adverse outcomes.

In conclusion, ACB but not polypharmacy was associated with in-hospital mortality in acutely ill older patients. We hope that the results of this study lead to further analytic and interventional studies on PIMs and ACB in older inpatients.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

AUTHOR CONTRIBUTIONS

Conceptualization, HWJ; Data curation, SM, SL, SJH; Investigation JHL, HWJ, IYJ; Methodology. JHL, HWJ, IYJ, SJH; Project administration, HWJ; Supervision, SJH; Writing-original draft, JHL, HWJ; Writing, review & Editing, SJH.

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Development of Health-RESPECT: An Integrated Service Model for Older Long-Term Care Hospital/Nursing Home Patients Using Information and Communication Technology

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Background: Korea, as one of the fastest-aging countries worldwide, requires an improved healthcare service model for older adults. We evaluated the current healthcare system and developed a service model based on information and communication technologies (ICT) for use in older patients in long-term care facilities (LTCF). **Methods:** We conducted a qualitative literature review, focus group interviews (FGIs), and structured survey to identify the current technology use and status of healthcare systems. We then developed a web-based platform with necessary, high-priority, and usable content for the care of older patients in LTCF. **Results:** We reviewed 60 (23 hypertension, 18 diabetes, and 19 heart failure) articles on iinformation and communication technologies (ICT)-based disease management for clinical effectiveness and improved patient satisfaction. FGIs and structured surveys were used to evaluate the inconvenience in patient and medical information transfer between hospitals and cost and time required for its process. Accordingly, we confirmed the unmet need for an ICT-based service model for management, monitoring, and consultation among older patients and developed the Health-RESPECT (integrated caRE Systems for elderly PatiEnts using iCT), a service platform for older patients residing in LTCF. The medical information exchange system was used to transfer medical information. Health-RESPECT includes an established algorithm for evidence-based comprehensive geriatric assessment and customized management; chronic disease management; management of potentially inappropriate medications; rehabilitation; and consultation and videoconferencing. **Conclusion:** This study identified the current status and unmet needs of healthcare systems for older adults. We developed an ICT-based system to manage older institutionalized patients. However, the Health-RESPECT service model requires further validation.

Key Words: Frailty, Care model, Digital medicine, ICT

INTRODUCTION

A "baby boomers" grow older Korea, is one of the fast-aging countries worldwide. In just 17 years, the aging population has doubled from 7% (an aging society) in 2000 to 14% (an aged society) in 2017 and is expected to grow to 20% (a post-aged society) by 2026.[1] Older individuals tend to have multiple chronic conditions, poor self-reported health status, and functional dependencies. As a result, older patients are institutionalized in long-term care hospitals (LTCH) or nursing homes (NH).[2,3] Thus, the costs of medical care for older adults is expected to increase exponentially, giving rise to the need for alternative, sustainable health and medical systems. However, fragmented medical services in Korea lead to challenges in providing integrated medical services to this population.

The management and care of older adults is a challenge because of their complicated multi-morbidities and variations in their functional, cognitive, and socio-economic statuses.[3] In Korea, due to the increase in the number of single-person households and the social activities of women, family support in the care of older adults is decreasing. Consequently, older adults are eventually admitted to LTCH or NH that provide both medical and care support. Particularly in Japan, where the proportion of the aging population is over 27%, long-term care costs have increased more rapidly than medical costs, especially among older adults living alone.[4] Thus, we need to respond to the growing demand and expanding costs of healthcare, comprising medical and long-term care costs, in older adults.

To offer sustainable healthcare systems to support active and healthy aging, Europe has developed and validated the Inclusive Introduction of Integrated Care (IN3CA) project as part of the eHealth Action Plan. The project is slated to run from 2012 until 2020 and uses information and communication technologies (ICT) to enable better and more efficient health care at a lower cost and with better continuity of care. The project showed that integrated care with joint care planning, shared clinical records, decision support tools, and care coordination through the use of ICT benefited patient experience, use of services, and costs.[5]

There is great potential for ICT service platforms to address present and future healthcare and long-term care management of older people.[6] ICT can positively affect both intergenerational and partner care by decreasing usability barriers and promoting attractive and collaborative environments for informal care. ICT platforms and communication channels also allow us to avoid duplication of efforts when dealing with patient diagnostic, therapeutic, rehabilitation, or monitoring and support needs.

Thus, in this study, we performed a qualitative literature review, focus group interviews (FGIs), and structured surveys to identify technologies and platforms useful for the management of older patients globally and the current healthcare systems for older patients in Korea. We then developed the Health-RESPECT (integrated caRE Systems for elderly PatiEnts using iCT) platform that focuses on the provision of care, support, and expert consultation to older adults admitted to LTCH or NH and requiring integrated care because of their multiple chronic diseases and functional decline.

MATERIALS AND METHODS

To develop the Health-RESPECT service model, we first conducted a qualitative literature review of existing ICT technologies or service models for the management of older adults and related research. Because research on ICT-based consultation or inter-professional relationships for chronic disease management is not sufficient, we included all types of research ranging from randomized controlled studies to observational studies. Under chronic diseases, we included diabetes and hypertension, which are the most prevalent diseases in older adults, and heart failure, which can be the most difficult to manage in long-term care facilities. The PubMed database was searched for relevant articles in English published in the last 10 years prior to the date of the search. The search strategies are shown in Supplementary Table S1.

We next conducted FGIs of medical staff, patients, and their family members. The interview focused on (1) difficulty in the management or care of older patients, (2) the current status of cooperative management between institutions, (3) the unmet needs for ICT-based integrated service models, (4) the specific content to be provided by ICT-based services, and (5) the requirements for the activation of ICT-based services.

On the basis of the results of FGIs, on- and off-line structured questionnaire surveys were designed and administered to measure quantified data from additional participants. The questions were organized to objectively describe the contents discussed in the FGI. The structured survey evaluated (1) the current status of cooperative management for older adults between institutions, (2) the current status and expected improvements in the use of comprehensive geriatric assessments (CGAs), and (3) comments on an ICT-based interdisciplinary service model for older adults. Because their major interests differed, medical staff (physicians/nurses) and patients/family members/caregivers were surveyed using different questions, and the data were analyzed separately.

On the basis of these findings, we developed the evidence-based Health-RESPECT, which included (1) CGA and customized management strategies, (2) a chronic disease management service including a decision support system, (3) a service to manage potentially inappropriate medications, (4) a tailored rehabilitation

service, and (5) a consultation and videoconference service.

The study protocol was reviewed and approved by the Seoul National University Bundang Hospital Institutional Review Board (No. B-1908/556-304).

RESULTS

Qualitative Literature Review

To identify recent technology trends, platform development cases, and usability and effects of ICT-based chronic disease management in older adults, we reviewed a total of 60 articles (23 on hypertension, 18 on diabetes, and 19 on heart failure) indexed in the PubMed database. The rapid increase in research on the management of chronic diseases through ICT since 2009 has been attributed to technology development. The consultation systems mainly used web or mobile-based online platforms or single-application technologies. In most studies, both patients and medical staff participated. For hypertension and diabetes, ICT-based chronic disease management led to significant reductions in blood pressure or blood sugar levels.[7-10] In the case of heart failure, faster communication between patients and medical staff improved patient satisfaction and reduce hospitalized costs.[11-13] However, little research has been conducted on a consultation service model between the medical staff of different institutions (Supplementary Table S2, Fig. S1).

Focus Group Interviews

Between June 4 and 28, 2018, FGIs were conducted with 6 medical staff (2 acute care hospital physicians, 2 long-term care hospital physicians, 1 acute care hospital nurse, and 1 long-term care hospital nurse), 1 patient, 2 family members, and a hired caregiver. Most of the interviewees indicated that inter-institutional consultation is not well-established in Korea; however, due to complex multi-morbidities among older patients, there is a strong need for coordinated management between institutions. In addition, due to the absence of common geriatric evaluation tools, communication regarding functional status is impossible between institutions. Therefore, these FGIs underscored the importance of a common format for the comprehensive assessment of multi-morbidity, medication, nutrition, and functional status for efficient information sharing. In addition, the participants indicated that an online consultation system would be helpful for the management of duplicate drugs and chronic diseases. To activate the ICT-based, inter-professional consultation system, the physicians indicated the need for reimbursement for the invisible resource input provided by personnel. Meanwhile, patients or family members indicated that they would be willing to pay for an ICT-based consultation system that substituted for regular outpatient care without having to visit a university hospital or large center. They also expressed hope that the sharing of medical information between institutions would be more convenient with the ICT-based system.

Structured Survey

The FGI revealed the difficulties in evaluating and managing older patients while the qualitative literature review identified the usefulness of ICT-based management or consultation services in older patients. To collect and request more specific opinions and components to be included in the ICT-based management and consultation service system, we conducted an on- and off-line structured survey from August 16 to September 30, 2018, of 114 medical staff and 50 patients/family members/caregivers. Among the 114 medical staff (53% male) who participated in the structured survey, 80% were physicians and 20% were nurses; 45% belonged to tertiary hospitals and the others to LTCH and NH. Most medical staff (94%) had over 1 year of experience in managing older adults. Among the 50 patients/family members/caregivers respondents, 76% were family members, 18% were hired caregivers, and 6% were patients.

The most difficult factors in the management or care of older patients were complex multi-morbidity (4.1/5 points), absence of assessment tools and reimbursement systems for older patients (4.04/5), management of duplicate medications (3.96/5), lack of information about previous medical records (3.93/5), and lack of information about patient's pre-morbid function (3.90/5) (Fig. 1). The most common information transferred at the time of referral to other institutions was medical certificates and prescription and medical records; laboratory results or imaging files were relatively lower in necessity. The respondents most frequently reported using paper (86.8%) to transfer medical information but reported being dissatisfied (2.6/5) with the amount, quality, and methodology. Medication and chronic disease management were among the services expected to be provided by the ICT-based management service. Among chronic diseases, the demand for management services was high in the order of diabetes, hypertension, and heart failure. In addition, as a management method, consultation on acute exacerbation, provision of the latest guidelines, and cumulative inquiry of results were preferred. However, the participants also expressed concerns about the lack of an adequate reimbursement system (4.33/5) and leakage of private or medical information (3.61/5). The types of rehabilitation services that most needed to be provided in the ICT-based service were swallowing, physical function, and cognitive rehabilitation.

Patients visited an average of 1.55 hospitals and met 2.66 physicians, with 42% having a history of transfer. The average travel time

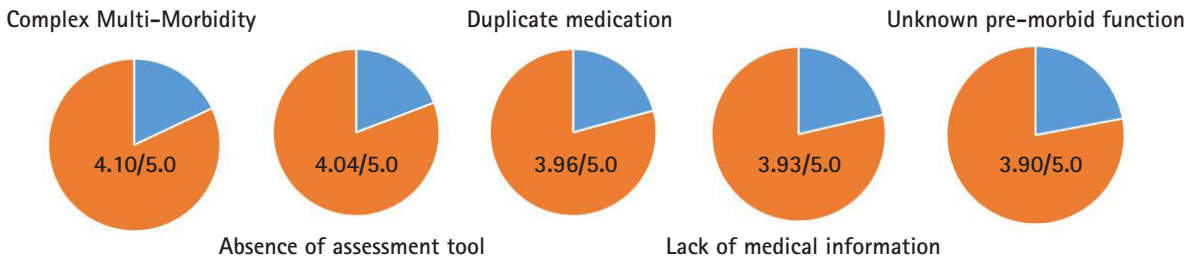

Fig. 1. Major difficulties in the management and care of older adults. The difficulties in the management or care of older patients included complex multi-morbidity (4.1/5 points), absence of assessment tools and reimbursement systems for older patients (4.04/5), duplicate medication management (3.96/5), lack of information about previous medical records (3.93/5), and lack of information about patients' pre-morbid function (3.90/5).

for outpatient/emergency visits was 1.72 hours, with an average cost of $41.22 per person. Depending on the patient's place of care, the greatest cost and time was required for the transfer of older patients living in NH or LTCH. We observed a positive response that the sharing of medical records through the ICT-based service would be helpful for treatment (4.16/5), prevention of duplicate prescription or drug abuse (4.26/5), increased convenience of delivering medical information (4.14/5), and money and time saving (3.92/5). Similar to the medical staff survey results, there were also concerns about the leakage of private or medical information (3.42/5). Regarding their willingness to pay for the ICT-based management and consultation system, we received above-average positive answers (3.50/5) from patients, family members, and caregivers.

Development of the Health-RESPECT

The ICT-based management and consultation service model was developed to provide proper high-priority services for the medical staff of LTCH or NH. The detailed contents of the service model were identified through a literature review, FGIs, and structured surveys (Fig. 2).

Since the healthcare workers in LTCH in Korea assess patient general function, comorbidity status, and cognitive status monthly to claim specified daily fees for care service, we developed CGA based on these data. The medical information exchange system is used to transfer information on prescribed medications, diagnoses, laboratory data, and vital signs from the electronic medical records (EMRs) of LTCH to the service platform. The CGA integrates (1) existing medical information received from EMRs of LTCH and (2) additional evaluated data required for disease management or rehabilitation services. A CGA encompassing the 6 domains of comorbidity, physical function, swallowing function, cognitive function, activities of living, and medication was developed to be administered to patients when they are initially included in the Health-RESPECT service platform. Physical function is evaluated by activities of daily living (ADLs) and instrumental ADLs (IADLs) with modified Barthel Index and Lawton and Brody Index.[14,15] Cognitive, swallowing, and physical functions are evaluated using the Korean version of the Mini-Mental State Examination (K-MMSE), the Standardized Swallowing Assessment (SSA), and the Functional Ambulatory Category (FAC), respectively.[16-18] Different versions of the MMSE (MMSE-K) used in long-term care facilities are substituted as needed. We used a validated self-report frailty questionnaire, based on the Korean version of the fatigue, re-

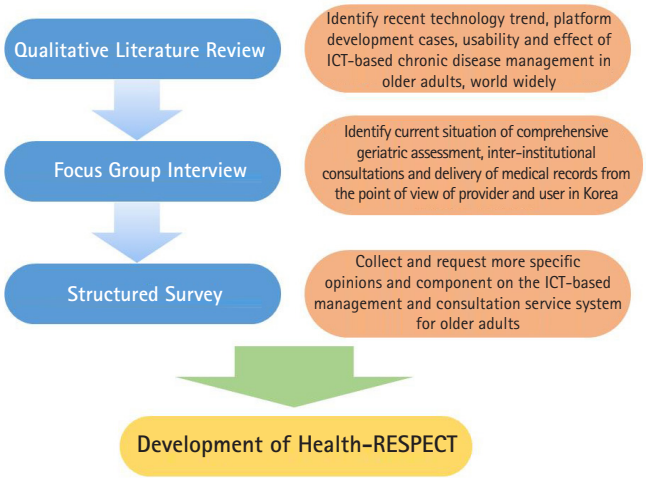

Fig. 2. Health-RESPECT development process. Qualitative literature review, focus group interview, and structured survey, as well as recent technology trends, inter-institutional consultations, and medical record delivery system identified the need for an information and communication technologies (ICT)-based system to manage older patients. The Health-RESPECT (integrated caRE Systems for elderly PatiEnts using iCT) was developed to reflect the requirements gathered in this process.

sistance, ambulation, illnesses, and loss of weight scale (K-FRAIL).[19] On the basis of Beers criteria, 2016 SNUBH Inappropriate Medication for Elderly Criteria, and guidelines for chronic diseases, a list of drugs inappropriate for older adults was developed to fit for their clinical significance and frequencies of clinical use in NH and LTCH.[20-24]

On the basis of the results of the CGA, we also developed an individualized challenge list and treatment targets that included chronic disease management (hypertension, diabetes, and heart failure), drug management, and rehabilitation (cognitive, swallowing, and physical functions). The drug management service was developed by screening the medication currently prescribed and providing the number and identity of drugs matching those on the absolute or potentially inappropriate drug lists each month.

The treatment targets for chronic diseases were set according to the patient frailty status (Table 1). A chronic disease management service was developed to provide information about recommended and non-recommended combinations of medications, screening, responses to adverse events during treatment (orthostatic hypotension, hypoglycemia), drug adjustment according to renal function, comorbidity screening and management (diabetes-dyslipidemia), guidance for acute decompensated conditions, and lifestyle modifications based on recent guidelines.[21-23]

In the rehabilitation service, video clips of exercise and swallowing rehabilitation of various levels are provided once weekly according to patients' physical and swallowing function, as evaluated by FAC or SSA. For example, patients who were non-functional ambulatory or ambulatory dependent on physical assistance (FAC 0–1) are provided with videos of pressure sore prevention or sitting exercises through correct posture while patients who could ambulate independently are provided with videos of more intensive exercise. The cognitive rehabilitation program was developed for increasingly difficult orientation, attention, memory and problem-solving training in which patients with MMSE scores of 10 or more and 21 or less participated three times weekly.

The Health-RESPECT service has a system for issuing warning alarms by message and written consultation service between institutions for vital or laboratory findings outside of the normal ranges or if the medical staff wish to do. Additionally, videoconferencing with acute care hospitals allowed regular management of patients living in LTCH or NH and participating in the Health-RESPECT service model (Fig. 3). Although the medical staff of long-term care facilities are responsible for primary decision-making, patients who may require changes in their assessment or prescription plans can be discussed bi-directionally through alarm messages, written consultations as needed or monthly video-conferencing.

To determine the expected clinical feasibility and usability of the various functions and tools included in the Health-RESPECT platform, we collected expert opinions from prospective users (medical staff from acute care hospital or long-term care facilities), who provided positive feedback, especially for the chronic disease and drug management tools. Additional corrections were made to the parts shown in these evaluations to be too complex or unusable.

Table 1. Treatment targets for hypertension and diabetes according to frailty status

	Robust	Pre-frail	Frail
Blood pressure (mmHg)	140/90	140/90	150/90
Glycated hemoglobin (HbA1c) (%)	< 7.5	< 8.0	< 8.5
Random glucose level (mg/dL)	≤ 190	≤ 210	≤ 230

Frailty status was evaluated using the Korean version of the Fatigue, Resistance, Ambulation, Illnesses, and Loss of Weight index (K-FRAIL). Scores of 3 and more, 1 to 2, and 0 were classified as frail, pre-frail, and robust, respectively.

DISCUSSION

This study identified the current status of the management or care for older patients in Korea through focus group interviews and a structured survey. In addition, we confirmed the necessity of an ICT-based platform for the exchange of medical information between institutions and for the treatment and care for older patients. The qualitative literature review identified that chronic disease management using ICT was also effective and efficient in older adults, leading to the development of the Health-RESPECT system with items and content suitable for older patients in Korea.

In Japan and Europe, where society aging has progressed further, government-supported policies and services actively use ICT to manage older populations in advance.[25,26] The use of ICT has allowed the development of service models and tools to support independent living, healthcare management through disease monitoring, fall detection, and emergency communication. For example, the DOREMI (Decrease of cOgnitive decline, malnutRition and sedEntariness by elderly empowerment in lifestyle Management and social Inclusion) project (Italy, 2013–2016) was developed to provide preventive strategies for senior citizens related to frailty, unhealthy nutrition, sedentariness, and cognitive decline.[27] The basis of the DOREMI environment is a context-aware and smart system able to learn and reason about older people, including their intentions, preferences, and purposes. Besides providing interventions, recording and monitoring information about the use of the system allows tracking of user performance over long periods, providing a potential alert to signs of malnutrition and physical and cognitive deterioration.

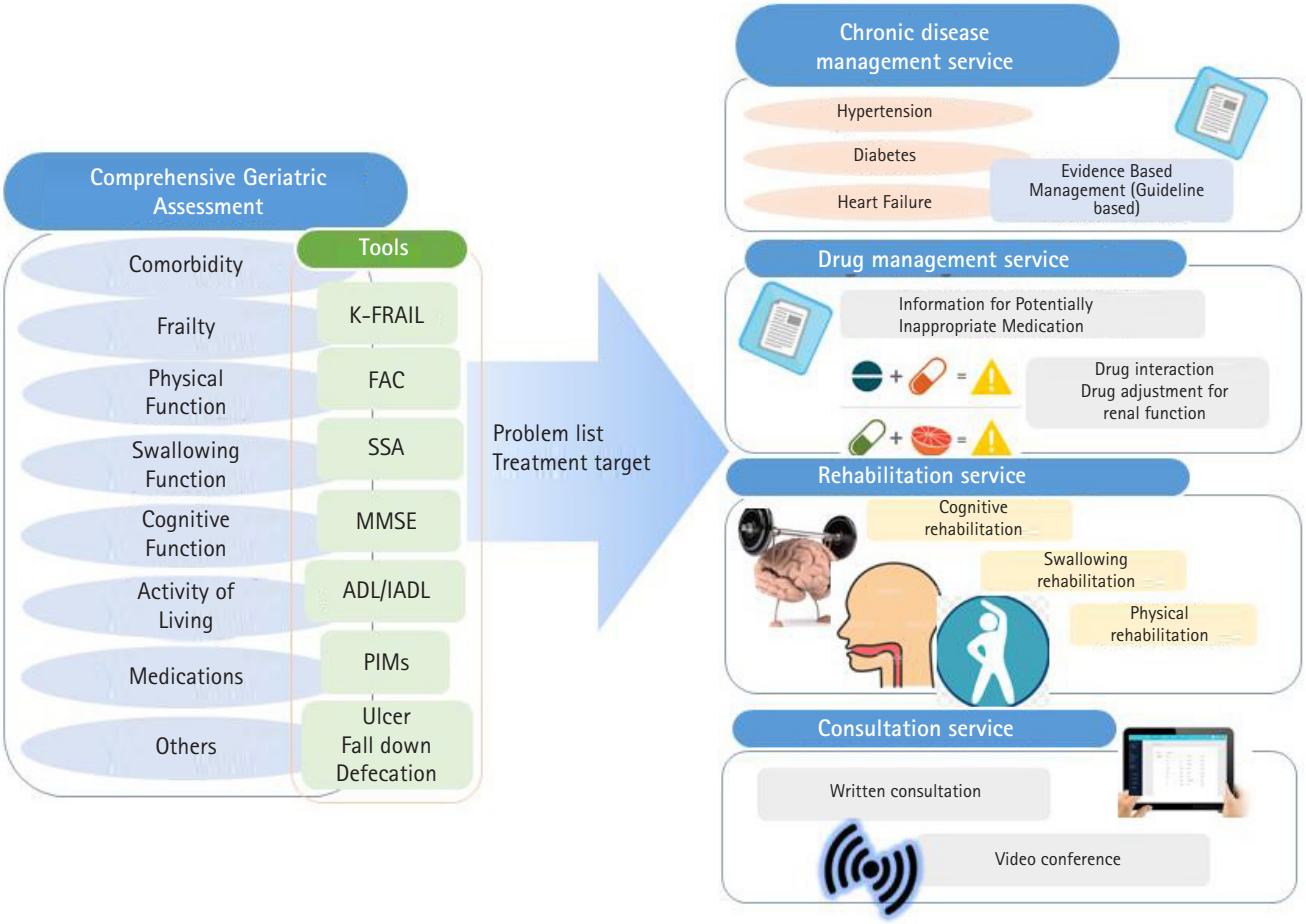

Fig. 3. Components of the Health-RESPECT program. We developed the Health-RESPECT (integrated caRE Systems for elderly PatiEnts using icT) system to provide tools for comprehensive geriatric assessment (CGA), individualized treatment strategies, chronic disease management, drug management, and rehabilitation programs. Systems for written consultation or videoconference allow for the management of acute exacerbation, aggravation, and patient transfer. K-FRAIL, Korean version of the fatigue, resistance, ambulation, illnesses, and loss of weight scale; FAC, Functional Ambulatory Category; SSA, Standardized Swallowing Assessment; MMSE, Mini-Mental State Examination; ADL, activities of daily living; IADL, instrumental activities of daily living; PIMs, potential inappropriate medications.

In Korea, many difficulties exist in the development and implementation of projects and the establishment of services to manage and care for older patients based on ICT. First, telemedicine, in which patients and doctors are not face-to-face, is legally prohibited in Korea. Therefore, we developed a usable ICT-based service platform for the management of older patients used by medical staff in LTCH and NH. The Health-RESPECT monitors for adverse events through an established algorithm and shared decisions can be made with distant professionals through consultation and videoconferencing. However, the system may also have a disadvantage in that additional effort and time may be required to use the new platform in addition to routine care. Approximately 30 minutes is required to perform CGA in new patients. Because of the nature of long-term care facilities, the patients have been hospitalized or institutionalized for long periods and the nurses in charge have a good understanding of the patients' medical or functional condition. Moreover, medical staff are familiar with the test tools (MMSE or ADL) because these tests are periodically performed for reimbursement purposes. A pilot study determined that CGAs required an average of approximately 10 minutes to evaluate one patient. However, it would be hard to maintain this process without additional reimbursement. Therefore, we propose a pilot clinical study to determine appropriate reimbursement through evaluations of the clinical effectiveness and perform an economic analysis.

There is a growing need to support the development of diversified service models and systems using new technology to effectively treat and manage older patients and to help them lead independent lives in the community as members of society.[28] In this sense, this study is meaningful as it used ICT technology to develop a system to manage older patients living in LTCH and NH. Howev-

er, as with most newly developed service models, the Health-RESPECT system requires validation through well-organized studies to provide evidence of its clinical effectiveness, utility, cost-effectiveness, safety, and the willingness of service users to pay.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization: JYC, KIK, JYK, JIK, HK ML, SKJ, DHL, JL, YIJ; Data curation, CJY; Funding acquisition, KIK; Investigation, JYC, JYK, HK, ML, SKJ, YIJ, IHO; Methodology, JYC, JYK, YIJ; Project administration, JYC; Supervision, KIK, HK, JYK; Writing original draft, CJY, YIJ; Writing, review & editing, KIK, HK.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.20.0006

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Adaptation of the Lawton Instrumental Activities of Daily Living Scale to Turkish: Validity and Reliability Study

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Background: The Lawton Instrumental Activities of Daily Living (IADL) scale is the most widely used scale for the assessment of IADL in the elderly population. The aim of this study was to adapt the Lawton IADL Scale in Turkish and to investigate the validity and the reliability of the scale in older adults. **Methods:** A total of 80 participants with a mean age of 71.6±5.8 years were included in the study. The independent living skills of the older adults were measured using Lawton IADL, Hodkinson Mental Test, Functional Independence Scale, Barthel Index, Katz Index, and visual analog scale. Lawton IADL was translated into Turkish, validated by professional reviewers, translated back into English, and then tested. Cronbach's alpha was used to measure reliability in a group of 34 participants and test-retest was performed 1 week after the first test. Pearson correlation analysis was used to show the relationship between Lawton IADL and other scales and indexes. **Results:** Internal consistency (Cronbach's alpha) value was 0.843 for the whole scale. The intraclass correlation coefficient value of the scale was 0.915. **Conclusion:** These results confirm that the Turkish version of the Lawton IADL scale has excellent reliability and validity.

Key Words: Rehabilitation, Geriatric assessment, Activities of daily living

INTRODUCTION

Functional capacity is a complex concept that includes basic activities of daily living (BADL), instrumental activities of daily living (IADL),[1] and advanced activities.[2] Since inadequacies in BADL affect daily activities, work performance, and leisure activities, BADL is one of the most important indicators of success to define the skill level, demonstrate the effectiveness of rehabilitation, and determine a person's ability to perform activities of daily living.[3,4] The BADL may decline due to age, a specific disease, or a variety of factors such as decreased muscle strength, muscle atrophy, degenerative changes in joints, impaired neuromuscular coordination, loss of vision, and postural changes.[5]

BADL represent the activities necessary for self-care (e.g., bathing, dressing, feeding, etc.) while IADL represent the activities that allow independence in social life.[6,7] In addition to some BADL, IADL also include outside activities such as shopping. Inadequacies in fulfilling IADL cause disability by decreasing the functional capacity of older adults. In 1969, Lawton and Brody[8] developed the Lawton Instrumental Activities of Daily Living Scale (Lawton-IADL) to measure disability levels and assess parameters in community-dwelling older adults. This scale comprises eight items, including the ability to use a telephone, shopping, food preparation, housekeeping, laundry, use of public transportation, managing self-medication, and handling finances. Responses to each of the eight items on the scale are scored as 0 (cannot perform or can partially perform) or 1 (can perform). The total score ranges from 0 (low-functioning, dependent) to 8 (high-functioning, independent). There are Spanish,[2] Hong Kong Chinese,[9] Korean,[10] and Persian[11] versions of the scale.

The Lawton-IADL is the most widely used scale for IADL assessment in older adults. The present study aimed to adapt the

Lawton-IADL developed by Lawton and Brody[8] to Turkish and investigate the validity and reliability of the scale in older adults.

MATERIALS AND METHODS

The study was approved by the Gazi University Ethics Committee (No. E.128338). Informed consent forms were obtained from all volunteers who participated in the study. Required permissions for the translation of Lawton-IADL to Turkish and its use were obtained via e-mail from Oxford University Press, Permissions, and Rights (Oxford University Press, Oxford, UK).

Study Group

The cognitive status of the older adults were assessed by the Hodkinson Mental Test (HMT). The study included 87 older Turkish volunteers aged ≥65 years (71.6±5.8 years) with HMT scores of ≥8 and without any visual or hearing impairments or mental illnesses (major depression, schizophrenia, psychosis, etc.). Individuals who had previously had a transient ischemic attack or stroke or had undergone orthopedic surgery in the last 2 years were excluded from the study. Since 5 of the 87 participants had HMT scores of ≤7 and two left the study willingly, the study finally included 80 volunteers—48 men (60%) and 32 women (40%). These participants resided in either Fethiye nursing home (Mugla, Turkey) or had applied to the Department of Physiotherapy and Rehabilitation at Gazi University Faculty of Health Sciences (Ankara, Turkey).

Assessment Criteria

Sociodemographic characteristics such as age, sex, weight, and height were recorded. The HMT, Functional Independence Scale (FIS), Barthel Index (BI), Katz Index of Activities of Daily Living, and visual analog scale (VAS) scores were used to evaluate patient status.

Hodkinson Mental Test

The HMT is a standardized test used for the assessment of cognitive functions that comprises 10 questions. It contains simple questions such as the date and patient name and address. The minimum score is 0 and the maximum score is 10.[12]

Functional Independence Scale

The FIS comprises motor scores including those for self-care, sphincter control, transfers, and mobility skills as well as cognitive scores including those for communication and social perception skills. The total score varies from 18 to 126. Higher scores indicate a higher level of independence.[13] The scale was adapted to Turkish in 2001 by Kucukdeveci et al.[14]

Barthel Index

The BI is used to determine the independence level of an individual in carrying out activities such as feeding, bathing, self-care, dressing, defecation and urine control, going to the toilet, passing from bed to wheelchair, using a wheelchair/walking, and climbing stairs. The index was developed by Mahoney and Barthel[15] and consists of 10 items with a total score ranging from 0 to 100. An increasing total score indicates increasing levels of independence. The Turkish version of the index was developed by Kucukdeveci et al.[16]

Katz Index of Activities of Daily Living

The Katz index, developed in 1963 by Katz et al.,[17] evaluates the activities that provide the basic requirements necessary for living. The Katz Index consists of 6 questions including information about bathing, dressing, using the toilet, mobility, excretion, and feeding activities. The Katz Index was adapted to Turkish by Arik et al.[18]

Visual analog scale

The VAS allows researchers to measure values that cannot be directly quantified. The VAS appears as a straight horizontal line with a fixed length, usually 100 mm, with the ends defined as the extremes of the parameter to be measured, orientated from the left (lowest) to the right (highest). The patient is asked to determine a point on the line for which the relevant situation makes sense for him/her. The length of the distance from where the relevant situation never takes place to the point that the patient has marked provides a numerical value.[19] In our study, the "ability to use a telephone" and "responsibility for taking their own medication" were assessed using the VAS.

Adaptation of the Lawton-IADL to Turkish

We used the proposals of Guillemin et al.[20] and Beaton et al.[21] for translation of the Lawton-IADL into Turkish and while investigating its validity and reliability. The English version of the Lawton-IADL was translated into Turkish by two independent groups, and the two versions were analyzed by an expert committee. The translations were evaluated considering Turkish cultural characteristics. A common version was then created by combining these translations. The created Turkish version was translated back into English by two native English speakers who were also fluent in Turkish. These two back translations were then combined and the English-translated version and original Lawton-IADL were compared by the committee. A pilot study was conducted with 30 vol-

unteers (15 men and 15 women) who met the inclusion-exclusion criteria to determine whether the questions were easily comprehensible. Then, the committee either confirmed the equivalence of the original Lawton-IADL and the Turkish version or made changes if necessary. Based on the findings, the scale was reviewed by the expert committee and minor changes were made. After being finalized, the Turkish version of Lawton-IADL was applied to the relevant population.

Statistical Analysis

All statistical analyses of this study were performed using SPSS version 22 for Windows (IBM, Armonk, NY, USA). The values of the analyses were expressed as mean ± standard deviation. The reliability of the Lawton-IADL was assessed using internal consistency and test-retest methods. Internal consistency was determined by Cronbach's alpha, while test-retest reliability was determined by calculating the intraclass correlation coefficient (ICC). Cronbach's alpha values of ≥0.70 and ICC values of ≥0.80 were considered significant.[22] Construct validity was assessed by conjoint analysis. Pearson correlation analysis was performed between the total score of the Lawton-IADL and those of the FIS, BI, and Katz Index for conjoint validity.[23] Similarly, Pearson correlation analyses were performed between the relevant subheadings of the Lawton-IADL and the Katz Index and between the VAS and the non-similar subtitles in the Katz Index. The results of these analyses were defined as excellent for values ranging from 0.81–1.00, very good for 0.61–0.80, good for 0.41–0.60, weak for 0.21–0.40, and bad for 0– 0.20.[24] p-values less than 0.05 were considered statistically significant.

RESULTS

A total of 80 people participated in this study, including 48 men and 32 women. Table 1 shows the sociodemographic characteristics of these older adults and the average scores of the scales.

Reliability of the Scale

Reliability is defined as the accuracy and repeatability of a measurement made with a scale.[25] To determine the reliabilities and test-retest of the Lawton-IADL, Cronbach's alpha and ICC were calculated, respectively. The Cronbach's alpha was 0.843 for the whole scale, indicating the high internal consistency of the scale. The test-retest analysis was used to evaluate the time-invariance of the scale. For this, the scale was applied again to 34 volunteers for 7 days. The ICC of the scale was 0.915. The test-retest correlation coefficients for each item varied between 0.74 and 0.98 ($p < 0.001$). The results of these analyses showed that the test-retest reliability of the subscales and the total scores were high, except for that of the ability to use a telephone (Table 2). These results demonstrated the high time-invariance of the Lawton-IADL.

Construct Validity

Validity is the degree of a scale's ability to measure what is intended for measurement.[25] To determine the conjoint validity of the scale, Pearson correlation analysis was performed between the total score of the scale and the total scores obtained from FIS, BI, Katz Index scores. The Lawton-IADL showed excellent correlations with the FIS, BI, and Katz Index scores ($p < 0.001$) (Table 3).

Pearson correlation analysis was performed using the Lawton-IADL subheadings and the similar subheadings in the Katz Index, and Pearson correlation analysis was also performed using non-similar subheadings and VAS. The construct validity of the scale was also investigated. The correlation coefficients of subheadings were between 0.263 and 0.843. Statistically significant

Table 1. Demographic information

Characteristic	Value
Age (y)	71.6 ± 5.8
Height (cm)	165.8 ± 10.2
Weight (kg)	76.8 ± 14.3
Sex	
Male	48 (60)
Female	32 (40)
Scale results	
HMT	8.6 ± 0.7
FIS	110.0 ± 24.5
BI	89.9 ± 20.0
Katz Index	26.0 ± 5.1
Lawton-IADL	6.1 ± 2.1

Values are presented as mean±standard deviation or number (%).
HMT, Hodkinson Mental Test; FIS, Functional Independence Scale; BI, Barthel Index; Lawton-IADL, Lawton Instrumental Activities of Daily Living.

Table 2. Test-retest reliability

Lawton-IADL	Cronbach's alpha	ICC
Ability to use a telephone	0.847	0.743
Shopping	0.813	0.876
Food preparation	0.850	0.921
Housekeeping	0.810	0.896
Laundry	0.815	0.875
Transportation method	0.806	0.868
Medication use	0.809	0.980
Handling finances	0.838	0.957
Total	0.843	0.915

Lawton-IADL, Lawton Instrumental Activities of Daily Living Scale; ICC, intraclass correlation coefficient.

Table 3. Correlation of the Lawton-IADL with the FIS, BI, and Katz Index

Scale	r	p-value
FIS	0.850	< 0.001
BI	0.843	< 0.001
Katz Index	0.896	< 0.001

Lawton-IADL, Lawton Instrumental Activities of Daily Living Scale; FIS, Functional Independence Scale; BI, Barthel Index.

moderate and strong correlations were observed among the subheadings (Table 4). These data supported the validity of the scale.

Table 4. Realationships of Lawton-IADL with the Katz Index and VAS by Pearson's correlation

Subheadings		r	p-value
Ability to use a telephone	VAS	0.553	< 0.001
Shopping	Katz Index	0.843	< 0.001
Food preparation	Katz Index	0.716	< 0.001
Housekeeping	Katz Index	0.619	< 0.001
Laundry	Katz Index	0.619	< 0.001
Transportation method	Katz Index	0.718	< 0.001
Use of medication	VAS	0.827	< 0.001
Handling finances	Katz Index	0.263	< 0.001

Lawton-IADL, Lawton Instrumental Activities of Daily Living Scale; VAS, visual analog scale.

DISCUSSION

Declining functional levels in older adults may be directly or indirectly related to their quality of life, major health problems, and mortality.[26,27] Assessment of the independence level of functions helps healthcare personnel to provide appropriate treatment, care, and counseling services by identifying the needs of older individuals and taking necessary measures.[28] This study adapted the Lawton-IADL, which is used to determine the IADL level in older adults, and analyzed its validity and reliability.

Our study group comprised adults more than 65 years of age with no acute health problems. The sociodemographic distribution of the patients showed that most were living alone and had one or more chronic diseases. These results were consistent with the population profiles in the current literature.[29] Similarly, most of the patients were not using any assistive devices (n = 63, 78.7%) and their final state assessment scale scores (FIS, 110.0 ± 24.5; BI, 89.9 ± 20.0; Katz Index, 26.0 ± 5.1; Lawton-IADL, 6.1 ± 2.1) indicated high functional levels.

Participants in our study had relatively high cognitive level (HMT, 8.6 ± 0.7). A decline in cognitive function can lead to deficiencies in decision-making ability[30] and subsequent ethical problems in both the clarity of the scale items and in obtaining informed consent. Laudisio et al.[4] observed normal and higher cognitive function adequacy in individuals with HMT scores above 7, while Chen et al.[31] reported that cognitive disorders negatively affected IADL performance. For these reasons, the present study used HMT scores of ≥ 8 one as an inclusion criterion. Therefore, during data collection, no difficult to understand part was reported from the volunteers for scale questions. Hence, authors believe that the study population is adequete to draw study conclusions of validities.

The Lawton-IADL results showed a higher inadequacy of the ability to use a telephone than other subheadings of Lawton IADL. Vergara et al.[2] also reported a higher inadequacy of this ability compared to the other subheadings of the Lawton-IADL. One possible explanation for these results may be the late entry of phone use in the lives of individuals over 65 years of age and the late increase in its prevalence. No widespread inadequacy was observed for other subheadings of the scale.

The Cronbach's alpha value, which indicates the internal consistency of the scale, was excellent (0.843). The Cronbach's alpha scores for the Chinese (Hong Kong), Korean, and Spanish and Persian versions were 0.86, 0.90, and 0.94, respectively.[2,9-11]

Our study evaluated the Lawton-IADL's temporal reliability by the test-retest method, with an ICC value of 0.915, compared to 0.96 for the original version of the scale.[8] The test-retest method was used to determine the reliability of the Chinese, Korean, and Persian versions of the scale, with values of 0.90, 0.90, and 0.99, respectively.[9-11] In the Spanish version of the study, the Comparative Fit Index was 0.99, with values > 0.90 considered satisfactory.[2] These results are similar to those of our study; the high ICC values in the Turkish version, show that the translation did not change the characteristics of the scores to a large extent.

Assessment of the test-retest correlation coefficients for the subheadings revealed the lowest value for the ability to use the telephone (0.74); however, even this value was above the threshold value for correlation.

The original version of the study investigated the correlations of the scale with the Physical Classification, Mental Status Questionnaire, Behavior and Adjustment rating scales, and Physical Self-Maintenance Scale (PSMS) scores. The Lawton-IADL showed a good correlation with the PSMS and moderate correlations with the other scales, thus supporting the validity of Lawton-IADL.[8] In the Chinese version of the study, the validity of the scale was examined by factor analysis, which identified nine content items.[9] The correlations between scale scores and disability levels in the Korean version of Lawton-IADL were -0.67 ($p < 0.001$) for men and -0.58 ($p < 0.001$) for women.[10] The correlations be-

tween the Spanish version compared to the BI, Medical Outcome Study (MOS) 12-items short form, Western Ontario and McMaster Universities Arthritis Index (WOMAC) short form, and Quick DASH (Disabilities of the Arm, Shoulder, and Hand) scales were above 0.40.[2] In the Persian version, Mehreban et al.[11] reported a correlation coefficient of -0.688 for the comparison of the scale with the Functional Assessment Staging test. Considering the results of other studies, the target older population, and the scale contents, the FIS, BI and Katz Index were considered appropriate to assess the validity of the Lawton-IADL. The total score of the scale showed excellent correlations with other indexes such as FIS (0.850), BI (0.843), and Katz Index (0.896). These findings indicate that IADL are related to the level of independence and BADL in older adults. The very high correlations between the Lawton-IADL and the FIS, BI and Katz Index supports that this scale is a valid tool for use in older populations.

Apart from the original scale and other version studies, the present study investigated the correlation of each Lawton-IADL subheading with another subheading with similar content. We observed that the Lawton-IADL was highly correlated with Katz Index subheadings similar to shopping, cooking, housekeeping, laundry, and transportation, and was poorly correlated with the subheading of handling finances. Although activities of daily living such as transportation, housekeeping, and food preparation are associated with physical health and independence, the handling of finances may be affected by mental health, educational level, and cognitive skill factors. In other words, it is not surprising that handling finances, an IADL, was not highly correlated with the Katz Index, a marker of activities of daily living.

We observed moderate correlations between the VAS scores and subheadings of the ability to use a telephone and medication. However, we obtained different results in the other subheadings, with a higher correlation using the Katz Index. The reason for this difference was that the Lawton-IADL subheadings included verbal and singular results, while the VAS score yielded quantitative and frequently plural results.

The high values, indicators of the validity and reliability of the Lawton-IADL, may be attributed to the fact that this scale is clear, feasible, and has a low scoring range.

Our study has some limitations. The study population comprised people from the same geriatric rehabilitation unit and nursing home environment, which may have affected the generalizability of the data. Including participants from two different cities (Mugla and Ankara) may also have affected the results, as participants from different cities may exhibit different sociodemographic characteristics. Also, the Lawton-IADL may not be sensitive enough to detect minor changes in IADL due to its scoring system. However, Yasuda et al.[32] compared the strengths of the scale to those of the Lawton-IADL for evaluating activities of daily living and reported that the strength of the scale was the ability to measure more complex function levels, increased sensitivity to detect serious dysfunctions since the person is likely to lose complex activities before simple activities, and more predictable detection in patients than that with an external performance assessment.

In conclusion, the Turkish version of the Lawton-IADL, which is widely used for the evaluation of IADL, is a valid and reliable scale for use in Turkish older adults.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

AUTHOR CONTRIBUTIONS

Conceptualization, EII, SB; Data curation, IU, SY; Funding acquisition, EII, SB, IU, SY; Investigation, SB, IU, SY; Methodology, EII, SB; Project administration, EII, SB; Supervision, SB; Writing_original draft, EII, SY, IU; Writing, review & editing, EII, SB.

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Ageism between Medical and Preliminary Medical Persons in Korea

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Background: We aimed to analyse the trends in ageism among health care providers and medical students in the Republic of Korea. **Methods:** We used the Fraboni Scale of Ageism (FSA), Relating to Older People Evaluation (ROPE) questionnaire, Anxiety about Aging Scale (AAS), and the Facts on Aging Quiz II to assess ageism in medical students (n=90), nurses (n=114), and physicians (n=83). We grouped health care providers based on the percentage of aged patients (over 65 years) that they treated. **Results:** Compared to the other groups, physicians had more knowledge about aging and the highest and lowest total scores in the FSA and ROPE, respectively. The total FSA scores were negatively correlated with the percentage of aged patients treated. Regarding the ROPE score, negative and positive ageist behaviors were positively correlated with the percentage of aged patients. **Conclusions:** Ageism and ageist behavior among physicians differed from previous reports and those of the other groups mentioned in the present study. Although physicians had more knowledge of aging, they had expressed a high levels of ageism. However, they did not act ageistically. Health care providers who treat a large number of older patients had minimal ageism but more ageist behavior. These findings indicate that continued education of geriatrics and ageism for medical staff and prospective medical personnel could help improve this situation.

Key Words: Ageism, Korea, Health personnel

INTRODUCTION

Butler[1)] defined ageism or age discrimination as "Prejudice by one age group towards other age groups". Iversen et al.[2)] defined ageism as negative or positive stereotypes, prejudice, and/or discrimination against (or to the advantage of) people based on chronological age or a perception of a person as being "old", "too old", "young", or "too young". Ageism should be treated like gender discrimination, racial discrimination, homosexual discrimination and discrimination against persons with disabilities because ageism results in differentiating, stratifying, and treating individuals differently based on attributes that they cannot change with effort or learning.

Ageistic behavior is an action resulting from ageism. For example, giving up one's seat to an older person and speaking loud to an older patient are considered positive ageistic behaviors. These actions result from preconceptions that older people have weak legs and cannot hear properly. Omitting detailed medical explanations or saying that older individuals are okay are considered negative ageistic behaviors arising from an age-based prejudice that older people have poor cognitive skills.

Ageism and ageist behaviors can significantly affect health care. Medical professionals should offer health care to all patients equally and patients should not be discriminated under any circumstances based on sex, nationality, religion, ethnicity, sexual identity, or age. However, in practice, age has served as a benchmark for setting treatment policy. Older women with breast cancer have typically fewer opportunities to receive breast conservative surgery than younger women.[3,4)] Furthermore, women over 70 years of age have a 40% greater probability of undergoing radical surgery than younger women. Similar findings have been reported world-

wide.[5,6] Nurse support for immunotherapy, breast reconstruction, and chemotherapy is less available for older breast cancer patients than for breast cancer patients who are younger. These trends reflect attitudes influenced by ageism.[7] Doctors and nurses reportedly perceive older patients differently from patients who are younger and treat older patients with lower priority.[8] In clinical studies, many trials excluded participants based solely on an arbitrary upper age limit.[9]

Briggs et al.[10] analyzed clinical trials in a teaching hospital over 3 years, reporting that, among 226 relevant trials, 31 used exclusion criteria to remove participants based on age. Most of the remaining trials also contained other exclusion criteria including cognitive function, which further limited participation of older people. These trials excluded older adults because of their seniority and not their inability to give informed consent.[11] Furthermore, older adults can buy many drugs over the counter without informational warning that the drugs may not have been tested on people of similar age, owing to age-related exclusion criteria of clinical trials for a number of these drugs. As the numbers of older individuals are increasing, ageism and age discrimination should be prohibited in areas related to public health care.

There are individual differences in the physical changes that occur throughout aging and the speed at which they occur. Simplifying the identification of patients over 65 years of age into a single "elderly" category encourages inaccurate medical judgments and unfair treatment.

To our knowledge, this study is the first to investigate ageism among health care providers and medical students in the Republic of Korea. Korea is a rapidly aging country. The average age of people is increasing faster than that in other developed countries.[12] Thus, there is a need to prepare social solutions for issues that aged individuals face across the nation. This study analyzed ageism trends among health care providers and medical students in the Republic of Korea to inform the planning of further studies on this topic.

MATERIALS AND METHODS

This study was approved by the Ethics Committee of the Catholic University of Korea College of Medicine (No. KC18QESE0532). This survey study investigated a sample of medical students (n = 90), nurses (n = 114), and physicians (n = 83) from one college of medicine and two tertiary university-based hospitals. The survey examined whether health care providers and medical students had completed geriatric classes. The geriatric classes included all undergraduate, post-graduate, and academic lectures. The medical personnel (physicians and nurses) were asked about the percentage of aged patients (65 years or over) they had treated in the total number of patients they had treated, Based on the percentage of aged patients that they had treated, the medical personnel were grouped as follow: Group I (0%–10%), Group II (11%–30%), Group III (31%–60%), and Group IV (61%–100%).

All gynecology doctors (n = 63) were asked about the treatment of uterine myoma. We asked these participants to respond to the following: "A patient with large uterine fibroid showing no increase in size comes to the hospital. The patient is in her 30s, 50s, 70s, and 80s. What treatment would you recommend for her? (a) Myomectomy, (b) Total hysterectomy, or (c) Observation". We wanted to determine if the treatment policy would vary based on patient age for the same medical conditions except for the respective age of the patient.

Instruments

The instruments used in this study included the Fraboni Scale of Ageism (FSA), Relating to Older People Evaluation (ROPE) questionnaire, Anxiety about Aging Scale (AAS), and Facts on Aging Quiz II.

The FSA[13] was used to assess ageism among the participants. The FSA contains 29 questions about ageism, each of which could be scored as 1 (strongly disagree), 2 (disagree), 3 (agree), or 4 (strongly agree). The total FSA score is the sum of scores for all 29 questions, with higher scores indicating greater ageism. To validate the Korean version of the FSA, Kim et al.[14] conducted exploratory factor analysis and confirmed a three-factor structure consisting of affective avoidance, discrimination, and stereotyping. This study used the same three-factor structure and total FSA score (Table 1). Eighteen of the 29 questions in Table 1 were included in the three-factor structures; the other eleven were included only in the total score.

The Korean version of the Facts on Aging Quiz II described by Palmore[15] was used to assess knowledge of aging. This questionnaire contain 25 questions about aging and older persons and is scored as correct or incorrect. The total score for this scale is based on the percentage of correct answers in which higher percentages of correct answers indicate greater knowledge on aging. Previous studies demonstrated a relationship between knowledge of aging and reduced ageism.

The AAS is used to measure a participant's fear of aging.[16] It consists of 20 questions, the answers to which are scored. The four interpretable factors measured in the AAS are fear of older individuals, psychological concerns, physical appearance, and fear of loss. Higher scores indicate more severe anxiety about aging.

The ROPE is a self-reported measure of the frequency and type of ageist behaviors. It is a 20-item questionnaire that measures per-

Table 1. Factor structures of the Fraboni Scale of Ageism

Structure	Item no.	Description
Affective avoidance	15	I personally would not want to spend much time with an old person.
	13	I would prefer not to go to an open house at a senior's club, if invited.
	26	I would prefer not to live with an old person.
	21	The company of most old people is quite enjoyable.
	7	I don't like it when old people try to make conversation with me.
	24	Most old people are interesting, individualistic people.
	6	I sometimes avoid eye contact with old people when I see them.
Discrimination	20	It is best that old people live where they won't bother anyone.
	16	Most old people should not be allowed to renew their driver's licenses.
	17	Old people don't really need to use our community sports facilities.
	8	Old people deserve the same rights and freedoms as do other members of our society.
	22	It is sad to hear about the plight of the old in our society these days.
Stereotype	5	Many old people just live in the past.
	10	Feeling depressed when around old people is probably a common feeling.
	28	Old people complain more than other people do.
	4	Many old people are not interested in making new friends preferring instead the circle of friends they have had for years.
	19	Many old people are happiest when they are with people their own age.
	3	Many old people are stingy and hoard their money and possessions.

sonal discrimination against older adults using 14 and 6 statements that reflect negative and positive types of ageism, respectively.[17] The responses to each question are scored as follows: 0 (never), 1 (sometimes), or 2 (often). The sums of the scores of questions reflecting negative types of ageism (defined as "negative ageistic behavior") and positive types of ageism (defined as "positive ageistic behavior") are calculated. The total score is summed and expressed as the proportion of the highest score possible for either the positive or negative dimensions. Higher scores indicate greater ageist behavior.

RESULTS

Demographics

The medical students were significantly younger than the other groups sampled. All nurses in our sample were female. The duration of university and post graduate education was significantly higher for the doctor group than for the other groups. However, the percentage of completed geriatrics classes was significantly higher in the nurse group than those in the other groups.

The percentage of correct answers in the Facts on Aging Quiz II and the FSA total score differed significantly among the three groups (Table 2).

Difference among groups according to their job

Physicians had more knowledge about aging than other groups, with the highest FSA total scores and lowest ROPE scores. This finding suggests that the doctors hold both knowledge and prejudices regarding aging individuals; The AAS scores were highest in the nurse group (Table 2).

Differences according to the completion of a geriatrics course

We grouped the participants based on whether they had completed a geriatrics course in college. The FSA total score was significantly lower in those who had taken a geriatrics course. However, the group showed significantly higher negative and positive ageist behaviors compared to the groups that had not attended a course (Table 3).

Differences according to the percentages of aged patients treated

The according to the percentages of aged patients treated (Table 4). The FSA total scores were negatively correlated with the percentage of aged patients treated by health care providers ($r = -0.63$, $p < 0.05$). Physicians or nurses who treated more older patients appeared to express less ageism. The "avoidance" and "stereotype" subscales of the FSA were both negatively correlated with the percentage of aged patients treated ($r = -0.8$ and $r = -0.7$, respectively, both $p < 0.05$). With respect to the ROPE measure, negative and positive ageist behaviors were positively correlated with the percentage of aged patients treated (Fig. 1).

With respect to the AAS, the "fear of old people" subscale was negatively correlated with the percentage of aged patients treated

Table 2. Demographic information and mean scores on administered measures

	Medical students (n = 90)	Nurses (n = 114)	Physicians (n = 83)
Age, mean (y)	24.1*	36.6	44.2
Sex (%)			
Male	40	0*	26
Female	50	114	56
Educational duration, mean (y)			
University***	3.6	4.6	5.7
Graduate school	1.5	1.3	3.1*
Completion of geriatrics class (%)	26.6	69.2	43.3
Questionnaire score			
Facts on aging quiz*** (% of correct responses)	59.8	66.3	71.3
FSA total score***	60.8	64.8	67.3
Avoidance	15.6	14.9	16.5
Discrimination	8.7	9.1	9.4
Stereotypes	12.6	14.5	14.9
Anxiety about Aging Scale	59.3	61.0*	58.2
Fear of losses	22.4	22.7	22.1
Fear of old people	12.7	12.4	13.1
Physical appearance	12.7	13.2	12
Psychological concerns	7.6	7.3	7
ROPE			
Negative ageist behavior	38.9*	27.2	26.2
Positive ageist behavior***	40.9	45.1	35.9

FSA, Fraboni Scale of Ageism; ROPE, Relating to Older People Evaluation.
* $p<0.05$, significant difference with the other groups.
***$p<0.05$, significant difference between three groups.

Table 3. Differences according to the completion of a geriatrics course

Did you take the geriatrics course?	Response		p-value
	Yes	No	
Facts on aging quiz (% of correct responses)	66.3	65.1	NS
FSA total score	63.3	65.5	< 0.05
Avoidance	15	16.3	< 0.05
Discrimination	8.8	9.4	< 0.05
Stereotypes	14.1	14	NS
Anxiety about aging scale	59.8	59.5	NS
Fear of losses	18.8	18.4	NS
Fear of old people	12.5	13	< 0.05
Physical appearance	12.9	12.4	< 0.05
Psychological concerns	7.2	7.4	NS
ROPE			
Negative ageist behavior	36.5	23.3	< 0.05
Positive ageist behavior	45.5	35.7	< 0.05

FSA, Fraboni Scale of Ageism; ROPE, Relating to Older People Evaluation; NS, not significant.

Table 4. Mean scores on administered measures based on the percentages of aged patients treated

	Group I	Group II	Group III	Group IV
Percentage of aged patients over 65 years	0–10	< 30	< 60	< 100
Facts on aging quiz (% of correct responses)	69.7	69	69	69.8
FSA total score	67.2	67.4	64	64.8
Avoidance	16.5***	16.2	14.8	14.8
Discrimination	9.2	9.9***	8.8	9.1
Stereotypes	14.8*	14.9*	14.5	14.5
Anxiety about aging scale	60.2	58.9	58.6	62
Fear of losses	6.9	7.2	6.9	7.7
Fear of old people	19	17.9	18.4	20
Physical appearance	13.4	12.9	12.4	12.3
Psychological concerns	12.7	12.2	12.9	13.2
ROPE				
Negative ageist behavior	24.5	27.2	26.5	28.5
Positive ageist behavior	37.3	38.4	43.6	44.9

FSA, Fraboni Scale of Ageism; ROPE, Relating to Older People Evaluation;
*$p<0.05$, significant difference with group III.
***$p<0.05$, significant difference with the other groups.

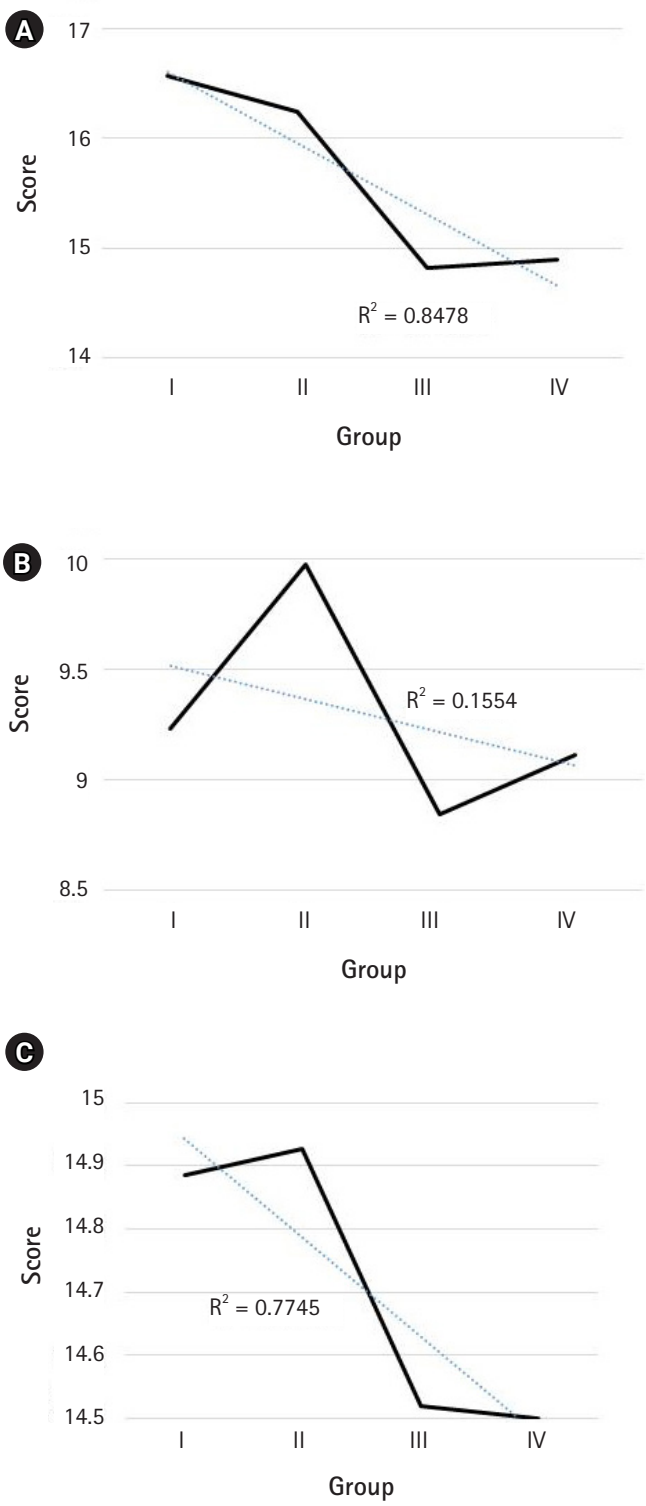

Fig. 1. The Fraboni Scale of Ageism scores and groups according to the percentages of aged patients. (A) Affective avoidance, (B) discrimination, and (C) stereotyping. Affective avoidance and stereotyping showed a negative relationship with the percentages of aged patients, indicating that the more medical providers see older patients, the lower their emotional avoidance or stereotyping.

by health care providers. Those treating a large number of aged patients expressed fewer fears and defensive attitudes toward them ($r = -0.9$, $p < 0.05$) (Fig. 2). Physical concerns and psychological concerns were positively correlated with the percentages of aged patients treated by the health care providers. The total AAS score was significantly higher in Group IV, which comprised practitioners who reported that over 70% of their patients were aged ($p < 0.05$).

With respect to the ROPE measure, negative and positive ageist behaviors were both positively correlated with the percentage of aged patients treated by the health care providers (Fig. 3).

Choice of treatment based on patient age

The answers to resort to total hysterectomy for uterine myoma increased with patient age but decreased for patients in their 80s. The answers to resort to uterus preservation, such as myomectomy, decreased with patient age (Fig. 4).

DISCUSSION

Ageism usually refers to negative attitudes and behavior toward aged adults; however, tax benefits for the aged, public service discounts for the aged, and medical care discounts for older adults demonstrate "ageism for the aged". It may be especially difficult to differentiate positive and negative ageism in health care services and among medical staff because age is usually used as a criterion for treatment indicators such as medication or surgery needs. Individuals above 65 years of age visit hospitals at an average of 12 times a year and precise knowledge of aging among health care providers is an important factor to ensure accuracy in disease diagnosis and sensitivity of efforts to differentiate between normal aging and disease.[18] Medical staff should differentiate between treatable diseases among aged individuals and normal physiological decline as a process of aging without prejudice or discrimination.

Prejudice toward older adults among health care providers may also cause over- and under-treatment. Increasing rates of prostate cancer screenings provide an example of over-treatment due to age-related biases.[19] Among health care providers, 65% agreed that "When somebody gets older, he/she feels more pain", 52% agreed that "When somebody gets older, it is easy to forget", and 14.7% agreed that "When somebody gets older, he/she is usually depressed".[18] These prejudices affect medical staff decision-making. When aged people complain of pain, fatigue, depression, or cognitive impairment, their symptoms are treated as less serious; moreover, these prejudices may interfere with disease diagnosis and prevent health care providers from providing necessary treatments. Health care providers should not assess patients primarily based

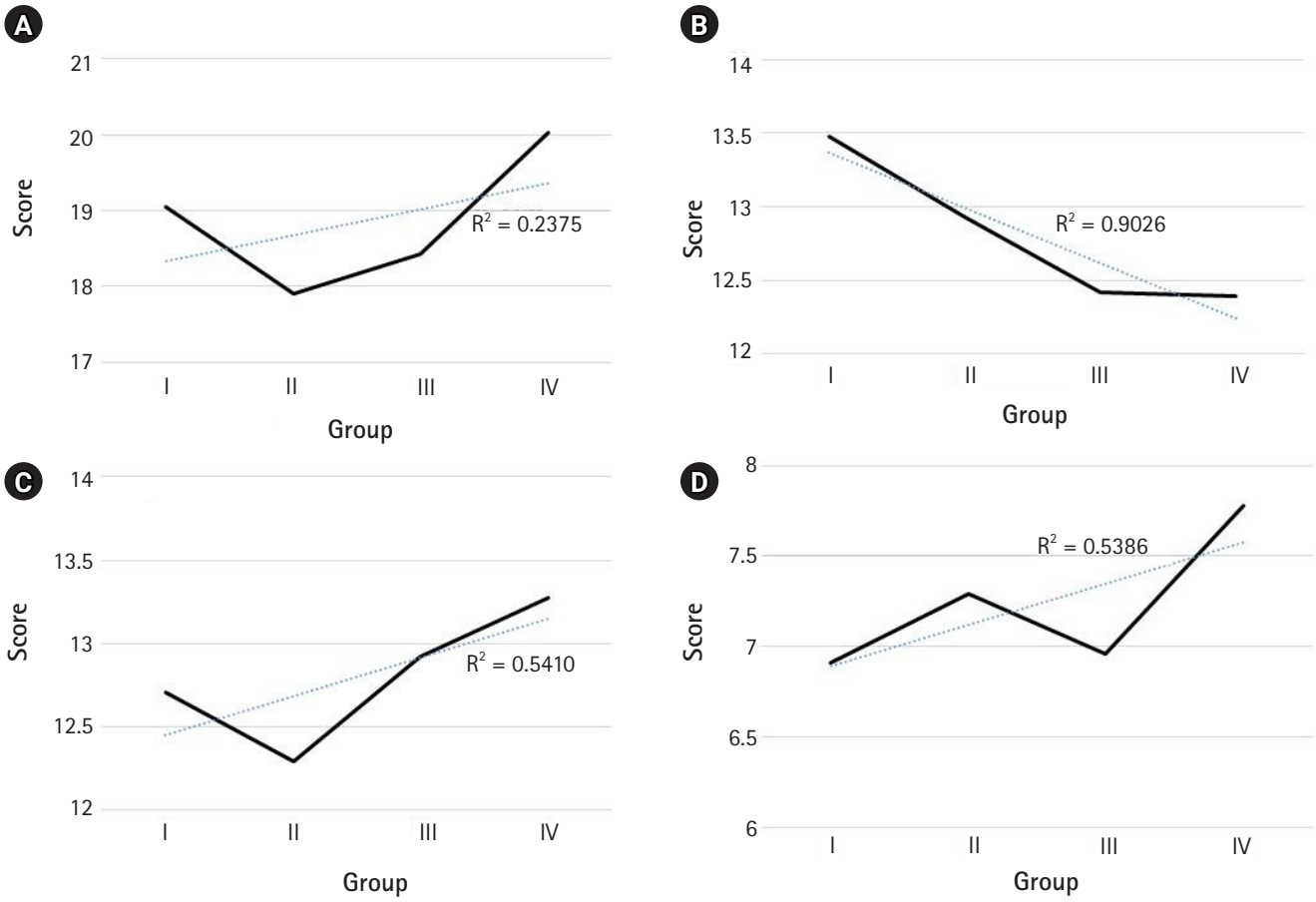

Fig. 2. The Anxiety of Aging Scale scores and group according to the percentages of aged patients. Fear about physical appearance showed a negative relationship with the percentage of aged patients. Physiological concerns and fear of loss showed a positive relationship with the percentage of aged patients. (A) Fear of older people, (B) physical appearance, (C) physiological concerns, and (D) fear of loses.

on age without considering their physical functioning or accompanying diseases. Patient life expectancy, cognitive ability, functional independence, and nutritional status are important indicators for assessing patient health and recommending adequate treatment.

Schroyen et al.[7] reported that immunotherapy, breast reconstruction, and chemotherapy are less commonly administered treatments among aged people and that ageism among nurses in oncology departments affects the rate of reconstructive breast cancer surgeries. The type of treatment that medical staff recommend is influenced by their degree of ageism.[20,21] If medical personnel have negative views related to aging, their behavioral engagement with older patients would be consistent with the negative views.[7]

Diseases requiring surgery are increasing in prevalence with age and age itself is not a contraindication to surgery for any disease.[22] In a study of 637 aged patients with head and neck cancer, higher age was not associated with increase postoperative complications or mortality.[23] Despite these results, heart surgery for patients in their 80s is not a treatment option[24] and reconstructive breast cancer surgery is usually only provided for those under 70 years of age.[6] Although cardiovascular disease (CVD) is more common in aged individuals, the percentage of patients administered intervention treatments for CVD is affected by their age. Intervention treatments are usually performed more often in younger patients, while medical rather than surgical treatments are administered to aged patients. Furthermore, with advanced age receive minimally adequate treatment after acute myocardial infarction.[25,26]

Ageism can be divided into conscious ageism and unconscious ageism.[27] Conscious ageism is explicit age discrimination, age-specific beliefs, emotions, and behaviors that are enforced in consciousness. Unconscious ageism refers to age-discriminating behaviors, beliefs, and emotions that occur unconsciously. Aged people consistently dissatisfied with their health represents conscious ageism. However, a health care provider not asking an older adult about their sexual life as a consequence of an unconscious belief

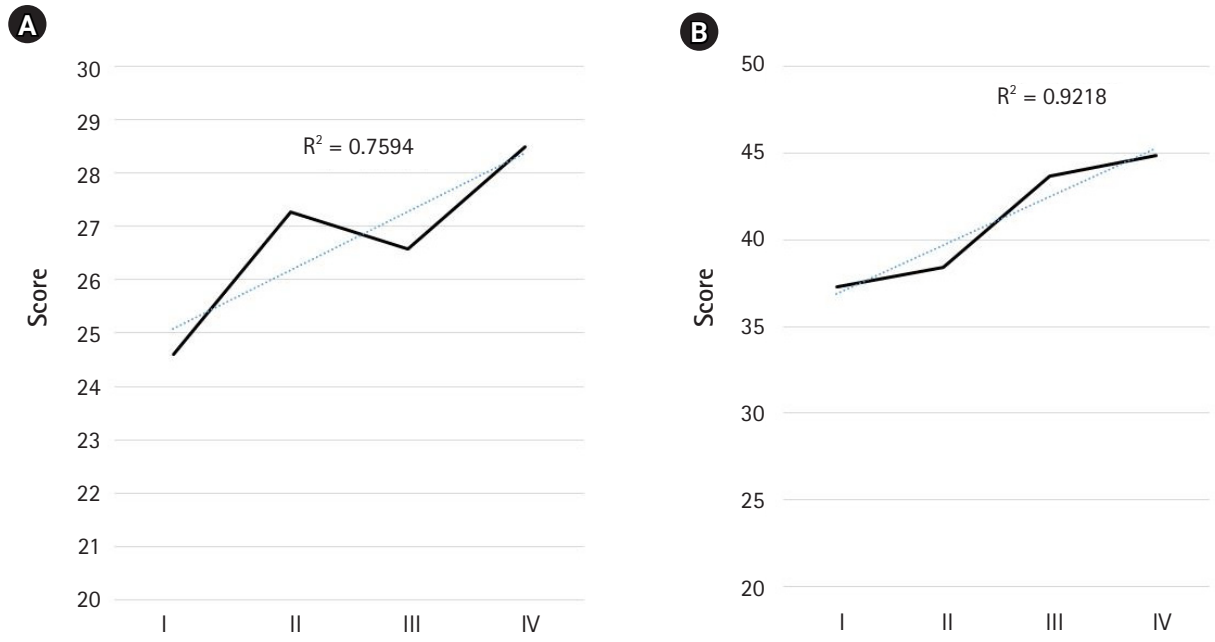

Fig. 3. The Relating to Older People Evaluation scores and groups according to the percentages of aged patients. (A) Negative ageist behavior and (B) positive ageist behavior. Negative and positive ageist behaviors were positively related to the percentages of aged patients, indicating that the more medical providers see older patients, the more ageistic behaviors they evidence.

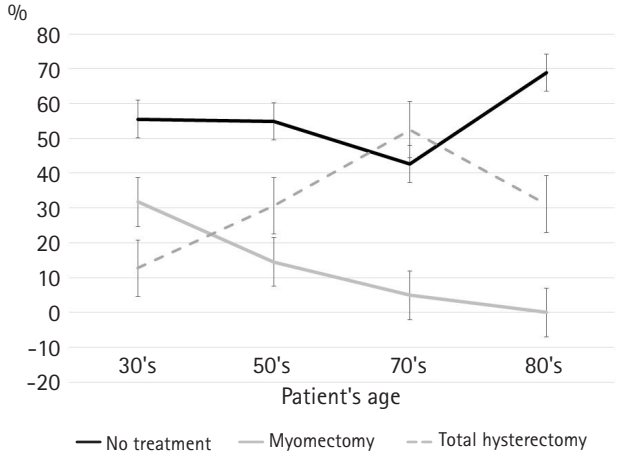

Fig. 4. Choices of treatment methods based on patient age.

that this population is not sexually active constitutes unconscious ageism. Jose et al. reported that many previous publications did not measure unconscious ageism because it required special tools to measure among older patients rather than considering older people as a more general group.[27] Unconscious ageism is more harmful to patients than conscious ageism because it can cause health care providers to mistakenly assign specific disease symptoms as normal changes associated with physiological aging. Health care providers often consider older patients to be too old to undergo invasive diagnostic tests. As such, these patients may not receive proper treatment or management due to unconscious ageism in their health care providers.[28] Unconscious ageism facilitates prejudiced treatment based on age, eliminating age-related criteria from clinical protocols. Guidelines are not adequate to minimize ageistic treatment.[29] Only targeting health care providers with continuous education and promotion of awareness about unconscious ageism can help to reduce this phenomenon.

In this study, the students were the youngest group, followed by nurses and physicians. Students showed the highest FSA score. In previous reports, conclusions regarding the association between ageism and age were unclear. Tuckman and Lorge[30] reported higher ageism in parents than in their children; however, a study that included college students and their parents found more favorable responses in parents than the students. Generally, older adults have more positive attitudes toward aging and old age; however, attitudes to aging are not defined by chronological age but may be determined by a more personal experience of aging.[31] The effects of age were not completely excluded, which is a limitation of this study.

Our identification of ageism and ageist behavior among a group of doctors differed from the findings of previous reports and other participant groups in this paper. In previous studies, knowledge about aging was negatively correlated with FSA score, while AAS

was positively correlated with FSA score;[11,32,33] contrary to the evidence in the present study. The physicians scored highest for knowledge about aging but also showed the highest FSA score. In a previous study, higher FSA scores typically represented higher consistency with ageist behavior;[32,33] however, the physician group showed the lowest ageist behavior scores. In other words, the physicians held the most knowledge and expressed a high level of ageism but did not act ageistically. There are two possible reasons for this finding. The first is that physicians do not act as they are usually thought of in doctor-patient interactions and do not show ageist behaviors toward aged patients. The second is that Asian Confucianism prevents ageist thoughts from manifesting into action, and many Koreans follow traditional Confucian ideas. Confucian values promote positive views of aging and teach younger people to respect, obey, and care for aged individuals. Confucianists do not act as they think (even if they have significant ageist thoughts) because of their social surveillance system. Vauclair et al.[34] performed a meta-analysis to compare attitudes toward older people in the east and west; they reported that competence, admiration, and personal attitudes about the aged were more inconsistent in participants from the east.

Previous reports demonstrated that qualified contact with the older adults helped to reduce ageism and anxiety about aging.[35] The present study showed lower FSA scores and anxiety about aging among health care providers who treated more patients over 65 years of age. Regarding ageist behavior, the numbers of older patients treated were positively correlated with ageistic behavior. Negative and positive ageist behaviors both increased in proportion with the percentage of the older patients treated. These results indicate that health care providers likely do not recognize their ageist behaviors.

Among all study participants, taking a geriatric class affected the total FSA score. Those that took the course showed lower FSA scores than those who did not. However, ageist behaviors were higher in those that took the class.

The traditional treatment policy for uterine fibroids in gynecology recommends uterine preservation surgery and hysterectomy in younger and older patients, respectively. After menopause, uterine myoma is observed without treatment because it decreases in size after menopause. The results of this study showed that patients in their 70s were recommended hysterectomy under the same medical conditions as women from younger age groups, while those in their 80s were recommended to undergo observation without treatment. Why not recommend surgery to women in their 80s? Thus, it is inappropriate to argue that doctors avoid surgery on older patients because of their prejudice toward aged people.

In conclusion, this study investigated age-related bias and prejudiced behaviors among medical students and health care providers in the Republic of Korea. We found that the completion of geriatric classes influenced ageism in medical staff and prospective medical practitioners. We also found ageist behavior in medical staff, even though they see more older patients. These results indicate that continued education of geriatrics and ageism for medical staff and prospective medical personnel could help improve this situation. This study is limited in the sense that it is difficult to apply the results to a broader population of Korean health care providers, as the study was conducted in two tertiary university hospitals. Future research on the effects of ageism education on the behaviors of health care providers should include more institutions.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

AUTHOR CONTRIBUTIONS

Conceptualization, HHC; Data curation, JYL, HSY, SRY; Investigation, MWK, SRY; Methodology, HHC, JYL, HSY; Project administration, HHC; Supervision, SRY; Writing original draft, HHC, JYL; Writing review & editing, HHC.

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Management Challenges in Atypical Femoral Fractures: A Case Report

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A 78-year-old woman presented with an atypical femoral fracture of her right femur associated with a left thigh stress fracture following 9 years of bisphosphonate therapy. The fracture was managed with femoral nailing. However, she represented 3 years later with peri-prosthetic infection, worsening of the left-side stress fracture, and low bone turnover in a bone metabolic study, consistent with an ongoing bisphosphonate effect. This case highlights the increased rate of postoperative complications in atypical femoral fractures even years after surgery as well as the challenging management issues for contralateral fracture and the risk of missing bilateral fractures.

Key Words: Bisphosphonate, Osteoporosis, Femoral fractures

INTRODUCTION

Bisphosphonates (BPs) have been used for decades to decrease bone fractures in individuals with osteoporosis and those on long-term glucocorticoid therapy.[1] A recent study in *The New England Journal of Medicine* reported good evidence that BPs can decrease the risk of fragility fractures in patients over 65 years of age with osteoporosis and even osteopenia.[2] According to the Australian Government's Pharmaceutical Benefits Scheme (PBS), BPs are used for primary prevention in osteopenic patients who have been using 7.5 mg or more of prednisone per day for at least 3 months.[3] As per revised criteria from the American Society for Bone and Mineral Research (ASBMR) task force report, Atypical Femoral Fractures (AFFs) are defined as fractures after no or minimal trauma with non-comminuted ones on femoral diaphysis from distal to the lesser trochanter to proximal to the supracondylar region; with complete ones extended to both cortices and incomplete AFFs involving just lateral cortex (Table 1).[1] The risk of AFFs usually increases after 3 years, with a median treatment of 7 years. The relative risk of AFFs is 2.1–128 in patients on BP therapy, with higher risks with long-term use (>100 per 100,000 person-years).[1] Management of these fractures and their complications is also challenging for physicians.

We report a case of AFF secondary to long-term BP treatment complicated by a peri-prosthetic wound infection 3 years later in addition to malunion of an incomplete fracture. Compared with other reports, our case highlights the challenging management of asymptomatic contralateral unhealed fractures as well as the risk of delayed postoperative complications even years after surgery in patients with AFFs.

CASE REPORT

A 78-year-old woman who presented to the hospital with right hip pain after a low-impact fall on her driveway in February 2016 was found to have a transverse fracture of the proximal shaft of her right femur with radiologic findings of AFFs consistent with ASMBR criteria (Table 1, Fig. 1).[1] At the same time, a contralateral left thigh radiograph confirmed cortical thickening of the femur, consistent with a stress fracture (Fig. 2). She had previously been treated with risedronate tablets (35 mg once weekly) for 9 years from 2006 and had discontinued their use in August 2015. The patient was also on long-term prednisolone (5 mg daily) to prevent asthma exacerbation. BP treatment was indicated on the basis of long-

Table 1. ASBMR Task Force 2013 revised criteria for atypical femoral fractures[1)]

Major criteria	Minimal or no trauma fracture
	Transverse fracture line originates from lateral cortex
	Complete fracture line involving both cortices associated with medial spike/incomplete fracture on lateral cortex
	Non-comminuted or minimally comminuted
	"Beaking" of fracture site
Minor criteria	Generalised increase in diaphyses cortical thickness
	Unilateral or bilateral prodromal symptoms
	Bilateral complete or incomplete femoral diaphysis fracture
	Delayed fracture healing

Fracture on femoral diaphysis from distal lesser trochanter to proximal supracondylar ridge.
At least 4 of 5 major criteria need to be present, none of minor criteria necessarily need to be present.
ASBMR; the American Society of Bone and Mineral Research.

Fig. 1. X-ray of right femur with anteroposterior view showing atypical subtrochanteric fracture in February 2016.

Fig. 2. X-ray of left femur with anteroposterior view showing stress fracture of left femur similar location to right femur in February 2016.

term steroid therapy and osteopenia detected on bone density scans by dual-energy X-ray absorptiometry (DXA). She also had past medical history of asthma, hypertension, and hysterectomy. She underwent antegrade femoral nailing. A survey for secondary causes of her osteoporosis, including evaluation of 25-hydroxyvitamin D, calcium, phosphate, parathyroid hormone (PTH), and thyroid-stimulating hormone levels, serum protein electrophoresis, and free light chain assay for multiple myeloma, showed normal results. Despite the incident fracture being considered as AFF, no intervention was considered for the left femur stress fracture because she was asymptomatic at the time. In the hospital, a physiotherapist started her on limited weight-bearing exercises for 6 weeks, which were gradually escalated to full weight-bearing exercises. She was then discharged with calcium and vitamin D supplementation. Her outpatient DXA scan in December 2016 showed an anteroposterior spine T score of -1.3, forearm T score of -0.6, and total hip T score of -1.6, features mainly consistent with those of osteopenia. Comparison with bone densitometry performed in 2015 showed minimal changes. Anabolic therapy with teriparatide

(TPTD) was considered inappropriate as she did not meet the criteria for the Australian PBS,[4] a program for the prescription of subsidized medications offered by the Australian Government.

In January 2019, the patient developed a fever associated with right-sided hip pain that worsened with mobility. A bone scan with technetium 99m-methyl hydroxy diphosphonate (^{99m}Tc-HDP) followed by a gallium scan with ^{67}Ga citrate for completion showed peri-prosthetic distal femoral nail infection and ongoing focal activity in the lateral cortex of her left proximal femur, consistent with the stress fracture that remained unhealed after 3 years (Fig. 3). She underwent right femoral nail removal and insertion of a new nail. However, fever, oozing from operation site, and sustained increased inflammatory marker levels after the operation mandated a second operation for removal of the right femoral nail, femur irrigation and debridement, and insertion of an antibiotic-impregnated intramedullary nail (Fig. 4). The patient was transferred to a rehabilitation center with a plan for completion of 6 weeks of intravenous antibiotic therapy in total. She was allowed to weight bear on the right leg and limited weight-bearing on the left leg with a walking frame. Repeated radiography of her left femur confirmed worsening of the stress fracture (Fig. 5).

During this admission, the bone turnover indices were as follows: urine N-terminal telopeptide (NTX), 70 nmol BCE/L (reference range, 26–124 nmol BCE/mmol creatinine in premenopause); NTX/creatinine ratio, 30 nmol BCE/L (> 50 in premenopause); ionized serum calcium, 1.28 mmol/L (1.12–1.32 mmol/L); plasma phosphate, 1.15 mmol/L (0.75–1.50 mmol/L); plasma

Fig. 4. X-ray of right femur with anteroposterior view showing new intramedullary nail in January 2019.

Fig. 3. Bone scan result showing focal activity of left femur consistent with stress fracture in addition to area of hypervascularity in right femur.

Fig. 5. Pelvis X-ray with anteroposterior view showing right femoral nailing as well as worsening of stress fracture on left femur 3 years later.

PTH 1.5 pmol/L (1.6–9.0 pmol/L), bone-specific alkaline phosphatase (BSAP), 0.69 U/L (30–110 U/L); serum 25-hydroxy vitamin D, 93 nm/L (> 50 nm/L), and urine calcium/creatinine ratio, 0.25 (0.1–0.58). These features were consistent with low bone turnover in the setting of an unhealed fracture. Prophylactic nailing of her left femur stress fracture was performed successfully 2 months after discharge (Fig. 6). The patient returned to baseline function and remained asymptomatic after 8 months of follow-up with callus formation in recovery.

Informed consent obtained from the patient.

Fig. 6. Anteroposterior view of left femur radiogram after prophylactic nailing in April 2019.

DISCUSSION

The ASMBR uses terms for "stress" and "insufficiency" fractures interchangeably, recognizing stress as augmented pressure on normal bone and insufficiency as excessive pressure on the abnormal bone.[1] They are transverse, located on the lateral cortex under the lesser trochanter with a "dreaded black line" appearance in contrast to conventional stress fractures, which are obliquely located on the medial cortex of the proximal femur. BPs can accumulate on stress fracture sites because of increased blood flow and callus formation, which leads to decreased remodeling and increased fracture size.[1,5]

A systematic literature review of 77 clinical trials including 834 people with complete or incomplete AFFs reported a mean healing time of 7.3 months (2–31 months). A higher failure rate was observed for non-operative treatment of incomplete fractures, whereas prophylactic surgery resulted in a 97% healing rate.[6] Moreover, almost 50% of incomplete fractures can progress to a complete fracture and could eventually require operative management.[6] Other studies also demonstrated delayed healing and increased revision rates.[7] Indeed, the ASMBR guideline considers delayed healing to be a minor criterion (Table 1).[1]

Despite conflicting opinions, intramedullary nailing is the favored treatment for complete AFFs.[1,6,7] In asymptomatic patients with radiologically incomplete fractures, stress reaction or stress fracture with no pain, the ASMBR guideline suggests limited weight-bearing exercises, calcium and vitamin D supplementation, discontinuation of BP therapy, and monitoring of bone edema until healing occurs. However, due to the high risk of complete fracture, prophylactic nailing is recommended if healing does not occur after 3 months.[1]

A case series reported an association between intramedullary nailing and with new bone formation in cortical defects in symptomatic incomplete AFFs.[8] However, justification of prophylactic surgery in asymptomatic patients can be difficult even in the presence of bilateral disease and previous contralateral fracture.[6,7] However, anecdotal studies showed improvement without surgery using TPTD as anabolic therapy.[9]

TPTD, a PTH(1-34) fragment, is another option for the treatment of incomplete AFFs. There is low-quality evidence that TPTD increases bone healing in patients with BP-related AFFs by enhancing bone turnover.[7] TPTD can be administered in high-risk patients with T scores of -3 or less with two or more minimal trauma fractures despite BP treatment for at least 12 months, according to PBS criteria. The treatment period is 18 months[4] and is usually followed by antiresorptive treatment to maintain the benefit, which is otherwise lost, which also presents an additional dilemma in patients with AFFs following BP treatment.

Zhang et al.[10] reported a case of a 71-year-old woman with osteoporotic vertebral fractures on BPs who developed left-side AFF that was treated with intramedullary nailing. The case was complicated by non-union 2 years later and was conservatively managed with TPTD. However, the patient required revision surgery 5 years post-operation and was also diagnosed with symptomatic incomplete right-side AFF at the same time of developing non-union on the left side. The former was treated with intramedullary nailing and TPTD with excellent bone healing after 3 months.[10] Similar to our study, this case also showed that healing can be prolonged in

asymptomatic AFFs.

In asymptomatic patients, there is always a chance of missing bilateral fracture if there are no symptoms and patients are not screened or monitored for it (radiography, bone scan, CT, or MRI). Another important point is whether to offer prophylactic nailing on the contralateral side, which can be critical for patients because of the risk of contralateral fracture. Good quality randomized clinical trials are needed to assess the benefit of conservative vs. surgical treatment, simply stopping antiresorptive therapy versus anabolic therapy, and other supportive strategies. This remains a dilemma and challenge without a clear answer, and decisions are made on an individual basis according to clinician experience and expertise and patient acceptance of the risks and benefits of each strategy.

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CONFLICT OF INTEREST DISCLOSURES

The researchers claim no conflicts of interest.

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Commentary
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Visualizing Domains of Comprehensive Geriatric Assessments to Grasp Frailty Spectrum in Older Adults with a Radar Chart

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Frailty, defined as vulnerability to possible stressors in older adults, reflecting decreased physiological reserve (Fig. 1), is widely accepted as a measure of human biological aging, a predictor of adverse outcomes, and outcome measures of interventions in geriatric research.[1,2] There remains controversy regarding frailty concepts and clinical definitions—i.e., physical frailty and frailty by deficit accumulation—although there is a growing consensus that both concepts are well correlated and generally point toward a systemic, biological aging phenotype in older adults.[1,3-5] Researchers have also attempted to separate varying features of the frailty spectrum, including social frailty, oral frailty, and cognitive frailty, to better understand heterogeneous aging phenotypes among persons.[6-8] Among these approaches toward frailty, the frailty index, based on deficits in parameters from comprehensive geriatric assessments (CGAs), is accepted as one of the most well-validated measures to predict mortality in older adults.[9,10]

However, there are caveats in utilizing CGAs and the frailty index in clinical practice for older adults. Because CGA results are usually presented using scales from multiple domains and narrative descriptions that are acquired through extensive examinations and interviews, imagining patients' clinical frailty status is an unfamiliar task for most non-geriatric healthcare providers. In contrast, the frailty index is presented as a single score from 0 to 1, and it provides a seemingly more tangible, quantitative feeling; however, domain-specific functional status is not apparent with the frailty index, as the scale is one-dimensional because of the aggregation of all parameters in the CGA domains.

To visualize multiple attributes from CGA data to simultaneously provide quantifiable features for better interpretation of CGA data and the concept of frailty, the author suggest the use of a domain-specific radar chart with an inner area indicating the physiologic reserve and an outer area indicating the frailty index (Fig. 2). Because the varying ranges of domain-specific instruments in CGA might be unfamiliar to non-geriatric specialists, this radar chart approach may facilitate communication between healthcare providers to foster shared inter-professional decision-making. Also, this type of plot can make the interpretation of CGA parameters, in order to grasp which domains are impaired, easier, allowing physicians to tackle those with deficits. For example, in Fig. 2, the radar chart of an imaginary person shows that cognitive performance is relatively impaired; thus, physicians can more vigilantly prevent delirium at hospitalization.[11] Furthermore, with accumulating re-

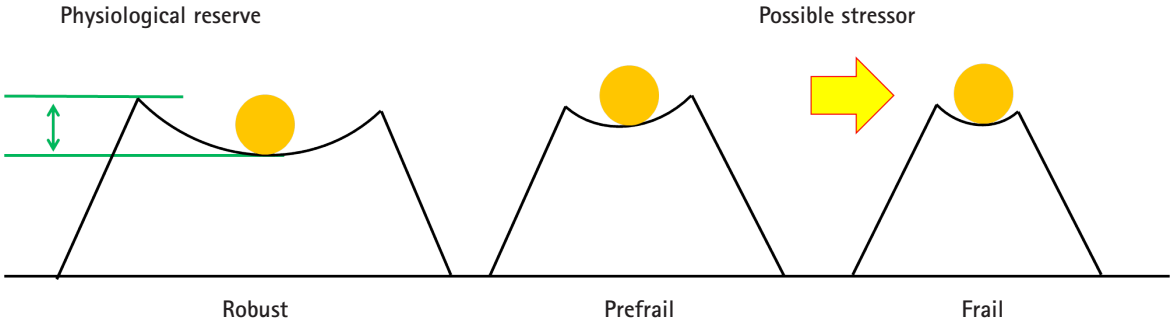

Fig. 1. Frailty status as a spectrum of physiological reserve and vulnerability to possible stressors.

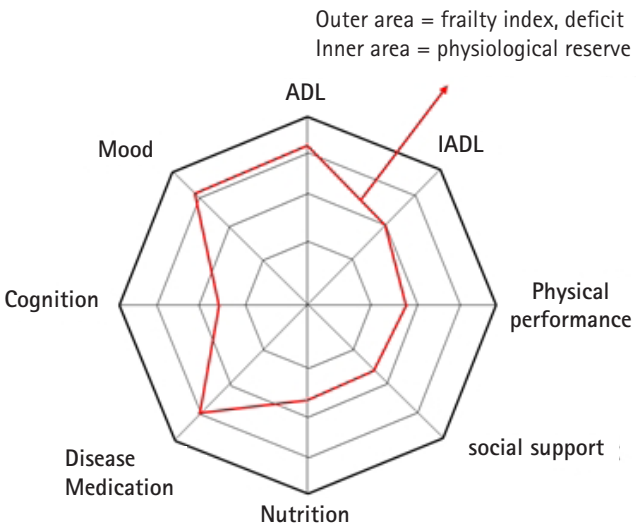

Fig. 2. Radar chart of a comprehensive geriatric assessment for an imaginary person. ADL, activity of daily living; IADL, instrumental activity of daily living.

search evidence showing that the frailty spectrum is amenable to structuralized interventions,[12] domain-specific longitudinal improvements of intervention programs might be more readily described with this radar chart.

Although qualitative or quantitative evidence on the advantage of visualizing CGA and frailty status is not yet available, I hope to see future studies utilizing this approach both in research and in clinical care for older adults.

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CONFLICT OF INTEREST

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What Should We Do to Help Lessen Older Patients' Pain?

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To the Editor,

I read the article by Akbar et al.[1] with great interest, as chronic pain in older persons is one of the most common conditions encountered by healthcare professionals, especially in acute-care hospitals. However, it is the least-heeded problem in hospitals, nursing homes, and home care. Pain is associated with substantial disability, falls, anxiety, sleep impairment, and isolation,[2] and it reduces mobility, affects activities of daily living, and disrupts both familial and social relationships.[3]

As the authors mentioned, cultural preferences and miscommunication between doctors and older patients are important barriers to pain management in older patients. Older patients admitted to acute-care hospitals assume that pain is the natural course of their acute illness and believe that it must be endured without treatment to recover from the illness, despite the available solutions to relieve pain. Furthermore, older people in Korea have often experienced poverty and are accustomed to enduring discomfort. To make the matters worse, some older patients mistakenly believe that they will become addicted to painkillers if they take them frequently. Therefore, it is important to ask patients about their pain during daily rounds and to constructively inform them that there are better solutions to relieve pain that avoid or reduce side effects.

Many hospitalized older patients have decreased cognitive function due to mild cognitive dysfunction, dementia, delirium, and other neurodegenerative disorders that affect pain assessment.[4] Moreover, delirium and behavioral and psychological symptoms of dementia can result from pain. Even if attending physicians use numeral rating scales or visual analog scales to assess pain in older patients, they cannot precisely determine a decrease in cognitive function. In these situations, a multidisciplinary team approach is very important. Caregivers, family members, nurses, physiotherapists, and occupational therapists can also provide valuable information or feedback.

We have all learned about the importance of pain control and appropriate pain treatment solutions, and we already know how to reduce pain. If we approach older patients from a humanistic perspective rather than as a patient subgroup to be studied and treated, we can provide better medical services and improve the fundamental human rights of older persons.

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

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

Reporting Guidelines for Specific Study Designs

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

Composition of Manuscripts

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

Table 1. Recommended maximums for articles submitted to AGMR

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

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[a]Maximum number of words is exclusive of the abstract, references, tables, and figure legends.
[b]Background, methods, results, and conclusion.

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A concise and factual abstract is required. The abstract should not

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Guidelines for the Main Body

- Introduction: State the objectives of the work and provide adequate background, avoiding a detailed literature survey or summary of the results.
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Reference Style

- Journal article:

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

- Book:

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

- Book chapter:

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

Press; 1995. p. 465-78.

- Website:

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

Tables and Figures

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

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Other Manuscript Formats

General guidelines are same as for original articles.

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