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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

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Editorial office
The Korean Geriatrics Society (Ann Geriatr Med Res)
#401 Yuksam Hyundai Venturetel, 20, Teheran-ro 25-gil, Gangnam-gu, Seoul 06132, Korea
Tel: +82-2-2269-1039 Fax: +82-2-2269-1040 E-mail: agmr.editorial@gmail.com

Printing office
M2PI
8th FL, DreamTower, 66 Seongsui-ro, Seongdong-gu, Seoul 04784, Korea
Tel: +82-2-6966-4930 Fax: +82-2-6966-4945 E-mail: support@m2-pi.com

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Editorial board

AGMR
Annals of Geriatric Medicine and Research

Contents

September 2022 Vol. 26, No. 3

Review Articles

Original Articles

AGMR
Annals of Geriatric Medicine and Research

Contents

September 2022 Vol. 26, No. 3

Case Reports

AGMR
Annals of Geriatric Medicine and Research

Review Article
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The National Programme for Health Care of the Elderly: A Review of its Achievements and Challenges in India

Lokesh Mukut Vaishnav, Shiv Hiren Joshi, Abhishek Upendra Joshi, Ashok Madhukar Mehendale

Department of Community Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (Meghe), India

Corresponding Author:
Shiv Hiren Joshi, MD
Department of Community Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (Meghe), 442001, India
E-mail: drshivjoshi93@gmail.com
ORCID:
http://orcid.org/0000-0001-7273-6058

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Aging care is critical. Projections for 2020 indicate that India's older population will comprise 6.57% of the overall population. The best-known newly developed technologies must be provided to the older population. Non-governmental organizations and private institutions are increasingly providing more door-to-door guidance and help. This study evaluated the impact of the National Programme for Health Care of the Elderly (NPHCE) in India and analyzed its achievements and challenges. The program's key strategies include providing preventive and promotional care and sickness management, empowering geriatric services, and guaranteeing optimal rehabilitation. The NPHCE is an excellent project for caring for a rapidly aging population. This study described the existing programs and schemes related to older people in India, with a focus on the NPHCE and an analysis of the program's achievements and challenges.

Key Words: Geriatric health services, National health program, Rehabilitation centre, Long-term care, Health policy, Research activities

INTRODUCTION

"For happy old age keep a goal." Aging is a process that converts a fit body into a frail one that is vulnerable to infections, injuries, and death.[1] In India, "senior citizens" are defined as older adults of Indian nationality aged 60 years and above. The National Policy for Older Persons was established in 1999 by the Ministry of Statistics and Programme Implementation and the National Statistics Office of the Government of India. The older adult population has increased from 24.7 million in the 1961 census to a projected 137.9 million and 158.7 million for the 2022 and 2025 censuses, respectively, accounting for 11.1% of the overall population.[2,3] This increasing older adult population leads to economic, social, and health concerns that require immediate and prompt responses from the government, enterprises, and society.[4,5] The onus of morbidity is immense. Diseases pose great threats to older adults, whose socioeconomic status is questionable. Disabilities worsen the daily living activities of old age.[6] While the United Nations Population Fund and Help Age India estimated that the senior population in India would increase to 173 million by 2026,[7] by 2001, India had surpassed that percentage (7.47%) and is predicted to reach 12.6% by 2025. Hence, India's aging population is drastically changing.[8] In India, the populations aged 0–14, 15–59, and 60 years and above comprised 30.8%, 60.3%, and 8.6% of the total population, respectively.[9] Older adults comprise 7.5% of the population, two-thirds of whom live in villages, with almost half in socioeconomically poor conditions.[10] Every program for older adults created in India aims to provide older persons with discrete, specialized, and complete health care at various levels of the Indian healthcare delivery system, in addition to outreach programs. Over 70% of India's geriatric population resides in rural areas, according to the 2011 census.[11] It has been said that care for older adults should be the same as that for children. One Indian report indicated that 8%–10% of older adults will be bedridden and will require utmost care for their survival. The dual challenges of aging care include ensuring that older adults can live healthy, dignified, and

productive lives and transforming them into partners rather than burdens on society.[12] The rise in the senior population has resulted in an "older adult boom" in several parts of the country.[13] The inequity and intricacies of India's demographic shift are obscured by summary numbers that ignore the disparities and complexities of demographic transition among Indian states with varying degrees of economic development, cultural norms, and political circumstances.[14] The main aim of this study is to describe the existing programs and schemes related to older people in India, with a focus on the National Programme for Health Care of the Elderly (NPHCE), and to analyze the achievements and challenges of this program.

MAIN FINDINGS

Issues Faced by the Older Population in India

Aging is a global phenomenon. India is in Stage 3 of the demographic transition, suggesting a fall in birth rate with the death rate remaining low and the population continuing to increase at a steady rate.[15] This leads to a growth of the older population, making it crucial for India to develop policies addressing their health-related concerns. Instead of the traditional fragmented approach, which caters to the individual health challenges of the older population through disease-based programs for non-communicable illnesses, cancer, and mental health, a comprehensive approach to older population health care is required.[16] Old age is associated with considerable mortality and morbidity, of which musculoskeletal pain is a major concern. This leads older adults to demand analgesics for pain relief. However, analgesics have detrimental effects on the body.[17]

The key issues faced by older adults in India are outlined in Table 1. Other issues include vulnerability to certain types of infection. For example, waterborne infections are more common among the older population in rural locations. Older adults may not be aware of proper hygiene measures that contribute to their risk of illness. Thus, there is a need to increase awareness of basic hygiene in this community to prevent bacterial illnesses.[18-21] Hence, older adults should be targeted for the prevention of bacterial infections.

Multimorbidity Patterns in Older Adults

According to the 2017 United Nations Population Fund report, performing activities of daily living is more difficult for older women than for older men.[22] Aging accounts for a high prevalence of musculoskeletal diseases such as those affecting muscles, the spine, bone (osteoporosis), and joints (osteoarthritis), leading to frequent fall injuries.[23] Aging is also influenced by various components, such as the surroundings in which older adults live, their families, their neighborhood, their communities, and their physical and mental capabilities, as well as their characteristics, including their sex, ethnicity, and socioeconomic status. The most crucial component that differs from younger populations is life experience. One of the pressing issues faced by the older population is depression, which manifests as social depression.[24]

Multimorbidity has been a concern in recent decades, with increasing prevalence. India is experiencing significant epidemiological and demographic changes that have caused people to move faster toward aging. Through this transient phase, more older people have experienced long-term diseases that affect all aspects of their lives. Multimorbidity is more common overall among the older population (32.96%) and women (34.69%). Arthritis/rheumatism (54.75%), hypertension (45.79 %), tooth loss (32.94%), cataracts (31.34%), diabetes (23.11%), and asthma are the most common disorders among individuals with multiple morbidities (21.06%). Multimorbidity is strongly correlated with population aging and sex is a significant predictor of multimorbidity. Reducing the burden of multimorbidity requires researchers and policymakers to collaborate to create effective intervention techniques and programs.[25-27]

To address this social issue, a screening program with timely review should be created. Multimorbidity patterns with robust epidemiological research for older adults will help mitigate the clinical complexities by targeting chronic diseases addressed by the healthcare delivery system from the grassroots to the national level.[28-30]

Table 1. Issues faced by the older population

Issues	Statements
Economic issues	With age, financial troubles get more severe. This affects self-esteem and health. Inadequate financial resources in old age are linked to sadness, anxiety, tension, and demotivation.
Physiological issues	Not only physical and anatomical but also mental health issues affect this age group. This alters their outlook on life, which may lead to a life devoid of ambition.
Housing-related issues	A house is one of the most important investments a person can make for a secure future. However, with declining health, the dwelling environment must be more acceptable, welcoming, and livable.
Crime against aged persons	This age group is vulnerable to crimes including murder, attempted murder, bodily harm, deceit, robbery, dacoity, and extortion.

Polypharmacy should be evaluated regularly, to eliminate overlapping or superfluous medicines.[31)]

Urbanization Effects on the Older Population

Urbanization has caused a transition by transforming the economics of rural society, transport systems, and socioeconomic status.[32)] The residential patterns also affect the health of older adults due to the in-migration of the older population and the out-migration of young persons.[33)] The variety exhibited by the older population is not random and is affected by physical and social settings, as well as the influence of these factors on the possibilities and health behaviors. Personal traits such as the family older adults were born into, their sex, and their race distort their connection to the environment, resulting in health disparities.[34)]

Older adults are frequently stereotyped as fragile, dependent, and a societal burden. These and other ageist attitudes must be addressed by public health professionals and society as a whole, as they can lead to discrimination, influence policy development, and limit healthy aging.[35,36)]

Globalization Effects on the Older Population

Globalization, technological advancements (e.g., in transportation and communication), urbanization, migration, and changing gender norms have direct and indirect effects on the lives of older people. A public health response must assess the present and future trends and formulate appropriate policies.[37)] The abuse of older adults has been a pressing topic for many decades, defined as a single or recurrent act, or a failure to act appropriately, which causes injury or distress to older adults in any relationship where trust is expected.

Around 1 in 6 people 60 years and older had experienced some form of abuse in community settings during the past year, including physical, verbal, psychological, sexual, and financial, abuse, as well as neglect. This issue can be prevented through monetary help, helplines, and emergency shelters.[38-41)] The Health Care of the Older population implemented core and characteristically accessible services for the older population. However, older individuals face challenges and are not informed of these issues, preventing them from receiving advice on how to resolve them.[42)] Table 1 briefly summarizes the issues faced by older adults.

COVID-19 and Care of the Older Population

Since the spread of coronavirus disease 2019 (COVID-19) worldwide, there has been a boom in polypharmacy in the senior population. This exponential rise has made the older population more vulnerable to the side effects of many medications. The imperative for a multidisciplinary approach is a focus on effective medicine prescriptions, which encompasses all stakeholders, healthcare professionals, and other personnel.[43)]

Stress Reduction in the Geriatric Population

The Common Yoga Protocol launched by the Ministry of AYUSH of the Government of India provided guidelines for practitioners treating COVID-19. Studies have shown that yoga reduces the incidence of acute respiratory infections. Thus, yoga may benefit the psychosocial treatment and rehabilitation of patients with COVID-19 under quarantine and isolation to reduce anxiety and phobias in this population.[44)]

Polypharmacy in the Older Population

The negative effects of polypharmacy include death, falls, bad medication reactions, extended hospital stay, and hospital readmission soon after discharge.[45,46)] Increasing drug prescriptions increase the risks of side effects and injury.[47)] Numerous variables, such as drug-drug and drug-disease interactions, may cause harm. Owing to their lower lean body mass and diminished hearing, eyesight, cognition, and mobility, older people are at increased risk of negative side effects.[48)] Rather than a mere numerical count of medications, which has no practical relevance, studies have advised the use of the phrase "appropriate polypharmacy" to distinguish between "many" and "too many" medications.[49)] A universally accepted definition of polypharmacy is required.[50)]

Diseases and Biological Variations in Older Populations

India is experiencing a high non-communicable disease burden and lifestyle-related consequences.[51,52)] Healthy life in the older population includes refraining from tobacco or alcohol use, regular physical work, and consuming healthy products to help reduce communicable and non-communicable diseases, which ultimately decreases dependency on care in old age.[53)] At the cellular level, molecules and cells mutate with age. Aging causes physical and mental decline, as well as increased risks of various illnesses and death.

Variations

Biological variations and circumstantial modifications, such as retirement, pension, new housing, family support, death of partners and friends, food, and security, are also linked with aging. Geriatric syndromes are characterized by frailty, urinary incontinence, delirium, dementia, pressure ulcers, and falls. Common conditions include osteoarthritis, cataracts, refractive errors, diabetes, stroke, hypertension, asthma, chronic obstructive pulmonary disease, hearing loss, back and neck pain, depression, and cancer.[3,54)] In India, potential health disparities occurring among older adults are

related to their economic class and require appropriate interventions to formulate actions to supervise achievements.[55,56]

The NPHCE

This program was initiated in 2010 to address the many health-related challenges faced by the older population. With the enunciation of the UN Convention on the Rights of Persons with Disabilities, the National Policy on Older Persons, and the Maintenance and Welfare of Parents and Senior Citizens Act 2007, Section 20, the Ministry of Health and Family Welfare envisioned this program. The goal was to develop a facility entirely dedicated to adults aged 60 years and above. However, these schemes have not been extensively analyzed to determine the increasing health burden of senior citizens in India.[57-59] The 12th Five Year Plan covered around 100 districts each year and established 12 more regional geriatric centers in the chosen medical tertiary care hospitals nationwide.[60]

NPHCE vision and strategies

The vision of the NPHCE is to facilitate the best long-term comprehensive and dedicated services for active and healthy aging by making society affordable and accessible to the aging population. Table 2 specifies the NPHCE strategies required to implement the program for delivering better healthcare delivery to the older population.[15,35]

All strategies were guided by state- and national-level governments at various levels of the healthcare system.[61]

Schemes and Programs of the Government of India for the Welfare of the Older Population

The Ministry of Social Justice and Empowerment is a key ministry for senior welfare. The Ageing Division of the Department of Social Justice and Empowerment's Social Defence Bureau is responsible for implementing policies and initiatives. The projects included help from the government, non-governmental organizations (NGOs), Panchayati Raj Institutions, local governments, and the general public. The policies implemented by the government also promote voluntary organizations to enhance support for family care and assistance to vulnerable individuals.[2,62]

An integrated program for older adults

The main goal is to improve the quality of care and provide justified shelter, food, and medical care to encourage productive active aging.[63] The agencies listed include Panchayati Raj or local bodies, NGOs, government-established autonomous bodies, and charitable trusts (Nehru Yuvak Kendra Sanghathan).

The national policy for older persons (1999)

This policy works with the assistance of the state to support and ensure the well-being of older adults. The policy's goal is to safeguard older persons from exploitation and abuse, while also allowing them to flourish by providing money, food stability, and housing. It also aims to build the best healthcare system to encourage self-sufficiency in this population. New amendments are in the process of finalization according to data.

Maintenance and Welfare of Parents and Senior Citizens Act (2007)

This act was based on the requirements of parents and older adults, as well as their prosperity. This act was not implemented in Jammu and Kashmir states, Himachal Pradesh, as these states have their own acts. Since the last decade, there has been a need to work on the provisions implemented nationwide with an aim for modernization. In 2019, the bill was amended in Lok Sabha of this Act,

Table 2. NPHCE strategies

Strategy	Points to implement
Preventive and promotive care with nutrition	The best life possible directed toward care to live a long and a healthy life.
Surveillance and management of illness	Managing diseases associated with old age with the utmost care, real-time monitoring and independent assessment of the program, as well as geriatric research and NPHCE implementation.
Health man-power development for geriatric services	A community-based primary health care strategy that includes home visits by qualified healthcare personnel.
Medical rehabilitation and therapeutic interventions at primary health or community health centers	Physiotherapy units and the supply of machinery, equipment, training, additional human resources (community health centers), information, education, communication, etc.
Information, education, and communication	To reach out to the target population, use mainstream media, folk media, and other communication channels.
District hospitals	10 bedded facilities with human resources and appropriate consumables and other resources.
Strengthening of regional geriatric centers	Offer customized tertiary-level medical facilities for the older population, including the introduction of postgraduate courses in geriatric medicine and in-service training for all levels of health workers.

NPHCE, National Programme for Health Care of the Elderly.

which included the definitions, monetary rewards, family maintenance amounts, and nodal officers for senior citizens in every police station.[34] In 2002, the Act was amended to state that older adults have the right to appeal for their necessities.[54]

Rashtriya Varishth Jan Swasthya Yojana (RVJSY)

This scheme provides government health insurance to families below the poverty line nationwide. AIIMS, New Delhi, and Madras Medical College, Chennai, are two National Centers for Aging (NCAs), where the NPHCE is conducted through the Centre for Health Informatics (CHI) to deal with data on geriatric facilities across the country.

Pradhan Mantri Jan Arogya Yojana (PM-JAY)

The Ministry of Health and Family Welfare, which is affiliated with Ayushman Bharat and the National Health Authority, has been approved to implement Ayushman Bharat (PM-JAY) nationwide, which is the second component under Ayushmann Bharat which was launched in 2018. It aims to cover approximately 50 crore (500 million) beneficiaries (vulnerable and poor families). Through the nation's public and private empanelled hospitals, it offers a health cover of Rs. 5 lakhs (500,000 rupees) per family per year for secondary and tertiary care hospitalization. Health benefit packages 2.0 covers 867 packages and is split across 1,573 procedures. There were no constraints on family size, age, or gender. The public sector continues to play an important role, particularly in the neglected areas of India.[64,65] The initiative has also aided in the management of this issue by encouraging COVID-19 worker transportation in various sections of the country.[66]

Indira Gandhi national old age pension scheme

The Indira Gandhi National Old Age Pension Scheme (IGNOAPS) was launched by the Indian Ministry of Rural Development under the National Social Assistance Program (NSAP) in 2007. It features senior citizens of India receiving monthly pensions and no contribution required from pensioners. People aged 60 to 79 years will be provided with a monthly pension of Rs. 200 and older adults above 80 years will receive Rs. 500 per month as a pension. States were asked to provide the same level of help as the central government. The eligibility criteria for the scheme were men and women adults aged 60 years and above.

The Pradhan Mantri Vaya Vandana Yojana (PNVVY)

The PNVVY was launched in 2017 exclusively for people older than 60 years of age. The scheme was extended until March 2023, with an association with the Life Insurance Corporation of India. This insurance scheme has been in place for 10 years, with the amount of insurance ranging from Rs. 162,162 to Rs. 1,500,000, which is paid monthly, quarterly, half-yearly, and annually. Other ministries, such as the Ministry of Finance, the Ministry of Road Transport and Highways, the Ministry of Railways, and the Ministry of Consumer Affairs, Food, and Public Distribution, also provide schemes to support older adults and make them self-sufficient. Table 3 shows other ministries implemented provisions considering health in the country.

Other plans and initiatives

Other plans and initiatives include the National Action Plan for the Welfare of Senior Citizens (NAPSrC), the Scheme of Integrated Programme for Senior Citizens, the State Action Plan for Senior Citizens, the Convergence with Initiatives of other Ministries/Departments in Government of India in the field of Senior Citizens Welfare (CWMSrC), National Awards for Senior Citizens-Vayoshreshtha Samman, the Rashtriya Vayoshri Yojana: Scheme for Providing Physical Aids and Assisted-Living Devices for Senior Citizens, and the Senior Citizens Welfare Fund, which provides provisions, programs, schemes, and Walkathons mostly on October 1 every year in India. All these schemes and programs have the same goals to protect and secure the lives of senior citizens, with an enhanced approach to hospitalization and greater financial security.

Packages of Services Provided to Older People under the NPHCE

(1) Subcenters (SCs): Provide services for healthy aging education by experts and routine domiciliary visits with family education to maintain the health of bedridden or older adult pa-

Table 3. Other ministries implementing health-based provisions

Ministry	Concession and facility
Ministry of Railways	For the comfort of certain people, particularly older adults, wheelchairs are offered at all intersections, District Headquarters, and other significant stations. Ramps have also been built for wheelchairs.
Ministry of Consumer Affairs, Food, and Public Distribution	The Antyodaya Scheme offers food grains to households below the poverty line and older adults at extremely low prices.
Protection of the Life and Property of Senior Citizens	A comprehensive Action Plan has been implemented for the protection of the lives and property of older adults.

tients who are disabled. They also provide suitable supportive devices from the primary health center to allow older patients to be ambulatory and run operational support groups in their localities.

(2) Primary health center (PHC): Provide a weekly geriatric clinic managed by a trained medical officer who maintains the records of the visit in a standard format provided by the government of India. PHCs conduct routine check-ups with basic clinical examinations, such as eye examinations, blood pressure, and blood sugar check-ups. In addition, free medicines are provided, with appropriate advice on chronic diseases. PHCs also raise health awareness and offer rehabilitation in health and village sanitation camps or days. Referral services are also provided to CHCs or district hospitals (DHs) as per requirements.

(3) Community health center (CHC): CHCs are considered the first referral unit from the PHC and lower levels. CHCs also implement two weekly geriatric clinics with physiotherapy and counseling units for older persons. The other provided services include domiciliary visits for bedridden patients and referrals to DHs.

(4) NCA: NCAs involve multidisciplinary clinical services of medical and surgical disciplines. They also provide day-care services with special clinics, such as memory/fall/syncope/frail/implants and cosmetic clinics. A special focus on patients aged 75 years and above is given to intensive care services and acute rehabilitation.

Thus, the NPHCE provides different levels of service packages. The program constitutes an integrated program in conjunction with the National Rural Health Mission and State and District Health Societies.

Dedicated Geriatric OPD Services under the NPHCE

While India has implemented numerous programs aimed at the senior population in recent decades, geriatric health clinics, geriatric physicians, and caregivers remain insufficient to provide proper care for older adults. Long-term care for older adults with physical and mental issues is referred to as geriatric or older adult care. Outpatient department (OPD) care is one of the most important and highly recommended services at all levels of the health care delivery system. Geriatric OPD is still in its infancy in India; however, a national survey showed that more than 80% of medical professionals and interns reported a need for specialized OPDs for geriatric services.[67]

(1) DHs: Provide regular dedicated OPD for the older age group with facilities for labs and investigations for ailments and routine check-ups. DHs consist of 10 bedded geriatric wards covering specialties such as medicine, orthopedics, and ophthalmology for acute and chronic ailments. Patients referred from PHCs and CHCs are treated, and camps are also conducted for screening. From DHs, patients with severe cases are referred to tertiary hospitals.

(2) Regional geriatric center (RGC): These specialized OPDs include 30 beds for geriatric inpatient wards, including departments such as medicine, neurology, surgery, urology, and psychiatry, and laboratory facilities with special collection centers. Patients are referred from medical colleges, DHs, and below.

Comprehensive geriatric outpatient care offers older adult patients a thorough treatment plan and access to social services, which lowers the demand for medical resources.

Achievements in the implementation of the NPHCE[6]

(1) The development of primary and secondary geriatric care services in all districts: One hundred districts were sanctioned for NPHCE services during the 11th plan period, while 421 districts were sanctioned to provide specialized geriatric OPD, inpatient department (IPD), physiotherapy, and lab services during the 12th plan period. All 713 districts were sanctioned for geriatric primary and secondary care services, including OPD, IPD, physiotherapy, and laboratory services, with the remaining 114 districts sanctioned in 2019–2020.

(2) Tertiary-level activities of the NPHCE: The "Rashtriya Varisth Jan Swasthya Yojana" (2016–2017)—NPHCE has sanctioned 19 RGCs at selected medical colleges in 18 states to provide tertiary care services in the form of specialist OPDs, 30-bed wards in RGCs, including earmarked beds in various specialties such as urology, orthopedics, and ophthalmology as well as personnel development and research activities. Currently, 18 RGCs provide outpatient treatment, 16 RGCs provide inpatient services, 14 RGCs provide physiotherapy, and 13 RGCs provide laboratory services. Two NCAs have also been established as Geriatric Care Centers of Excellence. A 200-bed NCA has been built and is active in the COVID ward at Madras Medical College in Chennai, while another NCA is under construction at AIIMS in New Delhi.

(3) Comprehensive geriatric care training modules: Three sets of training modules for medical officers, nurses, and community-based workers were established to provide comprehensive geriatric care. Chhattisgarh, Meghalaya, Haryana, and Punjab have held state-level training of the trainers of medical officers for comprehensive geriatric care. Tamil Nadu and Maharashtra produced approximately 236 state-level master trainers and 85

national master trainers, including 27 medical officers, 26 staff nurses, and 32 community-based workers.

(4) NPHCE website (https://main.mohfw.gov.in/major-programmes/Non-Communicable-Diseases/Non-Communicable-Diseases-1): This website provides detailed information about geriatric facilities and services via the CHI as the management information system.

(5) Information and education communication: Awareness of the myths, stereotypes, and social stigma is the most important step and makes stakeholders cognizant of geriatric care. Audio/video data are used for the geriatric age group. Other materials, including hard copy material and posters, should be available in English, Hindi, and all other regional languages.

(6) Monitoring and evaluation/audit: At all levels, the Union Ministry of Health and Family Welfare, as well as the Directorate General of Health Services, will continue to monitor and assess the program. Implementing World Health Organization's "Age-Friendly Primary Health Care Centres Toolkit" will assist persons of all ages to improve the quality of their care.[68] Village panchayats work best in monitoring health service delivery and also assist in planning reproductive and child health services.[69,70] The knowledge gap can also be addressed by enhancing communication between stakeholders.[71]

Advancements in the operationalization of programme activities, 2020–2021

According to the Progress Report, between April and December 2020, 19 RGCs, 18 operational OPD, 16 indoor wards, 14 physiotherapy services, and 13 laboratory services were sanctioned. A total of 718 DHs were sanctioned by the government, in addition to 584 operational OPDs, 507 indoor wards, 445 physiotherapy service units, and 539 laboratory services. A total of 4,869 CHCs were sanctioned, with 3,111 operational OPDs; however, no indoor wards were operational. Physiotherapy and laboratory services accounted for 1,131 and 2,408 units, respectively. A total of 18,407 PHCs were sanctioned, including 10,180 operational OPDs; however, no provision for indoor wards, physiotherapy, and laboratory services units was reported.

Provision of geriatric care services, 2019–2020

The Annual Progress Report from April 2019 to March 2020 listed nine services: OPD care services, indoor admissions, physiotherapy care, lab tests, number of older adults screened and given a health card, number of older adults provided home care services, number of older adults provided supportive devices, cases referred, and cases died in the hospital. These services were divided into RGCs, DHs, CHCs, PHCs, and SCs. Thus, the 133,545 OPD care services were provided in RGCs, 7,567,744 in DHs, 7,016,670 in CHCs, 9,032,922 in PHCs, and 2,843,211 in SCs, totaling 26 million. The total of 0.96 million indoor admissions included 9,992 in RGCs, 688,966 in DHs, 269,286 in CHCs. The 1.5 million physiotherapy care units comprised 34,637 in RGCs, 754,186 in DHs, and 2,348,922 in CHCs. The 9.07 million laboratory testing services included 230,749 in RGCs, 4,215,883 in DHs, 2,348,922 in CHCs, and 2,275,600 in PHCs. The 0.24 million older adults who received home care services included 11,157 in DHs, 92,657 in CHCs, 68,674 in PHCs, and 68,783 in SCs. The 0.047 million older adults who received supportive devices included 4,820 in DHs, 18,006 in CHCs, 7,256 in PHCs, and 17,502 in SCs. The 0.22 million referred case included 32,017 in DHs, 59,202 in CHCs, 65,057 in PHCs, and 64,119 in SCs. The 0.019 million deaths in hospitals included 17,026 in DHs, 2,156 in CHCs, and 384 in PHCs.

The expected outcomes of the NPHCE focus on most health issues.[72,73] Fig. 1 illustrates the implementation of the NPHCE in India.[74]

Human resource development

The Medical Council of India announced 15 MD geriatric medicine seats as a curriculum. This course provides more insights into geriatric care. Over 3,000 doctors have been trained and have provided service to geriatric patients in diverse areas for >16 years. NCAs were created in AIIMS, New Delhi, and Madras Medical College, Chennai, as part of the NPHCE, with key duties including interdisciplinary team training, research, and healthcare delivery in the field of geriatrics.[75]

Training manual for medical officers for older adult care

The care of older individuals requires a holistic approach, which is addressed in this training module. The manual outlines the components of geriatric evaluation, including physical, mental, psychological, and socioeconomic aspects, as well as comorbidity profiles, diet, and medical utilization.[76]

Challenges to the implementation of NPHCE

Table 4 layout the challenges with their assertion on what issues implementing NPHCE.[77]

Concerns regarding Tribal Populations

With 8.6% of the population being tribal, India faces challenges in closing the healthcare gap between tribal and nontribal residents. The current scenario inevitably results in lower levels of economic achievement,[78] with only 56% of children receiving all recommended vaccinations, as evidenced by an infant mortality rate of

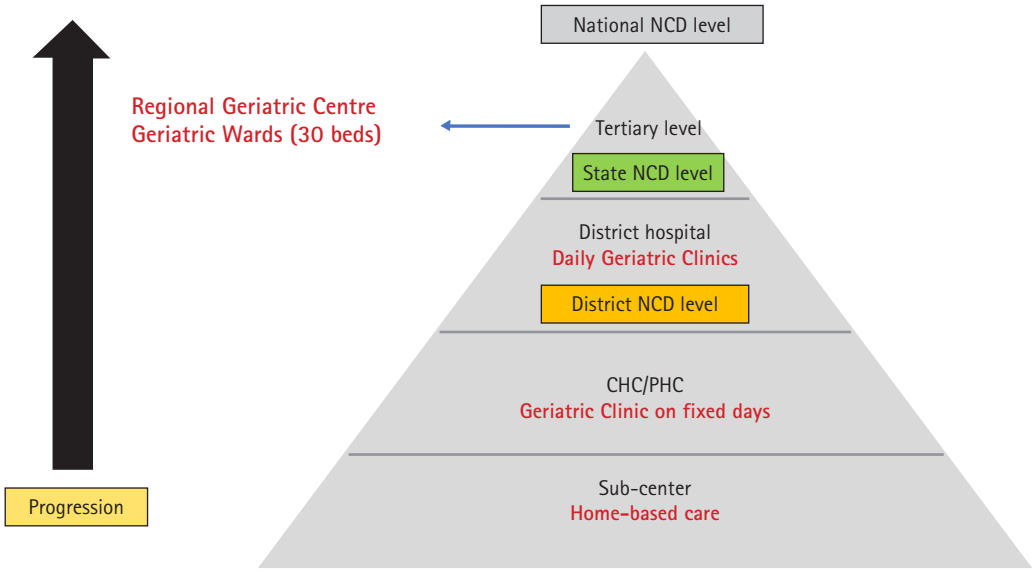

Fig. 1. The National Programme for Health Care of the Elderly (NPHCE) implementation pyramid. Modified from Operational Guideline of NPHCE.[6] NCD, non-communication disease; CHC, community health center; PHC, primary health center.

Table 4. NPHCE challenges[2,73]

Challenge	Statement
Demographic deviation	Population aging is caused by reduced fertility, lower mortality, and increased survival at later ages
Developing infrastructure for tertiary care	To create state-of-art centers and rehabilitation
Immunization and therapeutic approaches for the care of older persons	An organized, comprehensive approach to patient care by understanding the components of geriatric assessment
Treatments provided by medical professionals	Multi-dimensional treatment from all pathologies
Acute care of older adults	Mobile services for emergency care
Advocacy of public-private partnership as a collaborative strategy	Government initiatives involving private and public sectors
Merging and adapting service programs and monitoring data for older persons into the current monitoring system of the HWC.	Age-friendly environments, research on healthy aging by developing programs for sustainability, equitability, and equity
Health issues	Multiple disabilities with chronic diseases galvanize mental health problems

44.4% and an under-5-year mortality rate of 57.2%.[79] Additionally, 11% of the tribal population believes that nobody can stop diseases since it is God's will. Other research suggests that this population believes that sickness is caused by hostile spirits, ghosts, breaking certain taboos, and godly curses.[80] One of the most important challenges in providing healthcare for the tribal population is ensuring timely access. Older adults are more vulnerable to health conditions with multiple comorbidities. Hence, it is essential to work on the reorganization of service delivery mechanisms in tribal areas. A recent tribal India report suggested offering a broader range of 15 types of services, including geriatric and palliative healthcare services, through tribal health and wellness centers.[79]

Healthcare delivery to isolated older adults in such tribal settings can be aided by medical outreach camps and mobile health clinics. The attendance of tribal older people at health facilities may be increased by offering emergency transportation, hiring health workers from tribal communities, and establishing tribal counselors who make weekly visits to tribal hamlets to raise awareness of health issues and encourage healthy behaviors.[81]

Ongoing Research

Longitudinal Ageing Study in India (LASI)

In 2016, the Ministry of Health and Family Welfare in India began a country-level scientific review of health, economic, and social factors, and the aftereffects of India's aging population of 45 years and older. The International Institute for Population Sciences (IIPS) Mumbai was maintained as India's National Nodal Agency for the LASI survey. Technical support for Wave I of LASI was provided by the Harvard T.H. Chan School of Public Health

Table 5. Specific goals of the LASI

Goal	Activity
Survey	To design and conduct a longitudinal, nationally representative survey of adult health and aging in India.
Equivalence	To offer globally uniform data through the HRS and its sister studies worldwide, allowing for cross-national comparative research to learn more about how different institutions, cultures, and policies impact aging.
Research	To make unidentified data available to the scholarly community as quickly as feasible.
Policymaking	To provide statistics that will serve as a strong foundation for national and state-level legislation, as well as to aid policymakers and academics worldwide in analyzing how policies and programs affect population behavior, health outcomes, and the societal consequences that result.
Execution	To build a framework in India for innovative, rigorous, multidisciplinary research on aging that will inform policy.

LASI, Longitudinal Ageing Study in India; HRS, health and retirement study.

(HSPH) and the University of Southern California.[6,82,83]

LASI Initiation

Wave I of the LASI was conducted from April 2017 to December 2018 and enrolled 72,250 older adults. The LASI includes data from four domains: health, health care and health care financing, social, and economic. The findings of Wave I were released on January 6, 2021.[25,84,85] Table 5 specifies the goals for conducting the longitudinal aging study in India. The LASI is the largest global longitudinal aging study in terms of sample size, providing comprehensive and internationally comparable high-quality scientific data on the overall well-being of older adults in India. The LASI involves 30 states and 6 union territories, which cover 640 districts.

The LASI gathers information on four important subject areas[76]:

(1) Disease burden and risk factors in health (reported and measured).
(2) Healthcare and healthcare financing.
(3) Social: programs for older persons in the family, social networks, and social welfare.
(4) Economic: earnings, wealth, spending, employment, retirement, and pension.

A multivariate decomposition analysis of LASI data among older adults in 2017–2018 reported that older women are the highest priorities for health care professionals and necessitate the early prediction of disability, as well as the preservation of daily functioning.[86] The initial findings of the LASI revealed that older Indians face a wide range of health, social, and financial insecurities, with significant heterogeneity across several dimensions.[87]

CONCLUSION

While the NPHCE is a good initiative, it requires more monitoring and increased involvement of policymakers and stakeholders. These efforts are helping to develop a universal, accessible, and affordable long-term care service system with high-quality upstream prevention to postpone impairment and offer support services for family caregivers. The NPHCE prepares families for the worst circumstances and constructs a framework for each family to become a valuable participant in such programs. Public health measures could provide better national transport systems, provide buildings designed for the old people, adapt the course of the nature of the life cycle of older adults, and create a space for the psychological growth of newly experienced ideas.

This can be achieved through the education of health professionals, routine health check-ups, centralized specialized geriatric OPDs, and support and funding from the government at every level of the healthcare delivery system. Boys and girls from tribal communities with little formal education can be educated as community health workers and encouraged to work in their local neighbourhoods. LASI has performed a comprehensive nationwide study of the health, economic, and social factors, and implications of India's population ageing. It is necessary to look forward to preventing communicable and non-communicable diseases at each healthcare level. Efforts should be made in line with family support, social well-being, and measures to address psychological issues. Providing corporate statutes to geriatric healthcare services will galvanize the healthcare delivery system and encourage healthy ageing.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

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gation, LMV, SHJ; Methodology, LMV, SHJ; Project administration, SHJ, AUJ; Supervision, AUJ, AMM; Writing–original draft, LMV, SHJ; Writing–review & editing, LMV, SHJ, AUJ, AMM.

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A Meta-Analysis of the Effects of Dance Programs on Physical Performance: Appropriate Health Promotion for Healthy Older Adults

Suparat Sooktho[1], Nopparat Songserm[2], Somkiattiyos Woradet[3], Wanich Suksatan[4]

[1]Department of Aesthetic Sciences and Health, Faculty of Thai Traditional and Alternative Medicine, Ubon Ratchathani Rajabhat University, Ubon Ratchathani, Thailand
[2]Department of Health Sciences, Faculty of Public Health, Ubon Ratchathani Rajabhat University, Ubon Ratchathani, Thailand
[3]Department of Public Health, Faculty of Health and Sports Science, Thaksin University, Phatthalung, Thailand
[4]Department of Community Health Nursing, Faculty of Nursing, HRH Princess Chulabhorn College of Medical Science, Chulabhorn Royal Academy, Bangkok, Thailand

Corresponding Author:
Nopparat Songserm, PhD
Department of Health Sciences, Faculty of Public Health, Ubon Ratchathani Rajabhat University, Ubon Ratchathani, 34000, Thailand
E-mail: nopparat.s@ubru.ac.th
ORCID:
https://orcid.org/0000-0003-3741-367X

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Background: Dancing is a type of physical activity that has been associated with physical benefits in older adults. Regular dancing can help maintain physical function and improve the quality of life in this population. This review evaluated randomized control trials (RCTs) of the effectiveness of dance programs on the physical function of healthy older adults. **Methods:** We systematically searched four databases (PubMed, Google Scholar, Embase, and ThaiLis) through December 2021 for primary studies evaluating dance programs in healthy older adults aged 60 years and over. The meta-analysis used a random-effects model to compute the effect sizes using a forest plot and Cochran's Q and I^2 statistics as heterogeneity measures. **Results:** Eight types of dance programs showed significantly improved physical function. Muscle strength was assessed using the five times sit-to-stand test (I^2=89%; p=0.003), chair-sit-to-stand-30S test (I^2=75%; p=0.006), and 30-s arm curl test (I^2=22%; p=0.260). Static balance was evaluated using the Berg-balance scales test (I^2=0%; p=0.620) and the one-leg-stand test (I^2=32%; p=0.220). Dynamic balance was tested based on the time up-and-go and eight-foot up-and-go tests (I^2=51%; p=0.110). Flexibility was assessed based on the back-scratch (I^2=56%; p=0.130) and sit-and-reach test (I^2=0%; p=0.930). **Conclusion:** Dance exercise programs improved muscle strength, balance, and flexibility. Such programs are effective and safe for healthy older adults for use as daily exercise to promote health. Therefore, researchers, healthcare providers, and policymakers should establish properly organized dance interventions to improve physical function in healthy older adults.

Key Words: Exercise, Physical fitness, Healthy aging, Health promotion

INTRODUCTION

The world's population has transitioned into an aging population. Developed countries, such as the member states of Europe and North America, have become aging societies.[1] Japan, an Asian country, has also progressed to a super-aged community. Thailand is ranked second in aging societies among ASEAN countries after Singapore. The Office of the National Economic and Social Development Board (NESDB) has predicted that Thailand would become an aging society in 2021. That is, people aged 60 years or above account for 20% of the population. In 2036, Thailand is predicted to become a super-aged community, with 30% of the population aged 60 years and over.[2]

Dancing is a participatory activity, a method for socialization, and reflects the national culture of each country. International literature describes Chinese dance exercises, such as Tai Chi Chuan as popular and characterized by the inclusion of breath and body movement. These exercises also induce concentration and calm.[3,4]

The modified tap dance in the United States is a native American art form focusing on ankle and foot movement.[5] Korean traditional dance in Korea is a slow-tempo exercise to accompany the music.[6,7] In Thailand, exercises are performed with various musical accompaniments, including Muay Thai aerobic dance, Khon dance, Seng Sanai (Isan traditional dance), Applied Ancient Muay Dance, and Thai Dance. Indeed, studies in Thailand were consistent with international investigations of body movement exercises accompanied by music. This increased the research evidence related to dance and promoted good health in older adults.[8-11]

However, evidence from randomized control trials (RCTs) examining the effectiveness of dance programs on physical function among healthy older adults is limited. Most studies were in patients with Parkinson's, dementia, and lumbar stenosis. The results of these different studies were inconclusive regarding which program was appropriate to slow body deterioration in healthy older adults. A recent meta-analysis by Liu et al.[12] examined the effectiveness of dance on physical function in healthy older adults. The physical function outcomes were balance function, mobility function, endurance performance, gait, and general health. Likewise, Blanco-Rambo et al.[13] examined the effectiveness of dancing in reducing the risk of falls in older adults. Fall risk is assessed by time up-and-go (TUG), Berg-balance scales test (BBS), and one-leg-stand test. Physical function can be evaluated by measuring muscle strength based on the five times sit-to-stand test (FTSS), 30-s arm curl test (30AC), or chair-sit-to-stand-30S test (30CST). The present systematic review and meta-analysis collected data from previous studies to determine the effectiveness of various dance programs on relevant issues to make informed decisions about choosing the most appropriate dance program for older adults. Therefore, this study reviewed the literature on the effects of dance programs on physical function in healthy older adults to prevent and slow the deterioration of the body.

MATERIALS AND METHODS

Search Strategy

This review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)[14] checklist and flow diagram (Fig. 1) up until December 2021. We searched the PubMed, Google Scholar, Embase, and ThaiLis databases using keywords based on the PICO framework: P (healthy elderly), I (dance program), C (control group), and O (physical function) and the following keywords: "Dance program" ("Line dance" OR "Muay Thai aerobic dance" OR "Korean traditional dance" OR "Tai Chi Chuan exercise") AND "Physical function" AND "Healthy elderly" ("older adults" OR "elderly").

The criteria for inclusion in the meta-analysis were (1) published RCTs on the effects of dance programs (Line dance, Muay Thai aerobic dance, Korean traditional dance, and Tai Chi Chuan exercise) on the physical function of both female and male healthy older adults; (2) participant age 60 years and over without physical mobility limitations, and (3) sufficient data to perform the meta-analysis, including the mean, standard deviation (SD), and the sample size of both experimental and control groups. The exclusion criteria were qualitative research, review articles/editorial articles, proceedings, unavailable full text, and meta-analyses.

Search Outcomes

One researcher first searched the specified databases for data using the keywords above to identify studies meeting the inclusion criteria. Screening of the titles and abstracts revealed 18 relevant studies from PubMed, 49 from Google Scholar, 2 from Embase, and 42 from ThaiLis. Next, two researchers read the titles, abstracts, and research content carefully. A total of 52 publications were eliminated due to duplications (n = 21), systematic review and meta-analysis (n = 23), lack of focus on healthy older adults (n = 5), and pilot studies (n = 3). Differences of opinion between the two researchers were resolved through discussion with a third researcher. The systematic review and meta-analysis included a total of seven studies.

Quality Appraisal

We examined the heterogeneity of the seven studies based on fun-

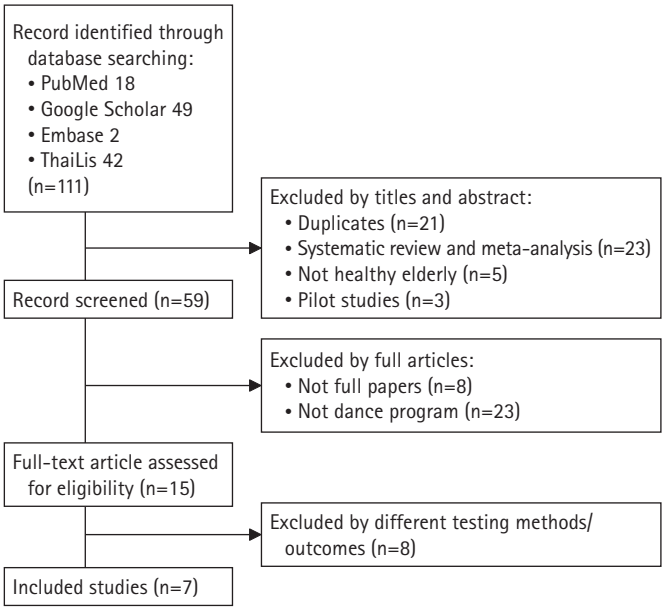


Fig. 1. Flowchart of study selection for meta-analysis. Adapted from the PRISMA Guidelines.[14]

nel plots using Review Manager (RevMan) version 5.4. The studies on the effects of dance programs on physical function tended to have publication bias in all four areas: muscle strength, static balance, dynamic balance, and flexibility. The assessment results of the risk of bias for each issue were classified according to selected research reports. We assessed the quality of the seven selected RCTs according to the PRISMA guidelines. The seven types of bias were evaluated and categorized as low, high, or unclear risk. The assessment results were 71.43% for random sequence generation (selection bias), 71.43% for allocation concealment (selection bias), 14.29% for blinding of participants and personnel (performance bias), 28.57% for blinding of outcome assessment (detection bias), 100% for incomplete outcome data (attrition bias), 100% for selective reporting (reporting bias), and 100% for other bias (Fig. 2).

Data Extraction

We developed a form to extract data to perform the systematic literature review. The details in Table 1 included the author's name, the publication year, the country of publication, the research objectives, information on the experimental and control groups, the details of the dance programs and assessment of the physical function of healthy older adults, and the research results.

Data Analysis

We synthesized the general data by summarizing the points of interest; namely, the effects of dance programs on the physical function of healthy older adults. We then analyzed the descriptive statistics using the available information from the samples. The mean, SD, and sample sizes of the experimental and control groups were used in the meta-analysis performed using RevMan version 5.4. The heterogeneity between each selected research study was tested using Cochran's Q and I^2. The statistical significance was set at the 0.05 level. The acceptable criteria for I^2 were: not significant (0%–24%), low heterogeneity (25%–49%), medium heterogeneity (50%–74%), and high heterogeneity (75%–100%).[15] The

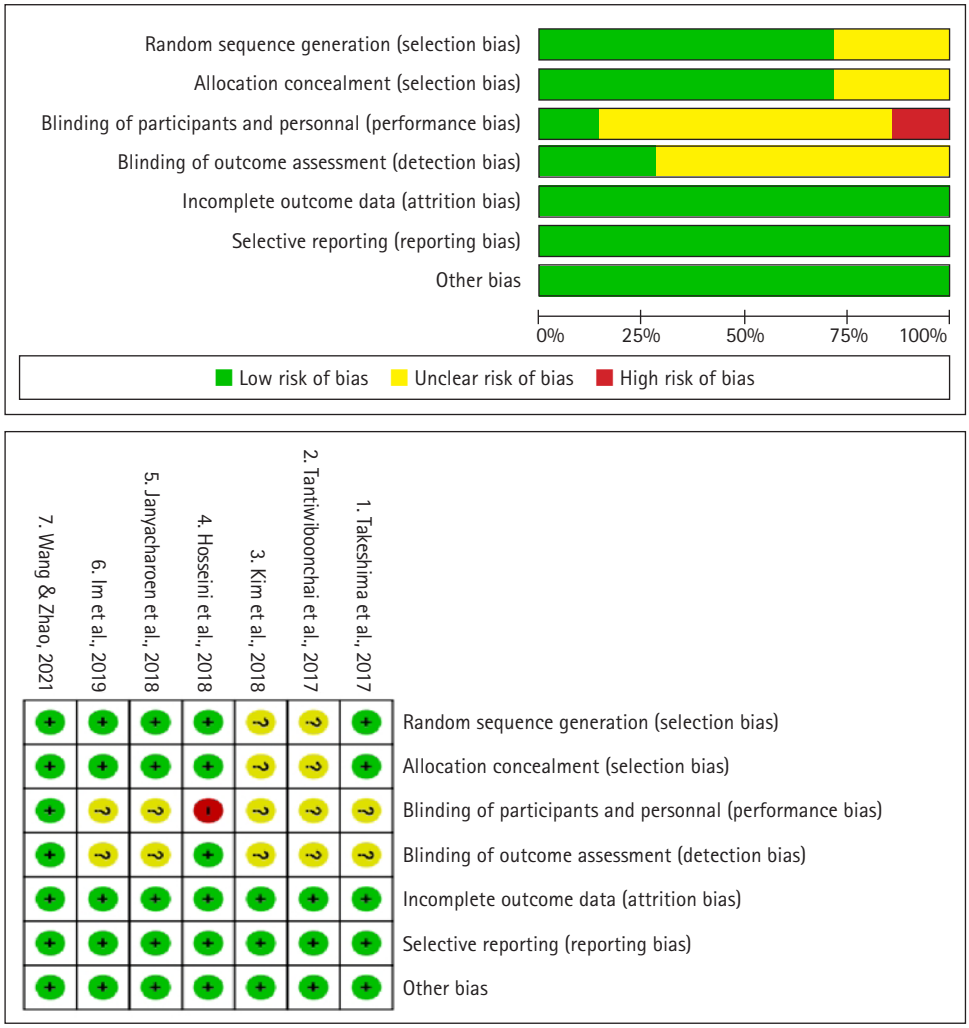


Fig. 2. Risk of bias graph and summary.

Table 1. Literature reviews dance programs' physical function of healthy older adults

Variable	Study, year	Country	Type of dance	Age (y)	Intervention period (wk)	Experimental group			Control group		
						n	Mean ± SD	Description	n	Mean ± SD	Description
Muscle strength											
Five times sit-to-stand test (FTSS)	Wang and Zhao,[5] 2021	USA	Modified Tap Dance	63.9 ± 4.21	12	22	6.4 ± 1.3	Modified tap dance program (MTD)	22	7.1 ± 1.2	Three health education lectures
	Janyacharoen et al.,[20] 2018	Thailand	Ancient boxing	65.9 ± 4.9	12	28	9.3 ± 2.0	Ancient boxing	28	12.2 ± 2.9	Education about the exercise and home program to aid in daily practice
30-s arm curl test (30AC)	Takeshima et al.,[3] 2017	China	Tai Chi Chuan	72.2 ± 5.0	12	25	32.5 ± 3.6	Tai Chi Chuan exercise	24	27.3 ± 3.9	Not change their physical activity habits
	Tantiwiboonchai et al.,[17] 2017	Thailand	Muay Thai Aerobic Dance	70.8 ± 4.4	16	20	22.0 ± 5.5	Muay Thai aerobic dance	20	14.5 ± 5.4	Routine physical activity
Chair-sit-to-stand 30S (30CST)	Takeshima et al.,[3] 2017	China	Tai Chi Chuan	72.2 ± 5.0	12	25	32.5 ± 4.7	Tai Chi Chuan exercise	24	27.2 ± 5.5	Not change their physical activity habits
	Tantiwiboonchai et al.,[17] 2017	Thailand	Muay Thai aerobic dance	70.8 ± 4.4	16	20	19.7 ± 6.8	Muay Thai aerobic dance	20	10.4 ± 5.0	Routine physical activity
	Kim et al.,[6] 2018	Korea	Korean traditional dance	78.0 ± 1.5	12	7	26.14 ± 5.27	Korean traditional dance	6	12.8 ± 1.8	Routine physical activity
	Im et al.,[7] 2019	Korea	Yoga and Korean dance	71.6 ± 3.2	12	14	19.4 ± 4.6	Yoga and Korean dance	11	13.7 ± 3.3	Supervised in the fitness center at the same frequency and time and performed sedentary physical activities
Static balance											
Berg balance scales	Janyacharoen et al.,[20] 2018	Thailand	Ancient boxing	65.9 ± 4.9	12	28	54.9 ± 1.5	Ancient boxing	28	51.2 ± 2.5	Education about the exercise and home program to aid in daily practice
	Bennett and Hackney,[24] 2018	USA	Line dance	65-93	8	12	50.4 ± 4.6	Line dance	11	48.1 ± 7.9	Normal daily activities
One-leg stance with eyes open	Tantiwiboonchai et al.,[17] 2017	Thailand	Muay Thai aerobic dance	70.8 ± 4.4	16	20	30.8 ± 30.0	Muay Thai aerobic dance	20	11.5 ± 11.0	Routine physical activity
One-leg balance with eyes closed	Kim et al.,[6] 2018	Korea	Korean traditional dance	78.0 ± 1.5	12	7	5.0 ± 3.5	Korean traditional dance	6	4.8 ± 2.9	Routine physical activity
Dynamic balance											
Eight-foot up-and-go test (UPGO)	Takeshima et al.,[3] 2017	China	Tai Chi Chuan	72.2 ± 5.0	12	25	4.3 ± 0.5	Tai Chi Chuan exercise	24	4.7 ± 1.4	Not change their physical activity habits
Time up-and-go test (TUG)	Hosseini et al., 2018[4]	China	Tai Chi Chuan	60-80	8	30	12.63 ± 4.13	Tai Chi Chuan exercise	30	18.7 ± 4.9	Did not receive any intervention
	Tantiwiboonchai et al.,[17] 2017	Thailand	Muay Thai aerobic dance	70.8 ± 4.4	16	20	8.4 ± 2.7	Muay Thai aerobic dance	20	16.4 ± 10.3	Routine physical activity
	Janyacharoen et al., 2018[20]	Thailand	Ancient boxing	65.9 ± 4.9	12	28	9.0 ± 1.7	Ancient boxing	28	7.5 ± 1.1	Education about the exercise and home program to aid in daily practice
Flexibility											
Back scratch test (BS)	Takeshima et al.,[3] 2017	China	Tai Chi Chuan	72.2 ± 5.0	12	25	-5.1 ± 12.1	Tai Chi Chuan exercise	24	-7.3 ± 12.8	Not change their physical activity habits
	Kim et al.,[6] 2018	Korea	Korean traditional dance	78.0 ± 1.5	12	7	10.0 ± 4.4	Korean traditional dance	6	1.8 ± 0.9	Routine physical activity
Sit-and-reach test (SRT)	Takeshima et al.,[3] 2017	China	Tai Chi Chuan	72.2 ± 5.0	12	25	14.9 ± 7.8	Tai Chi Chuan exercise	24	8.3 ± 15.1	Not change their physical activity habits
	Tantiwiboonchai et al.,[17] 2017	Thailand	Muay Thai aerobic dance	70.8 ± 4.4	16	20	10.8 ± 8.2	Muay Thai aerobic dance	20	4.1 ± 10.8	Routine physical activity
	Kim et al.,[6] 2018	Korea	Korean traditional dance	78.0 ± 1.5	12	7	33.2 ± 8.7	Korean traditional dance	6	24.8 ± 4.8	Routine physical activity

publication bias of the research was reported based on funnel plots. The statistical significance was set at the 0.05 level.

PHYSICAL FUNCTION OUTCOMES

Muscle Strength

FTSS

The FTSS is the most common method used to assess leg strength in older adults. Each participant is instructed to sit and stand from a chair repeatedly as quickly as possible with their arms folded across the chest to assess the risk of falling. The cut-off scores refer to the time used to categorize the participants as at risk or not at risk of falling. The cut-off scores are ≥ 11 seconds. Participants with FTSS times above this threshold are 4.40 times more likely to fall compared to those below the threshold. The FTSS test effectively predicts falls in older adults.[16)]

30AC

Each participant is instructed to sit on a chair with the dominant upper arm extended to the side. The forearm is placed parallel to the floor with the palm facing the body while holding a 2-kg dumbbell. After hearing the "start" signal, each older adult curls the arm holding the dumbbell by bending the elbow completely and then lowers the arm until the elbow is straight. The total number of controlled arm curls performed in 30 seconds is counted. The participants use their other hand to support the elbow of the curling arm to prevent injury. The score is the total number of arm curls performed in 30 seconds.[17)]

30CST (times)

30CST tests lower body strength. Each older adult is instructed to fold both arms across the chest and sit in the middle of a chair. After hearing the "start" signal, the participant must stand straight from the sitting position. The number of full stands and sits in 30 seconds is counted (the back of the participant must be straight against the wall or the assistant holds the back of the chair to prevent the chair from sliding backward during the test). The score is the total number of stands within 30 seconds.[18)]

Static Balance

BBS

The BBS measures the balance ability by performing 14 sitting and standing activities. Each activity is rated from 0 to 4 based on the participant's capacity, need for assistance, and the time spent performing the test. The total test score is 56 points. BBS scores < 45 points indicate a high risk of falls. The BBS is a highly accurate and reliable tool for balance assessment.[16)]

One-leg stance with eyes open and with eyes closed

One-leg stances with eyes open and closed are used to assess balance ability. The participant is instructed to stand with both heels on the edge of a drawn rectangle measuring 33 cm × 38 cm. The feet must be aligned and at shoulder width. The participant stands on the dominant leg and keeps the body upright and the hips straight. The non-dominant knee is then bent to 90°. The time elapsed from the start of the test to when the participant touches the ground with the non-dominant leg, felt the other leg, or could not bend the knee at 90° is recorded. The test is performed twice and the average time (in second) is used.[16)]

Dynamic Balance

TUG and UPGO

The TUG is a 3-m balance test used to measure the time required to rise from the chair, walk to turn around a cone and return to sit on the chair. Times ≥ 20 seconds to complete this task indicate a significant problem with dynamic balance. Times of 10–19 seconds indicate mild to moderate balance problems. Finally, times of < 10 seconds indicate an average dynamic balance.[16)] The UPGO is a test of balance over 2.44 m.

Flexibility

Back-scratch test

The back-scratch (BS) test upper body flexibility with the hands crossed behind the back and attempting to touch the fingers. The distance between the middle fingers of both hands is measured in inches. The measurements are performed twice, with the best value recorded.[19)]

Sit-and-reach test

The sit-and-reach test (SRT) test is used to evaluate lower body flexibility. First, the participant warms up by stretching the back and posterior leg muscles for 10–15 seconds 2–3 times on each other side. Next, the participant is instructed to remove their shoes and sit on the floor with their legs fully extended and the bottoms of their bare feet against the SRT testing box. The inner edges of both heels are aligned with the hip. The participants then slowly reach forward as far as possible with extended arms to place one hand on with the palms facing down. The stretch is held for approximately 2 seconds with the legs fully extended and knees straight. The furthest distance along the top of the SRT testing box

where the fingertip can touch the scales is measured. If the participant's knees are bent or if there is a jerky movement while testing, the attempt is not scored. The participant performs the test twice and the furthest distance is recorded.[17]

RESULTS

Muscle Strength

FTSS test

The analysis of FTSS test data applied a fixed mean difference. Among 100 healthy older adults from two full-text studies, 50 (50%) showed decreased FTSS test scores after receiving the dance intervention, with a mean difference of -1.16 (-1.79, -0.52) and an I^2 of 89%. The subgroup analysis included 100 subjects from two full-text studies. The asymmetric graph distribution on the funnel plot (Fig. 3) indicated that these studies were prone to publication bias. In addition, the fixed model was employed. The heterogeneity was high (75%–100%) ($I^2 = 89\%$; $p = 0.003$) (Fig. 4A).

30AC test

The analysis of 30AC test data applied a fixed mean difference. Among 89 healthy older adults from two full-text studies, 45 (51%) showed increased 30AC test scores after receiving the dance intervention, with a mean difference of 5.84. (4.06, 7.63) and an I^2 of 22%. The subgroup analysis included 89 subjects from two full-text studies. The asymmetrical graph distribution on the funnel plot (Fig. 3) indicated that these studies were prone to publication bias. In addition, the fixed model was employed. The het-

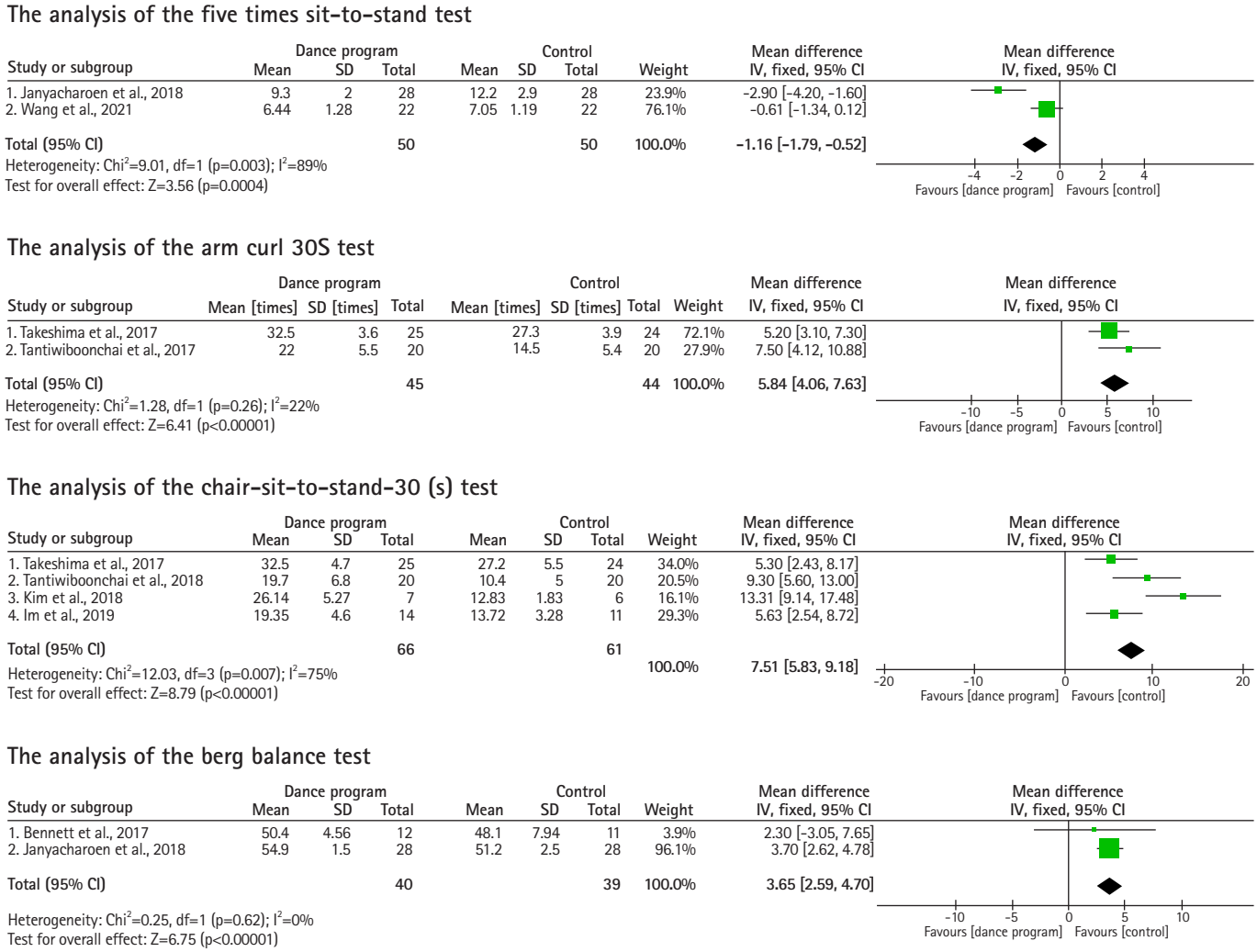


Fig. 3. Analysis of five times sit-to-stand test (FTSS), 30-s arm curl test (30AC), chair-sit-to-stand-30S test (30CST), and Berg-balance scales test (BBS) of healthy older adults.

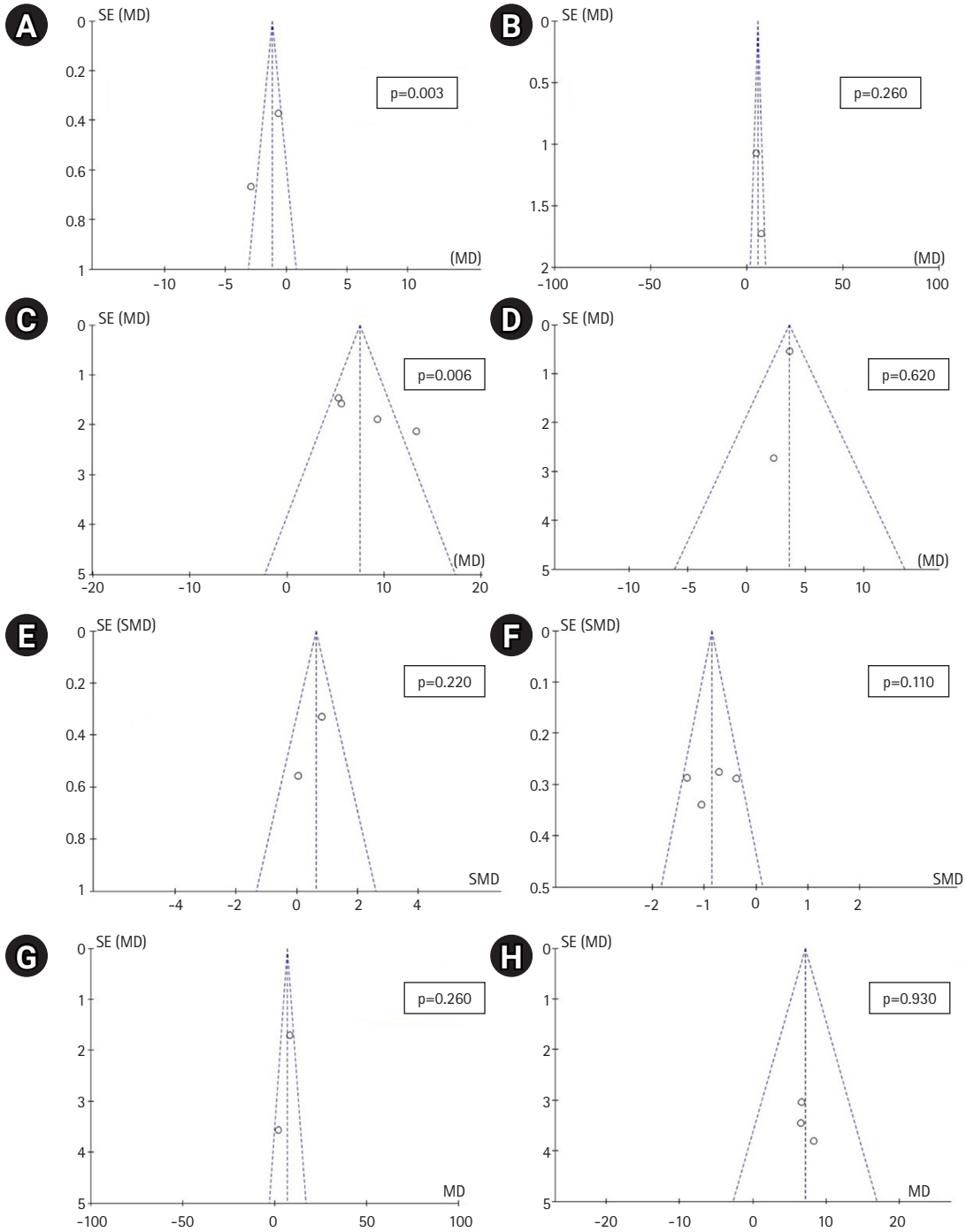


Fig. 4. Funnel plot analysis: (A) five times sit-to-stand test (FTSS), (B) 30-s arm curl test (30AC), (C) chair-sit-to-stand-30S test (30CST), (D) Berg-balance scales test (BBS), (E) one-leg stand test, (F) time up-and-go test (TUG) and eight-foot up-and-go test (UPGO), (G) back scratch test (BS), and (H) sit-and-reach test (SRT).

erogeneity was at the level of "not be important" (0%–24%) ($I^2 = 22\%$, $p = 0.260$) (Fig. 4B).

30CST test

The analysis of 30CST test data applied a fixed mean difference. Among 127 healthy older adults from four full-text studies, 66 (52%) showed increased 30CST test scores following the dance intervention, with a mean difference of 7.51 (5.83, 9.18) and an I^2 of 75%. The subgroup analysis included 127 subjects from four full-text studies. The asymmetrical graph distribution (Fig. 3) indicated that these studies were prone to publication bias. In addition, the fixed model was used. The heterogeneity was high (75%–

100%) (I^2 = 80%; p = 0.006) (Fig. 4C).

Static Balance

BBS test

The analysis of BBS test data applied a fixed mean difference. Among 79 healthy older adults from two full-text studies, 40 (51%) showed increased BBS scores after receiving the dance intervention, with a mean difference of 3.65 (2.59, 4.70) and an I^2 of 0%. The subgroup analysis included 79 subjects from two full-text studies who had received the dance intervention. The asymmetrical graph distribution on the funnel plot (Fig. 3) indicated that these studies were prone to publication bias.

In addition, the fixed model was used. The heterogeneity level was categorized as "not important" (0%–24%) (I^2 = 0%; p = 0.620) (Fig. 4D).

One-leg stance with eyes open

The analysis of one-leg stand test data applied a fixed standard mean difference. Among 53 healthy older adults from two full-text studies, 27 (51%) showed increased one-leg stand test scores, with a mean difference of 0.63 (0.07, 1.19) and an I^2 of 32%. The subgroup analysis of one-leg stand test results after receiving the dance intervention included 53 individuals from two full-text studies. The graph distribution on the funnel plot was asymmetrical (Fig. 5). Therefore, these studies were prone to publication bias. In addition, the fixed model was employed. The heterogeneity was low (0%–24%) (25%–49%) (I^2 = 32%; p = 0.220) (Fig. 4E).

Dynamic Balance

TUG and UPGO tests

The analysis of UPGO data used a fixed standard mean difference. Among 205 healthy older adults from four full-text studies, 103 individuals (50.25%) showed decreased UPGO scores following the dance intervention, with a mean difference of -0.85 (-1.14, -0.56) and an I^2 of 51%. The analysis of UPGO after the dance intervention in four full-text studies (subgroup analysis) included 205 individuals. The asymmetric graph distribution on the funnel plot (Fig. 5) indicated that these studies were prone to publication bias. In addition, a fixed model was employed. Medium heterogeneity (50%–74%) (I^2 = 51%; p = 0.110) was observed (Fig. 4F).

Flexibility

BS test

The analysis of BS test data used a fixed mean difference. The analysis of 62 healthy older adult samples from two full-text studies showed increased BS test scores in 32 individuals (52%) receiving the dance intervention, with a mean difference of 7.05 (4.03, 10.07) and an I^2 of 56%. The subgroup analysis included 62 subjects from two full-text studies. The asymmetric graph distribution on the funnel plot (Fig. 5) indicated that these studies were prone to publication bias. In addition, a fixed model was employed. Medium heterogeneity (50%–74%) was observed (I^2 = 56%; p = 0.260) (Fig. 4G).

SRT test

The analysis of SRT test data applied a fixed mean difference. Among 102 healthy older adults from three full-text studies, 52 (51%) showed an increased SRT test score following the dance intervention, with a mean difference of 7.09 (3.26, 10.93) and an I^2 of 0%. Subgroup analysis of SRT test results from three full-text studies included data from 53 older adults. The graph distribution of the funnel plot was asymmetrical (Fig. 5). Therefore, these studies were prone to publication bias. In addition, the fixed model was employed. The heterogeneity level was "not important" (0%–24%) (I^2 = 0%; p = 0.930) (Fig. 4H).

DISCUSSION

The results of the meta-analysis in this study demonstrated that dancing can help healthy older adults to move better. Based on the values of the variables, namely muscle strength, balance, and flexibility, the groups receiving dance interventions had better performance compared to the control group.

Muscle Strength

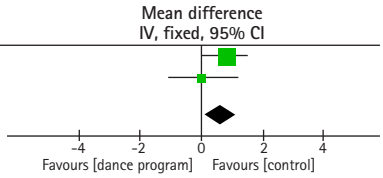
The analysis of the fixed mean differences in the FTSS, 30AC, and 30CST test results revealed that high heterogeneity in the FTSS and 30CST tests (I^2 = 89%; p = 0.003 and I^2 = 75%; p = 0.006, respectively). For the 30AC test, the heterogeneity was at the level of "not important" (I^2 = 22%; p = 0.260). Each dancing program had different dance moves, rhythm, exercise duration, and sample number.

The FTSS, 30AC, and 30CST tests are used to assess muscle strength. The FTSS and 30CST tests are used to evaluate the strength of the lower extremities while the 30AC test is used to measure the strength of the upper extremities. Previous studies reported significant increases in FTSS ($p < 0.05$) following the following dance interventions: ancient Thai boxing (from 10.06 ± 3.00 to 9.30 ± 2.00 seconds)[20] and modified tap dance (from 7.45 ± 1.51 to 6.44 ± 1.28 seconds).[5] Both dance programs required different upper and lower extremity movements. The

The analysis of the one-leg stand test

Study or subgroup	Dance program Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, fixed, 95% CI
1. Tantiwiboonchai et al., 2017	30.8	30	20	11.5	11	20	73.8%	0.84 [0.19, 1.49]
2. Kim et al., 2018	5	3.46	7	4.83	2.86	6	26.2%	0.05 [-1.04, 1.14]
Total (95% CI)			**27**			**26**	**100.0%**	**0.63 [0.07, 1.19]**

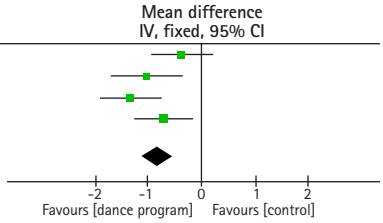
Heterogeneity: Chi^2=1.48, df=1 (p=0.22); I^2=32%
Test for overall effect: Z=2.22 (p=0.003)



The analysis of the time up and go test and eight-foot up and go test (UPGO)

Study or subgroup	Dance program Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, fixed, 95% CI
1. Takeshima et al., 2017	4.3	0.5	25	4.7	1.4	24	26.1%	-0.38 [-0.94, 0.19]
2. Tantiwiboonchai et al., 2017	8.4	2.7	20	16.4	10.3	20	18.9%	-1.04 [-1.71, -0.38]
3. Hosseini et al., 2018	12.63	4.13	30	18.7	4.85	30	26.4%	-1.33 [-1.89, -0.77]
2. Janyacharoen et al., 2018	7.5	1.1	28	8.7	2.1	28	28.6%	-0.71 [-1.25, -0.16]
Total (95% CI)			**103**			**102**	**100.0%**	**-0.85 [-1.14, -0.56]**

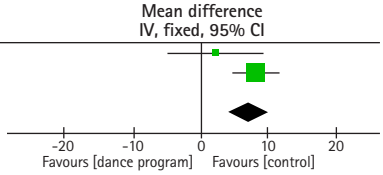
Heterogeneity: Chi^2=6.07, df=3 (p=0.11); I^2=51%
Test for overall effect: Z=5.75 (p=0.00001)



The analysis of the back scratch test

Study or subgroup	Dance program Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, fixed, 95% CI
1. Takeshima et al., 2017	-5.1	12.1	25	-7.3	12.8	24	18.7%	2.20 [-4.78, 9.18]
2. Kim et al., 2018	10	4.4	7	1.83	0.98	6	81.3%	8.17 [4.82, 11.52]
Total (95% CI)			**32**			**30**	**100.0%**	**7.05 [4.03, 10.07]**

Heterogeneity: Chi^2=2.28, df=1 (p=0.13); I^2=56%
Test for overall effect: Z=4.57 (p<0.00001)



The analysis of the sit and reach test

Study or subgroup	Dance program Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, fixed, 95% CI
1. Takeshima et al., 2017	14.9	7.8	25	8.3	15.1	24	32.0%	6.60 [-0.17, 13.37]
2. Tantiwiboonchai et al., 2017	10.8	8.2	20	4.1	10.8	20	41.6%	6.70 [0.76, 12.64]
3. Kim et al., 2018	33.14	8.67	7	24.83	4.75	6	26.4%	8.31 [0.85, 15.77]
Total (95% CI)			**52**			**50**	**100.0%**	**7.09 [3.26, 10.93]**

Heterogeneity: Chi^2=0.14, df=2 (p=0.93); I^2=0%
Test for overall effect: Z=3.63 (p=0.003)

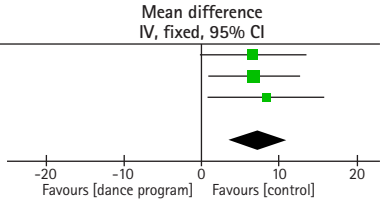


Fig. 5. Analysis of the one-leg stand test, time up-and-go test (TUG) and eight-foot up-and-go test (UPGO), back scratch test (BS), and sit-and-reach test (SRT) of healthy older adults.

modified tap dance program lasted 60 minutes. Each set from all eight groups focused on movements of the torso, ankles, knees, and arms. Every exercise set concentrated on increasing the muscle strength of the center of mass, in addition to coordination and agility.[21] Ancient Thai boxing was applied to the traditional boxing of Sakon Nakhon province, Phu Tai Noi, from the northeastern region of Thailand. The sessions lasted 40 minutes, divided into 5, 30, and 5 minutes. The exercise consisted of 14 movements of both arms and legs. However, the ancient Thai boxing exercise applied by Janyacharoen et al.[20] consisted of 12 moves. The FTSS test of both dance programs increased the strength of the leg muscles responsible for hip flexion and hip extension and the muscles responsible for knee flexion-extension, such as the quadriceps, femoris, and hamstring muscles.

Two dancing programs showed significant improvements in 30AC test results ($p < 0.05$); namely, Tai Chi Chuan (from 32.2 ± 3.7 to 32.5 ± 3.6 times)[3] and Muay Thai aerobic dance (from 18.20 ± 3.60 to 22.00 ± 5.50 times).[17] These programs focused on movements of the upper and lower extremities. Tai Chi Chuan lasted for 60 minutes, divided into 10, 40, and 10 minutes. This long-form Yang style includes 108 slow, soft, and stable movements. In contrast, the Muay Thai aerobic dance lasted for 40 minutes, divided into 10, 20, and 10 minutes. This intervention consisted of 11 and seven movements to exercise the lower and upper extremities, respectively. The 30AC test results of both dance programs indicated that exercising the arm muscles increased the strength of the muscles responsible for elbow flexion, including the biceps brachii.

Four dancing programs showed significantly improved 30CST results: Tai Chi Chuan (from 32.40 ± 4.60 to 32.50 ± 4.7 times),[3] Muay Thai aerobic dance (from 14.8 ± 4.6 to 19.7 ± 6.8 times),[17] Korean traditional dance (from 12.86 ± 1.95 to 26.14 ± 5.27 times),[6] and yoga and Korean dance (from 14.35 ± 3.05 to 19.35 ± 4.60 times).[7] These four programs focused on movements of the upper and lower extremities. Korean traditional dance consisted of 11 moves that lasted 60 minutes, divided into 10, 40, and 10 minutes.[6] Yoga and Korean dance lasted 60 minutes, divided into 5, 50, and 5 minutes. The exercise consisted of 4 positions of static balance (30 minutes) and six classes of dynamic equilibrium (20 minutes).[7] The 30CST test showed that all four dance programs focusing on the exercise of the hip and legs could increase the strength of the leg muscles responsible for hip flexion and extension and the muscles responsible for knee flexion-extension.

Therefore, each dance program helped improve muscle strength among healthy older adults. In addition, dancing increased leg and arm muscle power due to aerobic exercises. Moreover, repetitive movements can increase the endurance and strength of leg and arm muscles, which are linked to motor control and learning based on the following aspects. (1) Cognitive: learning each form of the exercise. (2) Movement: some movements of the dancing exercises may be anti-gravity, such as holding the leg up, resulting in new learning by the motor system. The resulting muscle contractions will help increase muscle strength. (3) Emotion: Before exercising by dancing, warm-up exercises are needed to prepare the muscles and prevent injuries. Moreover, cooling down after a workout relaxes and restores the body to its normal condition by stretching the muscles and slowing breathing.[22] Therefore, dancing exercise in healthy older adults can increase muscle strength and ultimately promote health, maintain good mobility, and reduce the risk of falls.

Static Balance

The analysis of the BBS and the one-leg stand tests by the fixed mean difference showed that "not important" heterogeneity for the BBS ($I^2 = 0\%$; $p = 0.620$) and low heterogeneity for the one-leg stand test ($I^2 = 32\%$; $p = 0.220$).

The BBS, one-leg stance with eyes open and one-leg balance with eyes closed are used to test static equilibrium. The BBS assesses balance by performing 14 rounds of sitting and standing. The one-leg stance with eyes open is used to evaluate balance with eyes open, while the one-leg balance with eyes closed is used to assess balance with eyes closed. Previous studies reported higher scores on these tests after dancing interventions. The BBS resulted in a significant improvement after ancient Thai boxing (from 52.10 ± 5.10 to 54.90 ± 1.50 points)[20] and a trend toward significance after line dancing (from 48.10 ± 7.94 to 50.40 ± 4.56 points).[23] Line dancing requires continuous leg and back movements in addition to weight transfer and posture control to move forward and backward, walk sideways, and turn the body. This dance style starts from easy to complicated movements. It requires 60 minutes, divided into 10, 40, and 10 minutes.[24] The BBS revealed that ancient Thai boxing and line dancing increased static balance. However, while line dancing showed improvement in the BBS, the difference was not statistically significant ($p > 0.05$), likely because the physical activity of line dance exercises did not alter the static balance in short-term studies.[24]

Muay Thai aerobic dance showed significantly improved one-leg stance with eyes open ($p < 0.05$, from 17.70 ± 21.70 to 30.80 ± 30.0 seconds).[17] The difference was higher, although without statistical significance ($p > 0.05$), for Korean traditional dance (from 3.71 ± 1.80 to 5.00 ± 3.46 seconds).[6]

The BBS, the one-leg stance with eyes open, and the one-leg balance with eyes closed improved because dance exercises increase leg and back muscle strength and may also enhance the coordination of the central nervous system, such as the cerebellum, which controls posture.[25]

Dynamic balance

The analysis of UPGO using a fixed standard mean difference showed a medium heterogeneity ($I^2 = 51\%$; $p = 0.110$). These two tests use a similar test method with slightly different measurement distances.

The UPGO is used to test dynamic balance. The TUG assesses emotional balance at a distance of 3 m, while the UPGO assesses dynamic balance at 2.44 m. (1) Tai Chi Chuan showed a significant improvement ($p < 0.05$) (from 19.23 ± 5.31 to 12.63 ± 4.13 seconds), lasting 55 minutes, divided into 5, 35, 5 minutes4); (2) Muay Thai aerobic dance (from 10.6 ± 2.0 to 8.4 ± 2.7 seconds)[17] and (3) ancient Thai boxing exercise (from 9.00 ± 1.70 to 7.50 ± 1.10 seconds) also showed improvements.[20] The UPGO test results were significantly improved ($p < 0.05$) after Tai Chi Chuan (from 4.40 ± 0.60 to 4.30 ± 0.50 seconds).[3]

Dance exercises can increase the strength of the muscles responsible for balance and motion and the nerve signals from the visual system, including postures, movements, and the vestibular system. Dancing could result in a better relationship between exercise and surroundings, allowing for better posture control during movement.[23]

Flexibility

The analysis of the BS and SRT tests using a fixed mean difference showed medium ($I^2 = 56\%$; $p = 0.130$), and not important ($I^2 = 0\%$;

p = 0.930) levels of heterogeneity, respectively.

The BS and SRT tests were used to assess upper and lower body flexibility, respectively.

Korean traditional dance significantly improved the BS test results (from 5.00 ± 1.38 to 10.00 ± 4.40 cm) ($p < 0.01$).[6] While Tai Chi Chuan improved the BS test results, the difference was not statistically significant (from -5.40 ± 12.20 to -5.10 ± 12.10 cm) ($p > 0.05$).[3] Both dance exercises increase upper body flexibility; namely, the muscles around the shoulder joints and arm muscles, as shoulder and arm movements are required to perform these exercises.

Muay Thai aerobic dance significantly improved the SRT test results (from 8.20 ± 6.90 to 10.80 ± 8.20 cm) ($p < 0.05$),[17] while Tai Chi Chuan and Korean traditional dance showed non-statistically significant improvements in SRT test results (Tai Chi Chuan: from 14.70 ± 7.70 to 14.90 ± 7.80 cm,[3] Korean traditional dance: from 28.93 ± 7.25 to 33.14 ± 8.67 cm, $p > 0.05$).[6] These three dance programs increased lower body flexibility; namely, lower back and posterior leg muscles, as these dances require body and leg movements.

Therefore, repetitive movements in each posture cause the muscles to relax. For example, static stretching before and after exercise causes the muscle fibers and tendons to stimulate the Golgi tendon and send signals to the alpha motor neuron, inhibiting muscle activity and inducing muscle relaxation.[24] However, Tai Chi Chuan showed no statistically significant improvement in BS and SRT test values.[3] Additionally, the Korean traditional dance exercises showed no statistically significant improvements in SRT test values.[6] These findings may be the result of complex and unfamiliar exercise postures, which resulted in no statistical differences even after 12 weeks of exercise.

LIMITATIONS

This meta-analysis has several limitations. First, we searched only four electronic databases, which might limit our findings and their generalizability. Future studies should include multiple databases (e.g., Scopus, Web of Science, and Cochrane) to increase the number of primary studies. Second, we focused only on peer-reviewed papers of RCTs assessing the effects of dance programs on physical function. Future studies should consider other study designs (e.g., quasi-experimental study), which might increase the uniqueness of the meta-analysis. Future studies should also include "gray" literature (e.g., unpublished studies, abstracts, or conference proceedings) to provide a balanced review and reduce publication bias. Third, we included only Thai and English languages. Future studies should include other languages in the evaluation of the effects of dance programs on physical function performance in healthy older adults. which may have been omitted. Finally, this study presented the results for various dance programs such as Tai Chi Chuan, Muay Thai aerobic dance, Line dance, Korean traditional dance, and ancient Thai boxing exercises. However, the differences in movements and rhythm, as well as duration may affect the results of the meta-analysis according to the variables, namely muscle strength, static balance, and flexibility. Therefore, research evidence is insufficient based on the analysis of these variables. In addition, the term "physical function" used in the search may be too broad, leading to the inclusion of a limited number of studies in the meta-analysis.

CONCLUSION

The results of the current meta-analysis confirmed that dance programs improve physical performance in healthy older adults. Moreover, these programs are valuable and safe for this population. The evidence in this study tends to support the American College of Sports Medicine. Furthermore, the dance programs resulted in significantly improved physical performance, e.g., muscle strength, static balance, dynamic balance, and flexibility. The programs were effective and safe; hence, they should be used as daily exercise to promote health in healthy older adults. However, this study did not consider older adults with health problems that require local rehabilitation, such as patients with osteoarthritis who cannot lose weight due to knee joints. Water walking is the recommended form of exercise in these patients, as the water helps support the body weight and reduces joint pressure. Therefore, researchers, healthcare providers, and policymakers should establish properly organized dance interventions to improve physical functions in healthy older adults or others according to context and appropriateness.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, SS, NS; Supervision, NS, SW, WS; Writing-original draft, SS; Writing-review & editing, NS, SW, WS.

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Convalescent Plasma in Older Adults with COVID-19: A Systematic Review and Meta-Analysis

I Gusti Putu Suka Aryana[1], Dian Daniella[2], Ivana Beatrice Paulus[3], Sandra Surya Rini[4], Siti Setiati[5]

[1]Division of Geriatrics, Department of Internal Medicine, Faculty of Medicine, Udayana University, Bali, Denpasar, Indonesia
[2]Department of Internal Medicine, Faculty of Medicine, Udayana University, Denpasar, Bali, Indonesia
[3]Wangaya General Hospital, Denpasar, Bali, Indonesia
[4]Department of Internal Medicine, North Lombok Regional Hospital, West Nusa Tenggara, Indonesia
[5]Division of Geriatrics, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

Corresponding Author:
Dian Daniella, MD
Department of Internal Medicine, Faculty of Medicine, Udayana University, Denpasar, Bali 80361, Indonesia
Email: dian.daniella@gmail.com
ORCID:
https://orcid.org/0000-0001-8698-1265

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Background: Among all patients infected with coronavirus disease 2019 (COVID-19), the older adult population was the most affected, with 80%–90% of fatalities occurring in this group. The effectiveness of convalescent plasma (CP) in older adults is considerably more restricted than that in adults, resulting in a demand for data on the efficacy of therapeutic CP in older adults. This meta-analysis of updated literature examined the effect of CP in older adults with COVID-19. **Methods:** Relevant literature was identified from studies indexed in the Cochrane, PubMed, and Google Scholar databases between December 2019 and April 2022. The primary outcome was all-cause mortality. Risk estimates were pooled using a random-effects model. The risk of bias was assessed by regression-based Egger test using the relative risk (RR) and upper and lower confidence intervals (CIs) of the three included studies. **Results:** Among 377 studies identified, three full-text studies that included 1,038 patients met the inclusion criteria. The results of our meta-analysis showed that CP administration lowered the mortality risk in older adults with COVID-19 (RR=0.47; 95% CI, 0.26–0.86; p=0.01; I^2=0%, p<0.81). CP therapy was more useful if delivered early in the course of the disease (within 72 hours of onset) and in less severe stages of the disease. Mortality tended to be lower in the high-titer group. **Conclusions:** CP treatment was significantly associated with a lower risk of mortality in older adults with COVID-19 than in patients not administered CP. The timing of CP administration is critical since earlier treatment after disease onset was associated with a better prognosis.

Key Words: Convalescent plasma, Immunization passive, Elderly, COVID-19, Mortality

INTRODUCTION

The epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that began in the city of Wuhan in the People's Republic of China in late 2019 has affected over 28 million people and caused nearly 900,000 deaths globally. This number has continued to increase, and it is now believed that SARS-CoV-2 has become endemic.[1)] Besides comorbidities, age is a poor prognostic factor in individuals with coronavirus disease 2019 (COVID-19). In Korea and Italy, approximately 80% and 90% of fatalities occurred in patients aged >70 years and 60 years, respectively. Similar patterns were observed in other countries affected by COVID-19.[2)] Older adults with COVID-19 also have a longer hospital stay, increased healthcare costs, and, even if they survive, an altered quality of life.

Age is a significant factor related to COVID-19 severity and clinical manifestations. Older adults with COVID-19 have a higher death rate because of the disease's high case fatality rate and symptomatic infection rate.[2)] Numerous studies have indicated that advanced age is a significant risk factor for COVID-19 mortality. Age

also affects the time between hospitalization and mortality, as well as viral clearance.[3] Inflammaging is a phenomenon in which the presence of systemic basal inflammatory mediators increases with age, regardless of acute immunological assaults. This chronic, low-grade inflammation has been hypothesized to be the cause of several chronic disorders related to aging.[4] Because inflammation is a major pathogenic mechanism in COVID-19, inflammaging may lead to worse prognosis in older adults with COVID-19.[5] Additionally, inflammation plays a significant role in immunosenescence, a term that refers to general changes that occur in the immune system with age, including a decreased ability to fight new infections.[4]

Few therapies for the treatment of COVID-19 are effective; some therapies have been abandoned and others are undergoing evaluation. Several techniques have been investigated, including the administration of particular antibodies found in convalescent plasma (CP).[6] While several meta-analyses investigating the benefits of CP in adults have failed to demonstrate its efficacy in decreasing death rates, the meta-analysis by Klassen et al.[7] demonstrated a lower death rate among CP-transfused patients with COVID-19 than among non-CP-transfused patients with COVID-19. The effectiveness of CP in older adults is considerably less studied than that in adults, resulting in a high demand for the evidence of the efficacy of therapeutic COVID-19 CP in older adults. Consequently, there remains a lack of consensus regarding the use of CP in older patients with COVID-19. Thus, we conducted this systematic review and meta-analysis to assess the existing data and provide evidence of the efficacy of CP for older adults with COVID-19. We also provided an overview of the prospective advantages of CP therapy in older adults with COVID-19.

MATERIALS AND METHODS

Eligibility Criteria

We included all research articles analyzing the outcomes of CP use in older adults with COVID-19. We independently screened eligible publications based on the following inclusion criteria: older adults with COVID-19, English language, and original articles. We excluded non-research articles (e.g., case reports or series, review articles, letters to the editor, study protocols, editorials, or commentaries) and studies with insufficient data.

Search Strategy and Study Selection

We performed this meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[1] We systematically searched the PubMed, Directory of Open Access Journal, and Cochrane Central Register of Controlled Trials databases using the search terms ("Coronavirus Disease 2019" OR "COVID-19" OR "novel coronavirus pneumonia" OR "2019-nCoV" OR "SARS-CoV-2") AND ("older adults") AND ("convalescent plasma") on January 30, 2021. The full search terms are presented in Supplementary Table S1. Duplicate results were excluded. We independently screened the abstracts of the remaining articles for relevance. We then read the remaining articles to include those that fulfilled our criteria. The final inclusion of the studies was based on the agreement of all authors. Any disagreement between the authors was resolved by consensus. We assessed the full texts of the remaining articles according to the inclusion and exclusion criteria and evaluated the quality of the observational cohort studies using the Newcastle-Ottawa Quality Assessment Scale. Study quality was categorized as poor (score 0–3), fair (score 4–6), or high (score 7–9). We assessed randomized controlled trials (RCTs) using a checklist guide from the Center of Evidence-Based Medicine.

Data Extraction

All authors independently performed data extraction using standardized forms that included the author, year of study, study design, country of study, number of samples, location of study, age, method of CP administration, and outcome. Disagreement among authors was addressed using a protocol for discussion to achieve agreement. The outcome of this study was mortality.

Definitions of Older Adults, COVID-19, and CP

Older adults were defined as those aged ≥ 65 years.[2] COVID-19 positivity was defined as a nasopharyngeal swab positive for SARS-CoV-2 by polymerase chain reaction assay. Standard care was provided to each patient based on the standard protocol of the respective centers. The convalescent plasma administration protocols were performed in the respective centers. The volume varied between 250 mL and 300 mL among studies based on patient clinical responses.

Statistical Analysis

We used Review Manager 5.4.1 (https://training.cochrane.org/online-learning/core-software/revman) and Stata version 16 (StataCorp LLC, College Station, TX, USA) to perform the meta-analysis. The effects of CP administration on mortality in older adults with COVID-19 were presented as relative risks (RRs). We calculated dichotomous variables using the Mantel–Haenszel formula. The RR was reported with a 95% confidence interval (CI) for dichotomous variables. The p-value was two tailed, and statistical significance was set at $p < 0.05$.

We assessed heterogeneity using the Q-statistic and I^2 tests. The

I^2 statistic measured the percentage of total variation across the studies due to clinical or methodological heterogeneity rather than chance. We applied a random-effects model in the analysis to better represent the population. To the assess small-study effect and publication bias, we performed a regression-based Egger test.[3] We did not perform a funnel plot analysis owing to the limited number of studies.

Ethics Approval and Consent to Participate

Ethical statements and consent for publication were not applicable to this review and meta-analysis. Our study is registered in PROSPERO (ID: CRD42022312006) and complied with the ethical guidelines for publication.[8]

This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[9]

RESULTS

Baseline Characteristics and Study Selection

The qualitative and quantitative syntheses (meta-analysis) included 1,038 patients from three studies (Fig. 1).[1,6,10] The characteristics of the included studies are presented in Table 1. The critical appraisals for each study are presented in Table 2. Two studies were observational, while one was a randomized, double-blind, placebo-controlled trial. Male patients comprised 46.89% of the study participants. The lowest mean age reported in the studies was 77.2 ± 8.6 years.[6]

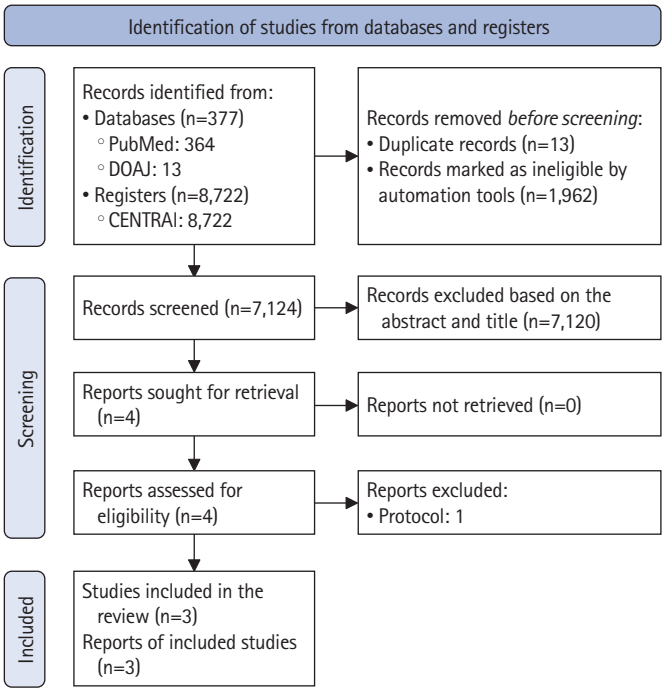

Fig. 1. Flowchart of the search strategy.

Table 1. Demographic and clinical characteristics of the included studies

Study	Year	Design	Country	Sample		Age (y)		Time administration	Volume and titer CP administration	Outcome
				Total	CP vs. control	Total	CP vs. control			
Franchini et al.[1]	2021	Observational	Italy	755	22 vs. 733	87 (82–90)	N/A	7 (4.5–8) days after symptoms	1 to 3 units of CP (300 mL per unit) (≥ 1: 160)	Mortality rates at 28 days and at the end of follow-up: 66 (48–80) days
Libster et al.[6]	2021	Randomized, double-blind, placebo-controlled trial	Argentina	160	80 vs. 80	77.2 ± 8.6	76.4 ± 8.7 vs. 77.9 ± 8.4	< 72 hours after symptoms	250 mL of CP (> 1:1000)	In-hospital mortality
Romon et al.[10]	2021	Observational	Spain	123	41 vs. 82	86.7 ± 5.02	86.7 ± 5.02 vs. 85.9 ± 4.39	7 (4–10) days after symptoms	300 mL of CP (low titer, < 1: 250; high titer, > 1: 250)	In-hospital mortality

Values are presented as median (interquartile range) or mean±standard deviation.
CP, convalescent plasma.

Table 2. Critical appraisal using the Newcastle-Ottawa Quality Assessment Scale (NOS) for the included studies

Study	Design	Selection	Comparability	Outcome	Validity	Importance	Applicability
Franchini et al.[1]	Observational	***		***			
Romon et al.[10]	Observational	****	*	***			
Libster et al.[6]	RCT				(+)	(+)	(+)

RCT, randomized controlled trial.
*, one point on NOS Scale. ***, three points on NOS Scale. ****, four points on NOS Scale. (+), yes.

The inclusion criteria differed among studies. Franchini et al.[1] included older adults with COVID-19 in a long-term care facility, in which 31.8% and 48.2% had moderate and severe COVID-19, respectively. Libster et al.[6] included patients with at least one of each sign or symptom in the following two categories for <48 hours: a temperature of at least 37.5°C, unexplained sweating, or chills and dry cough, dyspnea, fatigue, myalgia, anorexia, sore throat, dysgeusia, anosmia, or rhinorrhea. Romon et al.[10] included all adult patients with COVID-19 with radiologically confirmed pneumonia according to the criteria of the patient's physician and ability to receive standard treatment.

The methods of CP administration differed among studies. Franchini et al. provided the number of units of CP based on patient clinical response. Fifteen, six, and one patient received one, two, and three CP units, respectively. The median interval between the first and second CP administrations was 3 days (interquartile range [IQR], 3–12 days). The third CP unit was administered 3 days after the second CP unit.[1]

CP Administration and Patient Mortality

CP administration lowered mortality risk in older adults with COVID-19 (RR=0.47; 95% CI, 0.26–0.86; p=0.01; I^2=0%, p<0.81) (Fig. 2).

We also assessed the effects of CP administration on oxygen saturation, intensive care unit (ICU) admission, and length of stay as secondary outcomes; however, we did not carry out meta-analysis analysis because of the limited number of studies and lack of data. The following sections describe the outcomes.

Patient oxygen saturation increased after CP administration from 93% (91%–95%) to 96% (95%–97%; p<0.01) on day 3, 97% (95–97%; p<0.001) on day 7, and 98% (97%–98%; p<0.001) on day 14.[1] Severe respiratory disease developed in 13 patients (16%) in the CP group and 25 patients (31%) in the placebo group (RR=0.52; 95% CI, 0.29–0.94; p=0.03).[6]

Although Libster et al.[6] observed less severe respiratory disease in the CP group, Romon et al.[10] reported that ICU admission and length of stay did not differ between the CP and control groups. Two patients (4.9%) in the CP group and seven patients (8.5%) in the control group were admitted to the ICU (p=0.467). The median lengths of stay in the CP and control groups were 11 (9–16) and 11 (7.5–16) days, respectively (p=0.073).[10]

Publication Bias

We analyzed publication bias with a regression-based Egger test using the RR, upper CI, and lower CI of the three included studies. The regression-based Egger test showed no small-study effects (p=0.810).

DISCUSSION

Compared to without CP, CP treatment was significantly related to a lower risk of mortality in older adults with COVID-19 (RR=0.47; 95% CI, 0.26–0.86; p=0.01; I^2=0%, p<0.81). To date, few meta-analyses have investigated the effects of CP in older adults. Kloypan et al.[11] reported that CP significantly lowered the chance of all-cause mortality by 31% compared to usual therapy (pooled RR=0.69; 95% CI, 0.56–0.86; p=0.001; I^2=50.1%) in 47 patients; however, they included all adult populations and not specifically older adults. In contrast, in their meta-analysis, Janiaud et al.[12] reported that CP therapy had no meaningful effect on all-cause mortality or any other clinical outcomes in patients with COVID-19. Across all 10 RCTs, the summary RR was 1.02 (95% CI, 0.92–1.12). These contradictory results were most likely caused by differences in the time of administration, disease severity, and titer level. Several studies have demonstrated that the potential of CP to inhibit the course of COVID-19 is time dependent. Early (within 72 hours) delivery of high-titer CP to older adults with mild COVID-19 slowed disease progression. Early treatment resulted in reduced progression of the disease of 40%–60% compared to control.[1] In one study of patients in Houston, mortality was lower only among those who received CP within 72 hours of admission.[13] Moreover, a large multicenter study in the United States demonstrated lower 7-day mortality among hospitalized patients who received transfusions within 72 hours of diag-

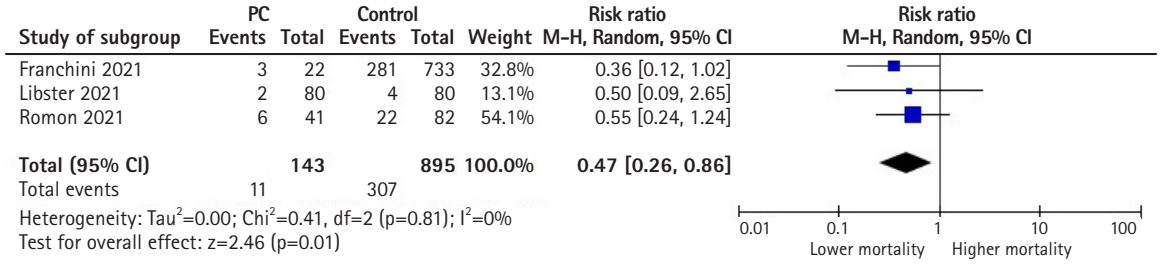

Fig. 2. Forest plot and relative risk for the association of convalescent plasma administration with mortality in older adults with COVID-19.

nosis than among those who received transfusions later.[14]

While more participants in the study by Libster et al.[6] showed relative mortality risk reduction of 48%, the trial administered 250 mL of CP with an IgG titer > 1:1000 within 72 hours after the onset of mild COVID-19 symptoms. The results of this trial demonstrated a dose-dependent IgG effect in CP infusions. Plasma with IgG titers of 1:3200 or higher reduced the risk of severe respiratory disease by 73%.[6] Similarly, Romon et al.[10] reported in-hospital mortality rates of 26.8% for controls and 14.6% for patients administered CP ($p = 0.131$). Moreover, the ICU admission rates were 8.5% and 4.9%, respectively ($p = 0.467$). Mortality tended to be lower in the high-titer group (9.5%) than in the low-titer group (20%) and in patients transfused within the first 7 days of symptom onset (10%) than in patients transfused later (19.1%).[10]

Franchini et al.[1] reported that 22 patients with COVID-19 were transfused with 30 CP units (median 1; IQR 1–2): 15 patients (68.2%) with one CP unit, six (27.3%) with two CP units, and one (4.5%) with three CP units. Each unit contained 300 mL. Seven CP units (23.3%) had a neutralizing antibody titer of 1:80, 18 (60.0%) had a titer of 1:160, and five (16.7%) had a titer of 1:320. The median interval between symptom onset and the first CP transfusion was 7 days (IQR 4.5–8 days). This study reported a significantly overall mortality rate of 13.6% (3/22) compared to the control group—38.3% (281/733), $p < 0.02$, corresponding to a 65% reduction in mortality risk.[1] Several parameters showed varying decreases in all tests performed (white blood cell, lymphocyte, and platelet counts and aspartate aminotransferase, alanine aminotransferase, ferritin, IL-6, CRP, lactate dehydrogenase, and D-dimer levels) during follow-up. In particular, ferritin levels decreased by 24% and 44% on days 3 and 14, respectively, following CP infusion. Similarly, IL-6 concentration decreased by 29% and 56%.[1]

CP collected from patients who have recovered COVID-19 and with humoral immunity against the virus includes many antibodies that can neutralize SARS-CoV-2 and eliminate the pathogen from blood circulation and pulmonary tissues.[11,15] In older adults who are severely or critically ill, lung alveoli macrophages or epithelial cells can release large amounts of pro-inflammatory cytokines and chemokines, which attract monocytes and neutrophils to the infection site to remove the virus and infected cells, resulting in uncontrolled inflammation. This results in increased macrophage infiltration and consequently, reduced lung function. Thus, the most important aspect of CP is that antibodies can kill or stop SARS-CoV-2 and prevent viral replication.[11] In patients with COVID-19, including immunocompromised people, CP treatment enhances SARS-CoV-2 clearance, indicating an antiviral effect. Viral neutralization is hypothesized to suppress the inflammatory response, thereby decreasing the risk of excessive immune response and preventing lung injury, disruption of gas exchange, and mortality.[7] Antibody-mediated interference with viral replication could lead to increased tissue repair and lower mortality. In addition, patients who received CP transfusions expressed fewer inflammatory markers, such as chemokines, IL-6, and CRP.[16]

Although our meta-analysis did not specifically analyze oxygen saturation and ICU length of stay owing to limited study findings, we aimed to describe how CP administration might also help enhance oxygen saturation and decrease the duration of ICU stay. Oxygen saturation improved following CP injection, from 93% (91–95%) to 96% (95–97%; $p < 0.01$) on day 3, 97% (95–97%; $p < 0.001$) on day 7, and 98% (97–98%; $p < 0.001$) on day 14.[1] Severe respiratory disease developed in 13 patients (16%) in the CP group and 25 patients (31%) in the placebo group (RR = 0.52; 95% CI, 0.29–0.94; $p = 0.03$).[6] This finding is also consistent with that reported by Allahyari et al.[17] who found that CP administration dramatically improved oxygen saturation and ameliorated acute respiratory distress syndrome (ARDS) when administered early in the disease course. They also reported that patients with mild ARDS administered CP ($PaO_2/FiO_2 > 200$ and < 250) recovered significantly more quickly than healthy control ($p = 0.046$). While the proportion of discharged patients with moderate ARDS ($PaO_2/FiO_2 \geq 100$ and ≤ 200) was similarly higher in the plasma group (55.6 % vs. 33.3 % in the control group), the difference was not statistically significant. Both groups discharged the same number of patients with severe ARDS ($PaO_2/FiO_2 < 100$) (1 of 4 patients, 25%). Therefore, CP therapy may be more useful if delivered early in the course of the disease and before the patient become critically ill, thus bolstering the concept of CP efficacy in less severe stages of the disease.

The impact of timing of administration on outcomes may be due to macrophage activation. Older adults with COVID-19 may experience higher macrophage activation and innate immune cell migration to lung tissues, resulting in more severe inflammation and pulmonary injury. Inhibition of this system may help prevent cytokine storms and lung injury. This was also reinforced by a recent study that reported increased chemokines for innate immune cells in patients with COVID-19 within the first 7 days of infection.[18] Furthermore, in the absence of an acute injury, aged individuals have a higher stage of inflammation. Therefore, providing CP in the early stages of illness may minimize the degrees of systemic inflammation and cytokine storm.

Romon et al.[10] reported that ICU admission and length of stay did not differ between the CP and control groups. Two patients (4.9%) in the CP group and seven patients (8.5%) in the control group were admitted to the ICU ($p = 0.467$). The median lengths

of stay in the CP and control groups were 11 (9–16) and 11 (7.5–16) days, respectively ($p = 0.073$). This lack of difference was most likely due to the late administration of CP in their trial. The median times between symptom onset and hospitalization to CP administration were 7 days (IQR 4–10) and 1 day (IQR 0–2), respectively. A previous study suggested that the early administration of CP based on symptoms and less severe disease may have a greater effect on CP therapy. Abolghasemi et al.,[19] reported that CP transfusion within 3 days of hospitalization resulted in a greater overall proportion of patients (98.2%) who were discharged compared to Allahyari et al.,[17] in which a median time from symptoms to CP administration of 4.41 days showed a lower percentage of patients who recovered and were discharged (78.1%). Thus, CP transfusion improved patient clinical outcomes by reducing the duration of stay in the hospital, the requirement for non-invasive mechanical ventilation and intubation, and the fatality rate.

This meta-analysis had some limitations. First, some studies were observational cohorts that provided weaker strength of evidence compared to RCTs. Second, the limited number of studies may have produced false-positive results. Third, we did not consider comorbidities in predicting the mortality risk. However, older adults often have multiple comorbidities that affect mortality risk.

In conclusion, compared to patients not administered CP, CP treatment was significantly associated with a lower risk of mortality in older adults with COVID-19. The timing of CP administration is critical since earlier onset of disease are associated with better prognosis.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, IGPSA, DD, IBP, SSR; Methodology, IGPSA, DD, IBP, SSR; Formal analysis, IGPSA, DD, IBP, SSR; Investigation, IGPSA, DD, IBP, SSR; Data curation, IGPSA, DD, IBP, SSR; Writing-original draft, IGPSA, DD, IBP, SSR; Writing-review & editing, IGPSA, DD, IBP, SSR, SS.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.22.0045.

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Calf Circumference Measurement Protocols for Sarcopenia Screening: Differences in Agreement, Convergent Validity and Diagnostic Performance

Melissa Rose Berlin Piodena-Aportadera[1], Sabrina Lau[1,2], Justin Chew[1,2], Jun Pei Lim[1,2], Noor Hafizah Ismail[2,3], Yew Yoong Ding[1,2], Wee Shiong Lim[1,2]

[1]Department of Geriatric Medicine, Tan Tock Seng Hospital, Singapore
[2]Institute of Geriatrics and Active Aging, Tan Tock Seng Hospital, Singapore
[3]Department of Continuing and Community Care, Tan Tock Seng Hospital, Singapore

Corresponding Author:
Wee Shiong Lim, MBBS, MRCP, MMed, MHPEd, AGSF, FAMS
Department of Geriatric Medicine, Institute of Geriatrics and Active Aging, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Novena, Singapore 308433
E-mail: wee_shiong_lim@ttsh.com.sg
ORCID:
https://orcid.org/0000-0003-3975-7230

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Background: Although recommended by the Asian Working Group for Sarcopenia 2019 consensus (AWGS'19) as a screening tool for sarcopenia, there remains no consensus regarding the position (sitting, standing) or laterality (right, left) for the measurement of calf circumference (CC). This study aimed to determine the agreement between CC measurements, correlations with muscle mass and function, and diagnostic performance for sarcopenia screening. **Methods:** We studied 176 healthy community-dwelling older adults (mean age, 66.8±7.1 years) from the GERILABS-2 study. CC was measured using non-elastic tape in four ways: left and right sides in the sitting and standing positions. Sarcopenia was diagnosed using the AWGS'19 criteria. We produced Bland-Altman plots to assess the agreement, partial correlations for muscle mass and function to compare convergent validity, and area under the receiver operating characteristic curve (AUC) to compare diagnostic performance. **Results:** The prevalence rate of sarcopenia was 17.4%. Sitting CC was larger than standing regardless of laterality (right 35.31±2.95 cm vs. 34.61±2.74 cm; left 35.37±2.96 cm vs. 34.70±2.83 cm; both $p<0.001$), consistent with the systematic bias on Bland-Altman plots showing the overestimation of sitting over standing measurements (right bias=0.70 cm; 95% confidence interval [CI], -0.48–1.88; left bias=0.67 cm, 95% CI, -0.35–1.68). After adjusting for age and sex, CC was significantly correlated with appendicular skeletal mass, hand grip strength, knee extension, gait speed, chair stand, and short physical performance battery. Although right-sided CC measurements had better diagnostic performance (AUC=0.817), the difference was not statistically significant compared to the other positions ($p>0.05$). The optimal cutoff was <34 cm for all measurements, except for the left standing position (cutoff <35 cm). **Conclusion:** Standing CC measurements are recommended for sarcopenia screening in community-dwelling older adults because of their good agreement without systematic bias, convergent validity, and diagnostic performance.

Key Words: Sarcopenia, Screening, Protocol

INTRODUCTION

Sarcopenia is a geriatric syndrome characterized by age-related loss of muscle mass, impaired muscle strength, and physical performance.[1] Sarcopenia is highly prevalent, especially in older men, and results in an increased risk of frailty and negative outcomes including disability, falls, and mortality.[2] Given the implications for disease burden and public health, early detection by screening for individuals at risk in the community or primary care setting is a priority.[3] Calf circumference (CC) is recognized by the Asian Working Group for Sarcopenia 2019 consensus (AWGS'19)[1] and the World Health Organization[4] as a marker of muscle mass in

older adult individuals. The results from different studies support the utility of CC as a surrogate marker for muscle mass measurement.[5-8] CC shows a good correlation with measurements of skeletal muscle mass using dual-energy X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA)[6] and moderate to high sensitivity and specificity in predicting sarcopenia.[5,7,8] In addition, CC predicts the disability risk in older adults.[9] Unsurprisingly, the AWGS'19 recommended CC as a screening tool for sarcopenia in the community setting.[6,8,10]

At present, there is wide variation in how CC is measured for sarcopenia screening due to the heterogeneity in measurement protocols. While the AWGS'19 recommends measuring the maximum value of both calves using a non-elastic tape, it offers no specific guidance on the position (standing vs. sitting) and laterality (left vs. right) for measurement. In terms of position, several studies[10-13] have used the sitting position, similar to the Mini Nutritional Assessment (MNA) protocol, to assess the risk of malnutrition,[14-16] albeit using higher cut-offs than the MNA for sarcopenia screening. Other studies have used the standing position,[6,7,17] consistent with recommendations from the International Society for the Advancement of Kinanthropometry (ISAK).[18] While there is a consensus to measure CC at the widest part of the calf, there is less guidance in terms of laterality. Some studies specifically measured the non-dominant calf,[11,12] while others used the average calf measurements[6,7] or the maximum value of both calves according to the AWGS'19 recommendations.[5,13,19]

Thus, there is currently a lack of agreement regarding the position (standing or sitting) and laterality (right or left) in CC measurement protocols for sarcopenia screening. It is unclear whether the lack of standardization in measurement protocols leads to systematic differences that can affect the reliability and validity of the readings. Currently, there is a paucity of studies directly comparing different CC measurement protocols. A recent Korean study reported a larger area under the curve in receiver operating characteristic analysis for CC measurements in the standing position compared to sitting for sarcopenia diagnosis.[19] The authors concluded that CC measurement on either side in the standing posture, regardless of the dominant hand, was an optimal method for screening for sarcopenia among community-dwelling older adults. However, the study did not compare the agreement or construct validity between the different CC measurement protocols.

As CC measurement is a simple and easy-to-use tool that can serve as a proxy for expensive and non-accessible diagnostic imaging modalities to assess muscle mass, knowledge of the ideal protocol to measure CC is essential for standardized measurements to ensure the reliability and accuracy of sarcopenia screening. Therefore, the primary aim of the present study was to determine the agreement between four different CC measurements (right standing, right sitting, left standing, and left sitting). The secondary aims were to compare the convergent validity via correlation with muscle mass and function and the diagnostic performance for sarcopenia screening among healthy community-dwelling older adults.

MATERIALS AND METHODS

Study Population

This cross-sectional study included 176 participants from the "Longitudinal Assessment of Biomarkers for characterization of early Sarcopenia and Osteosarcopenic Obesity in predicting frailty and functional decline in community-dwelling Asian older adults Study" (Geri-LABS-2). The details of this study were described previously.[20] In brief, the Geri-LABS-2 is a prospective cohort study with an annual follow-up of 230 healthy community-dwelling older adults aged 50–99 years who are functionally independent in both basic and instrumental activities of daily living (bADL and iADL), have no history of dementia or cognitive impairment (modified Chinese Mini-Mental State Examination [mCMMSE] score < 21),[21] and can walk 8 m independently. For the study duration (between September 1, 2020, and April 30, 2021), we contacted 211 participants for a second follow-up visit, of which 35 (16.6%) declined. Thus, our study comprised 176 (83.4%) participants who completed the assessments during the second follow-up visit. Written informed consent was obtained from the participants in the presence of a trained research assistant. This study was approved by the Institutional Review Board of the National Healthcare Group (No. NHG DSRB 2017/00850).

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

Data Collection

We collected baseline demographic information, including age, sex, ethnicity, and cardiovascular risk factors (hypertension, hyperlipidemia, diabetes, ischemic heart disease, atrial fibrillation, stroke or transient ischemic attack, and smoking). Anthropometric measurements, including weight, height, body mass index (BMI), and CC, were recorded. We assessed cognition using the locally validated mCMMSE,[21] mood using the 15-item Geriatric Depression Scale (GDS),[23] and nutritional status using the MNA.[14-16] Functional status was assessed using the Modified Barthel Index (MBI)[24] for bADL, Lawton and Brody's Index for iADL,[25] and the Frenchay Activities Index for everyday activities.[26] Frailty and sarcopenia were assessed using FRAIL[27] and SARC-F,[28] respec-

tively.

We measured relative appendicular skeletal mass (ALM) using multi-frequency bioimpedance analysis (InBody 770; InBody, Seoul, Korea). Fat-free lean body mass in the four limbs was summed and standardized using the square of the height to obtain the relative appendicular skeletal mass. Muscle function was assessed based on muscle strength and physical performance. For muscle strength, we measured the maximum hand grip strength using a hydraulic hand dynamometer (North Coast Medical Inc., Gilroy, CA, USA) and knee extension strength using an electronic push/pull dynamometer (BASELINE 12-0342; Fabrication Enterprises Inc., White Plains, NY, USA).[29] For physical performance, we assessed the usual gait speed based on the time taken to walk 3 m and also measured the time taken to perform five chair stands with a sitting stop. The Short Physical Performance Battery (SPPB),[30] a three-component test comprising balance, gait speed, and repeated chair stands, was administered as a gauge of overall physical performance. Sarcopenia was defined using the AWGS'19 criteria as follows: (1) low muscle mass (< 7.0 kg/m^2 in male and < 5.7 kg/m^2 in female); along with (2) low handgrip strength (< 28 kg in male and < 18 kg in female) and/or slow usual gait speed (< 1.0 m/s).[1]

Calf Circumference Measurement

We conducted four CC measurements: right-standing, right-sitting, left-standing, and left-sitting. Three trained research assistants performed the CC measurements in a standardized manner. The widest part of the calf was measured using a non-elastic tape. The tape was snugly applied flat on the skin and parallel to the floor in, taking care not to compress the calf. Sitting CC was first measured with the knee and ankle bent at a right angle and the feet flat on the floor. Standing CC was then measured with the feet at a shoulder-width distance for equal distribution of body weight. Altogether, we obtained four readings: the left and right sides in the sitting and standing positions, respectively.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). Statistical tests were two-tailed, with the level of significance set at 5%. Quantitative or continuous variables are expressed as mean ± standard deviation or median (interquartile range). Categorical variables are expressed as absolute and relative frequencies and percentages. We first performed paired t-tests to compare CC measurements according to position (standing and sitting) and laterality (right and left). We then constructed Bland-Altman plots to determine the agreement between the CC measurements. Systematic bias was calculated as the mean difference between the methods, and the 95% limits of agreement were calculated as the bias ± 2 SD for the differences between the methods. To ascertain the construct validity of the different CC measurements, we determined the partial correlation with relative appendicular skeletal mass and muscle function, adjusted for age and sex.

To compare diagnostic performance, we generated receiver operating characteristic (ROC) curves against the AWGS'19 criteria for sarcopenia as the reference standard. The area under the ROC curves (AUCs) were compared using the DeLong method. We determined the optimal cut-off value using the Youden method and derived the corresponding sensitivity, specificity, positive predictive value, and negative predictive value (NPV). We then performed a sex-stratified analysis to obtain the corresponding values for male and female.

We used MedCalc for Windows, version 21.111 (MedCalc Software, Ostend, Belgium) to calculate the sample size based on the evaluation of the Bland-Altman plot between sitting and standing CC measurements. We estimated that a sample size of 155 paired results would provide 80% power to detect a mean difference of 0.46 ± 0.4 with a maximum allowed difference between methods of 1.4, at an alpha level of 0.05. This yielded a final sample size of 172 participants, to accommodate a dropout rate of 10%.

RESULTS

Baseline Characteristics

We studied 176 community-dwelling older adults with a mean age of 66.8 ± 7.1 years (male, 69.3 years; female, 64.8 years) who were predominantly Chinese (94.3%) (Table 1). The most prevalent cardiovascular risk factors were hyperlipidemia (61.4%), hypertension (34.1%), and diabetes (12.5%). The participants were cognitively and functionally intact (CMMSE, 26.49 ± 1.47; MBI, 100 (95–100); Lawton & Brody's Index for iADLs: 23 (22–23), with no significant depressive symptoms (GDS, 1.38 ± 1.71) or malnutrition (MNA, 27.5 ± 1.7). The prevalence of sarcopenia was 17.4% based on the AWGS'19 criteria. The CC measurements ranged from 34.61 to 35.37 cm, with male having higher readings than female. Although most participants were right-handed (92.6%), the left CC measurements were higher than the right CC measurements, regardless of position.

Agreement between CC measurements

The sitting CC measurements were larger than the standing CC measurements regardless of laterality—right-sitting 35.31 ± 2.95 cm vs. right-standing 34.61 ± 2.74 cm ($p < 0.01$); left-sitting 35.37 ± 2.96 cm vs. left-standing 34.70 ± 2.83 cm ($p < 0.01$) (Table 2). For male,

Table 1. General characteristics

Variable	Total (n = 176)	Male (n = 48)	Femalen (n = 128)	p-value
Demographics				
Age (y)	66.8 ± 7.1	69.3 ± 6.7	64.8 ± 7.0	0.950
Race				0.106
Chinese	166 (94.3)	43 (89.6)	123 (96.1)	
Malay	2 (1.1)	1 (2.1)	1 (0.8)	
Indian	6 (3.4)	2 (4.2)	4 (3.1)	
Others	2 (1.1)	2 (4.2)	0 (0)	
Cardiovascular risk factors				
Hypertension	60 (34.1)	20 (41.7)	40 (31.3)	0.194
Hyperlipidemia	108 (61.4)	28 (58.3)	80 (62.5)	0.613
Diabetes	22 (12.5)	8 (16.7)	14 (10.9)	0.306
Ischemic heart disease	3 (1.7)	2 (4.2)	1 (0.8)	0.122
Atrial fibrillation	5 (2.8)	2 (4.2)	3 (2.3)	0.517
Stroke/TIA	5 (2.8)	1 (2.1)	4 (3.1)	0.711
Smoking	3 (1.7)	2 (4.2)	0 (0)	< 0.001*
Cognition and mood				
CMMSE (0–28)	26.49 ± 1.47	26.58 ± 1.28	26.46 ± 1.55	0.333
GDS (0–15)	1.38 ± 1.71	1.23 ± 1.25	1.44 ± 1.85	0.119
Functional ability				
bADL (0–100)	100 (95–100)	100 (100–100)	100 (95–100)	0.050
iADL (0–23)	23 (22–23)	23 (22–23)	23 (22–23)	0.841
FAI (0–45)	30.90 ± 4.69	29.92 ± 5.28	31.28 ± 4.44	0.153
Nutritional status				
MNA (0–30)	27.5 ± 1.7	27.6 ± 1.6	27.5 ± 1.8	0.596
Frailty and sarcopenia				
FRAIL score (0–5)	0 (0–1)	0 (0–1)	0 (0–1)	0.986
SARC-F score (0–5)	0 (0–1)	0 (0–1)	0 (0–1)	0.004*
Sarcopenia, AWGS'19	40 (17.4)	13 (27.1)	27 (21)	0.323
Anthropometric measurements				
Weight (kg)	58.29 ± 9.35	64.53 ± 9.58	56.05 ± 8.21	0.245
Height (cm)	1.57 ± 0.08	1.66 ± 0.07	1.54 ± 0.05	0.004*
BMI (kg/m^2)	23.48 ± 3.32	23.42 ± 3.49	23.50 ± 3.28	0.817
Calf circumference (cm)				
Right standing	34.61 ± 2.74	35.28 ± 2.81	34.37 ± 2.67	0.344
Right sitting	35.31 ± 2.95	36.00 ± 3.02	35.05 ± 2.89	0.462
Left standing	34.70 ± 2.83	35.60 ± 3.20	34.36 ± 2.62	0.064
Left sitting	35.37 ± 2.96	36.23 ± 3.29	35.05 ± 2.78	0.104
Handedness				0.317
Right	163 (92.6)	46 (95.8)	117 (91.4)	
Left	13 (7.4)	2 (4.2)	11 (8.6)	

Values are presented as mean±standard deviation or median (interquartile range) or number (%).
TIA, transient ischemic attack; CMMSE, Chinese Mini Mental Status Examination; GDS, Geriatric Depression Scale; bADL, basic activities of daily living; iADL, instrumental activities of daily living; FAI, Frenchay Activities Index; MNA, Mini-Nutritional Assessment; AWGS, Asian Working Group for Sarcopenia; BMI, body mass index.
* $p<0.01$.

Table 2. Comparison between calf circumference measurements in different positions

	Total			Male			Female		
	Right (cm)	Left (cm)	p-value[a)]	Right (cm)	Left (cm)	p-value[a)]	Right (cm)	Left (cm)	p-value[a)]
Standing	34.61 ± 2.74	34.70 ± 2.83	0.137	35.28 ± 2.81	35.60 ± 3.20	0.011*	34.37 ± 2.67	34.36 ± 2.62	0.972
Sitting	35.31 ± 2.95	35.37 ± 2.96	0.407	36.00 ± 3.02	36.23 ± 3.29	0.053	35.05 ± 2.89	35.05 ± 2.78	0.913
p-value[b)]	< 0.01	< 0.01		< 0.01	< 0.01		< 0.01	< 0.01	

[a)]Paired t-test, comparing right and left calf circumferences in the same position.
[b)]Paired t-test, comparing standing and sitting calf circumferences on the same side.
*p<0.05.

the right-standing CC was slightly smaller than the left-standing CC (35.28 ± 2.81 cm vs. 35.60 ± 3.20 cm; p = 0.011). We observed no significant differences in CC measurements based on laterality in the standing position for female and the sitting position for both male and female.

Fig. 1A–1D show the Bland-Altman plots comparing the agreements between CC measurements in the standing and sitting positions. The agreement was affected by position (standing vs. sitting) on both sides. We observed a systematic bias, with an overestimation of CC values in sitting compared to standing positions for both sides—right-sitting vs. right-standing (bias = 0.70 cm; 95% confidence interval [CI], -0.48–1.88); left-sitting vs. left-standing (bias = 0.67 cm; 95% CI, -0.35–1.68).

Conversely, we observed no evidence of systematic bias for right vs. left sides in both sitting and standing positions—right vs. left-standing (bias = -0.09 cm; 95% CI, -1.66–1.48); right vs. left-sitting (bias = -0.06 cm; 95% CI, -1.89–1.77).

Correlations of CC Measurements with Muscle Mass and Function

Table 3 shows the correlations of CC measurements with muscle mass and function. Adjusted for age and sex, CC showed significant correlations, including a good correlation for relative appendicular skeletal mass (r = 0.640 to 0.677, p < 0.05), a modest correlation for hand grip strength (r = 0.317 to 0.346, p < 0.01), and weak correlations for knee extension (r = 0.204 to 0.236, p < 0.01), gait speed (r = -0.048 to -0.078, p > 0.05), chair-stand (r = 0.161 to 0.194, p < 0.05), and SPPB (r = -0.196 to -0.240, p < 0.05).

Diagnostic Performance for Sarcopenia Screening

The diagnostic performance did not differ significantly between CC measurements in the standing and sitting positions (right AUC = 0.817 vs. 0.816, p = 0.904; left AUC = 0.790 vs. 0.786, p = 0.696) (Table 4). Similarly, although right-sided measurements had better diagnostic performance, the difference in AUCs was not significant (p > 0.05). Standing CC measurements had higher sensitivity and NPV compared to sitting CC regardless of laterality (right sensitivity = 85.0% vs. 75.0%, NPV = 93.3% vs. 90.7%; left sensitivity = 92.5% vs. 72.5%, NPV = 96.0% vs. 89.5%). The optimal cutoff was < 34 cm for all measurements, except for the left standing position (cutoff < 35 cm). In sex-stratified analyses, the left-standing position had the highest AUC in male compared to the right-standing position in female. The optimal cut-off was < 35 cm in all positions except right-standing (< 34 cm) for male, whereas the optimal cut-off was < 34 cm in all positions for female.

DISCUSSION

Despite being recommended by the AWGS'19 as a screening tool for community screening for sarcopenia, the methods for CC measurement vary widely. To our knowledge, this is the first study to directly compare different CC measurement protocols across the comprehensive domains of agreement, construct validity, and diagnostic performance for sarcopenia screening. Our results were based on an earlier comparative study by Jeong et al.,[19] which highlighted the importance of measurement position (standing vs. sitting) in CC-based screening for sarcopenia in the community setting (Table 5). Our demonstration of the systematic overestimation of sitting measurements supports the use of standing CC protocols. This corroborates the AWGS'19 recommendations for sarcopenia screening and highlights the distinction from CC protocols for malnutrition detection (such as the MNA), which typically utilize the sitting position.[14-16] Furthermore, comparisons of the four positions showed the highest correlation of right-standing CC measurement with muscle mass and function, as well as the best performance for sarcopenia diagnosis.

We demonstrated a systematic bias with the overestimation of CC by approximately 0.70 cm in the sitting position compared to the standing position, regardless of laterality. These findings were similar to those of an earlier study involving community-dwelling older adults in Korea[19] and suggest that CC measurements are not interchangeable between positions. Such variations can be explained by the differential movement of blood and extracellular fluid with changes in external hydrostatic pressures from sitting to

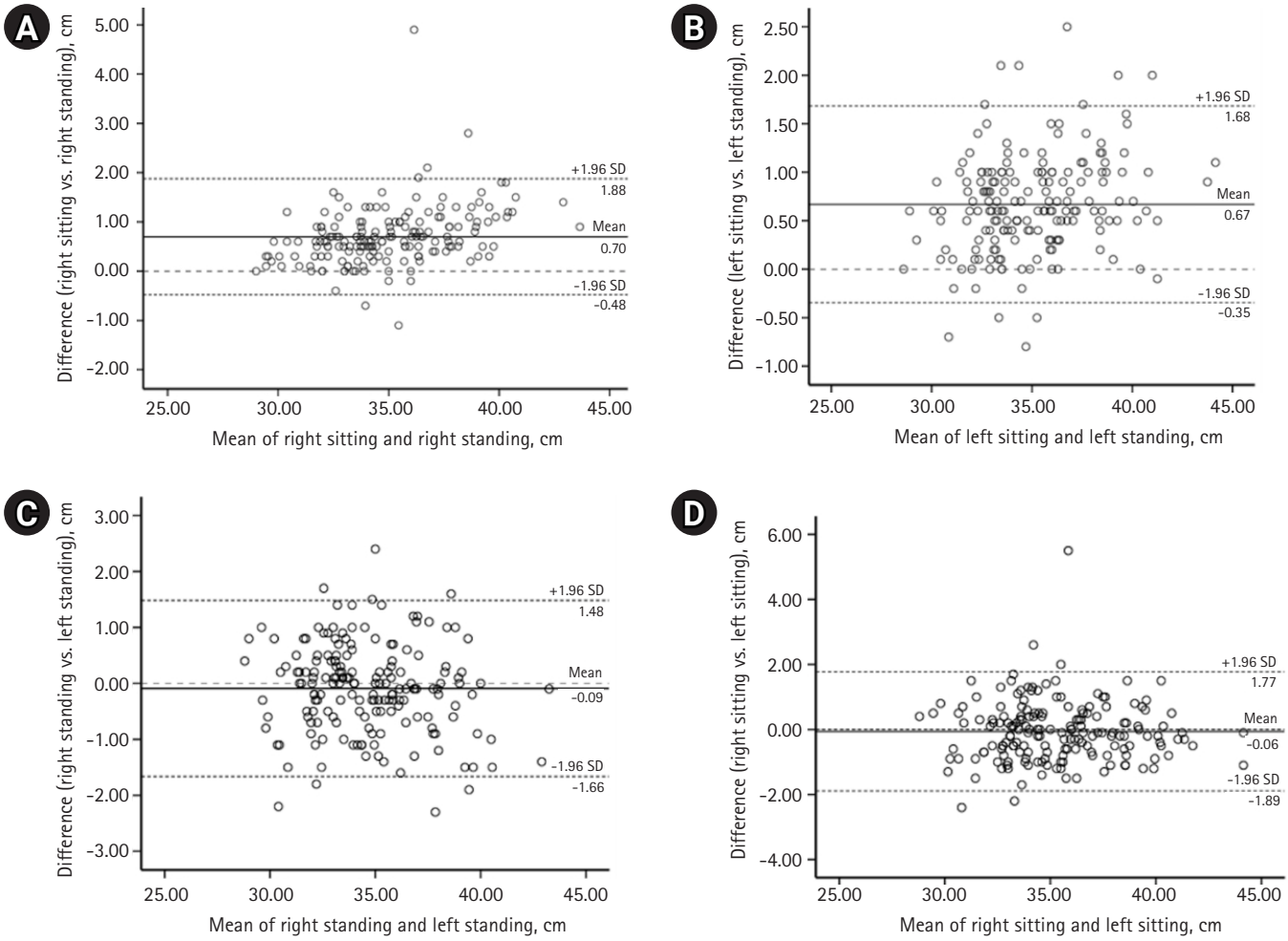

Fig. 1. Bland-Altman plots comparing the agreements between CC measurements in the standing and sitting positions. (A) Right sitting vs. right standing. (B) Left sitting vs. left standing. (C) Right standing vs. left standing. (D) Right sitting vs. left sitting.

Table 3. Correlation with muscle mass and function

	RASM	Hand grip	Knee extension	Gait speed	Chair stand	SPPB total
Right standing	0.677**	0.339*	0.236*	-0.078	0.194**	-0.240**
Right sitting	0.644**	0.317*	0.220*	-0.069	0.193**	-0.222**
Left standing	0.656**	0.346*	0.204*	-0.053	0.168**	-0.207**

Partial correlation, adjusted for age and sex.
RASM, relative appendicular skeletal mass; SPPB, Short Physical Performance Battery.
*p<0.01, **p<0.05.

standing[31] and altered length-tension relationships with increased muscle contraction while standing, thereby increasing the adhesion between muscle and superficial adipose tissue, resulting in standing smaller CC values compared to those in the sitting position.[31] We postulate that the contraction of the gastrocnemius muscle, the largest muscle in the calf, which passes both the knee and the ankle joint, contributes to smaller CC readings in the standing position.

Therefore, standing and sitting CC measurements should not be used interchangeably, as sitting measurements may result in a consistent overestimation of CC values, which in turn leads to the under-detection of sarcopenia. This systematic bias is especially salient in borderline cases, where the measurement error arising from the measurement position of the CC can result in misclassification with consequent under-detection of cases. For instance, an older adult gentleman with a CC reading of 34.5 cm in the sitting

Table 4. Diagnostic performance of CC measurements for sarcopenia screening

	AUC (95% CI)	Sensitivity (%)	Specificity (%)	PPV	NPV	CC cutoff (cm)
Right standing	0.817 (0.743–0.890)	85.0	64.6	42.5	93.3	< 34
Male	0.815 (0.677–0.953)	84.6	71.9	55.0	92.0	< 34
Female	0.830 (0.744–0.916)	85.2	62.2	38.3	93.8	< 34
Right sitting	0.816 (0.740–0.891)	75.0	75.4	48.4	90.7	< 34
Male	0.817 (0.673–0.962)	84.6	71.9	55.0	92.0	< 35
Female	0.825 (0.736–0.913)	81.5	73.5	45.8	93.5	< 34
Left standing	0.790 (0.710–0.869)	92.5	55.4	38.9	96.0	< 35
Male	0.826 (0.695–0.956)	92.3	75.0	60.0	96.0	< 35
Female	0.791 (0.694–0.888)	85.2	59.2	36.5	93.5	< 34
Left sitting	0.786 (0.706–0.866)	72.5	72.3	44.6	89.5	< 34
Male	0.813 (0.671–0.954)	69.2	78.1	56.3	86.2	< 35
Female	0.788 (0.693–0.883)	74.1	70.4	40.8	90.8	< 34

CC, calf circumference; AUC, area under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

position would be classified as non-sarcopenic (i.e., ≥ 34 cm), whereas in reality, the corresponding reading of 33.8 cm in the standing position should be classified as sarcopenia (i.e., < 34 cm) according to the AWGS'2019 criteria.

The results of our study demonstrated significant correlations between CC and both muscle mass and function. This affirms the construct validity of CC measurements and supports the use of CC for sarcopenia screening according to the AWGS'19 recommendations.[1] The good correlation with muscle mass was unsurprising and consistent with findings from earlier studies that supported the utility of CC as a surrogate for muscle mass measurement.[5-8] Comparisons between positions showed the highest correlation between right-standing CC and knee extension strength and muscle function (i.e., gait speed, repeated chair stand, and SPPB), thus supporting its role as a possible surrogate gauge of lower limb strength and function. This is a germane finding, as muscle function has been consistently shown to be a more powerful predictor of clinically relevant outcomes than muscle mass per se.[32]

The recommendation to use standing CC measurements for sarcopenia screening was further underscored by its superior diagnostic performance in the ROC curve analysis. This was mainly attributable to the superior sensitivity and negative predictive value, regardless of laterality, which resulted in better case detection of sarcopenia. In our study, right-standing CC showed the best diagnostic performance, although it was not statistically superior to the other positions. The optimal overall cut-off of < 34 cm in the right standing position was comparable to the AWGS'19 criteria (< 34 cm in male and < 33 cm in female). Notably, the cut-offs for sarcopenia screening are higher than the corresponding cut-off of < 31 cm for malnutrition in the MNA.[14-16] The differences in cut-off values are indicative of the underlying construct being measured, with sarcopenia involving both muscle mass and function, whereas CC serves as a surrogate for muscle mass for malnutrition assessment.

This study had several limitations. This study was conducted in a predominantly Chinese Asian population that was cognitively and functionally intact. Thus, the results may not be generalizable to other ethnic groups or older adults with frailer health status. The cross-sectional design also limited definitive conclusions regarding causality; moreover, reverse causality cannot be excluded from the demonstrated associations. The small sample size, with most subjects being right-handed, as well as the absence of data on calf dominance, precluded further analyses to understand the influence of handedness on CC measurements at different positions. Similarly, the differences in the sex-stratified cutoff values for sarcopenia screening from our single-population study (< 34–35 cm for male and < 34 cm for female) compared to those proposed by AWGS'19 (< 34 cm for male and < 33 cm for female) may also be related to the small sample size and should be interpreted with caution. Thus, larger studies with longitudinal follow-up in other Asian populations are warranted to verify the superior diagnostic performance and construct validity for right-standing CC measurement. Lastly, although the mean age in our study was fairly comparable to that in previous validation studies in Asian populations,[7,19] we included 26 participants (14.8%) aged 50–59 years, which is younger than the 60–65 years cutoff of the AWGS'2019 recommendations. Nonetheless, except for more female, the bADL, frailty status, nutrition, SPPB, and CC measurements did not differ significantly compared to those in participants aged ≥ 60 years. Sensitivity analysis excluding the < 60 age group revealed similar results for the comparisons of CC measurements and diag-

Table 5. Comparison of key characteristics and findings of calf circumference measurement protocol studies

Study	Year	Study aim	CC measurement protocol	Population	Results	Cutoff
Jeong et al.[19]	2020	-To evaluate the effect of body position, side and dominant hand on CC measured in community dwelling ambulatory older adults -To investigate the validity of CC for screening sarcopenia	-CC was measured using an inelastic tape, with a resolution of 1 mm, by investigators trained in standardized measurement methods to ensure excellent reliability. -To measure CC of the right and left calves in the standing posture at a time, the participant stood upright with their feet shoulder width apart. -Subsequently, they sat with their knee and ankle at a right angle, and both feet resting on the floor to measure CC in the sitting position. The inspector wrapped the tape around the calf at the widest part, taking care not to compress the subcutaneous tissue, and recorded the measurement.	1,439 participants from the Korean Frailty and Aging Cohort study Mean age: 75.9 ± 3.8 years (47.7% male)	Rt. CC, standing: AUC = 0.716; 95% CI, 0.684–0.749 Sensitivity 68.8%; Specificity 64.2% Lt. CC, standing AUC = 0.714; 95% CI, 0.682–0.746 Sensitivity 69.6%; Specificity 64.7% Rt. CC, sitting AUC = 0.707; 95% CI, 0.674–0.740 Sensitivity 61.6%; Specificity 70.7% Lt. CC, sitting: AUC = 0.703; 95% CI, 0.670–0.736 Sensitivity 62.0%; Specificity 69.8%	Based on AWGS'2019 criteria < 34 cm for male < 33 cm for female
Lau et al.[20]	2020	-To determine the agreement between 4 CC measurements -To compare convergent validity via correlation with muscle mass and function -To compare diagnostic performance for sarcopenia screening	-CC measurements were performed by three trained research assistants in a standardized manner. -The widest part of the calf was measured with a non-elastic tape applied flat on the skin and parallel to the floor in a manner that fits snugly, taking care not to compress the calf. -Sitting CC was first measured with the knee and ankle bent at right angle and feet flat on the floor. Standing CC was then measured with the feet at shoulder-width distance for equal distribution of bodyweight. Altogether, four readings were taken—left and right sides in the sitting and standing positions, respectively.	176 robust community-dwelling older adults from Geri-LABS-2 study Mean age: 66.8 ± 7.1 years (69.3% male)	Rt. standing: AUC = 0.817; 95% CI, 0.743–0.890 Sensitivity 85.0%; Specificity 64.6% Rt. sitting: AUC = 0.816; 95% CI, 0.740–0.891 Sensitivity 75.0%; Specificity 75.4% Lt. standing: AUC = 0.790; 95% CI, 0.710–0.869 Sensitivity 92.5%; Specificity 55.4% Lt. sitting: AUC = 0.786; 95% CI, 0.706–0.866 Sensitivity 72.5%; Specificity 72.3%	< 34 < 34 < 35 < 34

CC, calf circumference; AUC, area under the curve; CI, confidence interval.

nostic performance in different positions.

In conclusion, the results of this direct comparative study of four CC measurement protocols builds upon the body of evidence by demonstrating the importance of position (standing vs. sitting) when used for sarcopenia screening in a community setting. The standing position should be used owing to its good agreement without systematic bias, construct validity, and diagnostic performance. Although our results support that right standing CC measurement over the left standing position, this requires validation in future studies.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, MRBP, SL, WSL; Funding acquisition, JC, JPL, WSL; Methodology, MRBP, SL, JC, JPL, NHI, YYD, WSL; Supervision, WSL; Writing-original draft, MRBP, SL; Writing-review & editing, MRBP, SL, JC, JPL, NHI, YYD, WSL.

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A Malay Version of the Attitude to Ageing Questionnaire: Its Adaptation, Validation, and Reliability in the Malaysian Older Adult Population

Nazihah Rejab[1], Noor Azimah Muhammad[2], Hizlinda Tohid[2], Noorlaili Mohd Tohit[2], Pok Wen Kin[3], Ismail Drahman[4]

[1]Seremban Health Clinic, Ministry of Health, Jalan Rasah, Negeri Sembilan, Malaysia
[2]Department of Family Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia
[3]Department of Internal Medicine, Hospital Kuala Lumpur, Ministry of Health, Kuala Lumpur, Malaysia
[4]Department of Psychological Medicine, Faculty of Medicine and Health Science, Universiti Malaysia Sarawak, Sarawak, Malaysia

Corresponding Author:
Noor Azimah Muhammad, MBBS, MMed(FamilyMedicine), PhD
Department of Family Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Kuala Lumpur, Malaysia
E-mail: drazimah@ppukm.ukm.edu.my
ORCID:
https://orcid.org/0000-0001-6598-0060

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Background: The Attitude to Ageing Questionnaire (AAQ) was developed to assess perceptions of the aging process among older adults. The 24 items were framed into three factors. This study aimed to translate the AAQ from English to the Malay language (AAQ-M) and determine its factorial structure and validity in a Malaysian population. **Methods:** The original AAQ underwent a standard translation process, as well as content and face validation, to produce the AAQ-M. The construct validity of the AAQ-M was then assessed in 254 older adults aged 60 years and above attending a public primary care clinic in Seremban, Malaysia. **Results:** Exploratory factor analysis showed a three-factor model for the AAQ-M with acceptable reliability and Cronbach α values ranging from 0.71 to 0.82 for each factor. A total of five items were omitted for poor factor loadings (<0.32) or because they did not conceptually fit into the factor they were loaded onto. Of the final 19 AAQ-M items, seven were physical change factors, eight were psychosocial loss factors, and four were psychological growth factors. This three-factor model explained 37.9% of the total variance. **Conclusion:** The AAQ-M version confirmed that the three-factor model, namely physical change, psychosocial loss, and psychological growth, was similar to that of the original AAQ. The AAQ-M is a valid and reliable instrument for assessing the three aspects of attitudes toward aging in the Malaysian older adult population.

Key Words: Older adults, Aging, Malay, Validation, Questionnaire, Translations

INTRODUCTION

The population of older adults, defined as people aged 60 years and above,[1] has increased in recent decades. Worldwide, there were 1 billion older adults in 2019, a number that is expected to increase to 1.4 billion by 2030.[1] This significant increase is because of the increase in life expectancy of the population, which is closely related to improvements in health literacy and care, as well as to health systems in general. In Asia, including Malaysia, the older adult population is expected to double in 2030.[2,3] Malaysia is a multiracial country, with Malays, Chinese, Indians, and indigenous Bumiputra being the major races. Malay is the most common language.

Aging is a challenging phase of life that involves changes in employment, working environment, and physical and cognitive functioning. Aging is viewed as a reflection of individual accomplishments of their life goals.[4] The experience of getting old is subjective and influenced by various factors such as physical elements, psychological status, and sociocultural values. Attitude to aging, which plays an important role in its successful development, is how a person perceives and experiences the aging process, which is reflected in the affective, cognitive, and evaluative components of behavior.[5] A positive attitude to aging is associated with superior physical, mental, emotional, and social well-being,[6-9] whereas a

negative attitude to aging is associated with depression, anxiety, and poor quality of life.[10,11] Thus, a goal of living toward healthy or successful aging is of the utmost importance.

One instrument that has been developed to assess older adults' attitudes toward aging is the Attitude to Ageing Questionnaire (AAQ), which assesses psychological growth, physical change, and psychosocial loss domains.[12] The AAQ is a self-administered questionnaire with 24 items that reflect both the positive and negative aspects of aging based on an individual's experience and general opinion of the aging process.[12] The questionnaire has been translated into various languages and validated in many countries, including Canada, Spain, Brazil, Iran, Norway, and Belgium.[8,13-15] To our knowledge, no validated tool was available in Malay to measure the attitude toward aging among older adults in Malaysia. Research on the attitudes of Malaysian older adults toward aging is also limited. Hence, this study aimed to translate the English version of the AAQ into the Malay language (AAQ-M) and assess its validity among a group of Malaysian older adults. Hopefully, more studies among Malaysian older adults will be performed using this validated tool, which could allow a better understanding of their attitudes toward aging. This is an initial but important step in planning better health promotion and education programs.

MATERIALS AND METHODS

The AAQ

This study used the validated AAQ developed by Laidlaw.[12] The AAQ was used to assess subjective perceptions of aging based on three factors, namely physical change related to health and physical functioning (eight items: items #7, 8, 11, 13, 14, 16, 23, and 24); psychological growth, referring to wisdom in aging (eight items: items #1, 2, 4, 5, 10, 18, 19, and 21); and psychosocial loss related to the experience involving psychological and social loss throughout the aging process (eight items: items #3, 6, 9, 12, 15, 17, 20, and 22).[12] The response to each item used a five-point Likert scale between 1 ("strongly disagree" or "not at all true") and 5 ("strongly agree" or "extremely true"). Overall, the total score was the sum of all three subscales, with reverse scores for the psychosocial loss subscale. The mean of the total score was used to interpret the result. A higher mean score indicated a positive attitude toward aging.

Translation, Content Validation, and Face Validation

Four independent translators performed a forward and backward translation procedure on the original AAQ. Two forward translations into the Malay language (AAQ-M) were performed by a linguist and a medical doctor who could speak, read, and write in both English and Malay. Subsequently, another pair of linguists and medical doctors performed a backward translation of the AAQ-M into English. The researchers re-examined the translated versions against the original AAQ to form a harmonized AAQ-M version while ensuring that the translated items maintained the meaning of the original AAQ.

Subsequently, the AAQ was subjected to content validation by an expert panel comprising a psychiatrist, geriatrician, and family physician with special interests in geriatric care. We contacted panel members via email and provided both the original and translated versions of the questionnaires. The panel members were requested to give their expert opinions on the appropriateness of the items to be used, check the accuracy of the translated items in assessing the intended context of the respective original items, and suggest any additional items specific to the Malaysian population. Based on their suggestions, necessary amendments were made to produce the final version of the AAQ-M.

This final version was then administered to 10 older adults for face validity to check the comprehensibility of the questionnaire. These participants were patients aged ≥60 years attending a primary health clinic in Negeri Sembilan in the first week of June 2018. They were selected based on criteria similar to those used to select the intended population of the construct validity study and were not included in further studies. The selected participants were individually met and provided with the final AAQ-M. They were requested to review all items on their own. Subsequently, the field researcher checked their understanding of each item and indicated whether any of the questions were culturally insensitive, irrelevant, or inappropriate. The participants were also asked to attempt and provide their answers to each item using the response format.

Study Design, Setting, and Participants for Construct Validity

We conducted this cross-sectional validation study at the same primary health clinic in Negeri Sembilan, Malaysia. The participants attended the clinic from June to September 2018 and were older adults aged ≥60 years who could read and understand Malay. The exclusion criteria were older adults with cognitive impairment and those who had been involved in the face validity assessments. The sample size was based on a participant-to-item ratio of at least 10:1.[16] Hence, this study required a minimum of 276 participants, with an additional 15% needed to allow for non-responses. During the data collection period, a field researcher went through the list of clinic attendees and performed convenience sampling by approaching older adults while they waited for their medical consultations. The older adults who met the study criteria were briefed on the study and invited to participate. Individuals who agreed to

participate were requested to complete the AAQ-M questionnaire at their convenience. The completed questionnaires were collected on the same day before the participants left the clinic.

Ethical Considerations

This study was registered in the National Medical Research Registry (NMRR-17-3167-37451) of Malaysia and received approval from the research and ethics committee of the Universiti Kebangsaan Malaysia Research and Ethics Committee (UKM PPI/111/8/JEP-2018-069) and the Malaysia Medical Research and Ethic Committee (NMRR-17-3167-37451 (IRR)). We also obtained permission to conduct the study at the government primary health clinic from the Negeri Sembilan State Health Department and the family medicine specialists in charge. Kenneth Laidlaw, the original author of the questionnaire, granted us permission to use and translate the AAQ from English into the Malay language. The participation of older adults was voluntary, and only those who provided written consent were included in this study. Anonymity was maintained throughout the study.

This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[17]

Statistical Analysis

The analysis was performed using IBM SPSS Statistics version 22.0 (IBM, Armonk, NY, USA). A descriptive analysis was performed to describe sociodemographic profiles of the participants. The underlying structure of the 24-item AAQ-M was determined using exploratory factor analysis (EFA) with principal axis factoring and direct oblimin rotation. Oblimin rotation was used because factors were expected to be correlated with each other.[18,19] The number of factors to be extracted was based on the Kaiser criterion, scree plot, and Monte Carlo principal components analysis (PCA) for parallel analysis. Items with a factor loading < 0.32 were considered poor.[18] Items with poor factor loading or those that grouped into factors other than those in the original AAQ were examined qualitatively before a decision was made to exclude or retain them. Once a clean factorial structure was determined, the items were subjected to reliability testing of their internal consistency based on Cronbach's alpha (α) values.

RESULTS

Content and Face Validity

The content experts concluded that all 24 items were relevant and culturally appropriate in the Malaysian setting. They agreed that the translated AAQ-M version covered content similar to the original version and was suitable for testing in the older adult population. Minor amendments were made, mainly for item wording, to produce the finalized version of the AAQ-M. No additional items were suggested by the experts. During the face validity assessment, the participants felt that the questions were relevant and reported no difficulties in understanding the questions. They could answer them independently and took approximately 10–15 minutes to complete the questionnaire. They felt that the questions were both culturally relevant and appropriate.

Construct Validity and Factor Analysis

This study initially identified 276 older adults who met the study criteria. However, 11 refused to participate, seven did not return the questionnaire, and four gave incomplete responses. Thus, the analysis included feedback from 254 older adults, corresponding to a response rate of 92.0%. The participants' ages ranged from 60 to 88 years, with a mean ± standard deviation of 66.46 ± 5.37 years. The proportions of men (48.8%) and women (51.2%) were almost equal. More than half of the participants were Malays (56.3%) and had secondary school education (58.3%). Almost all participants were married (95.3%) (Table 1).

We initially conducted free EFA without restricting the analysis to a certain number of factors. The Kaiser-Meyer-Olkin value was 0.84, while Bartlett's test of sphericity was significant and the p-value was < 0.001, indicating that the data were adequate for factor analysis. Five factors from this first EFA explained 40.9% of the total variance. However, the average communalities were < 0.6 and

Table 1. Characteristics of the participants

Characteristic	Value
Age (y)	66.46 ± 5.37 (60–88)
Sex	
Male	124 (48.8)
Female	130 (51.2)
Ethnicity	
Malay	143 (56.3)
Chinese	47 (18.5)
Indian	62 (24.4)
Ohers	2 (0.8)
Marital status	
Married	242 (95.3)
Single	9 (3.5)
Divorced	3 (1.2)
Educational status	
No formal education	7 (2.8)
Primary school	54 (21.3)
Secondary school	148 (58.3)
College/university	45 (17.7)

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

thus did not meet the required assumptions for Kaiser's criterion in deciding the number of factors number of factors.[20]

Unlike Kaiser criterion, the scree plot suggested that three factors should be retained, whereas the Monte Carlo PCA for parallel analysis suggested two factors. If three factors were retained, which would be similar to the constructs of the original AAQ, they would account for 34.6% of the total variance. If two factors were retained, they would account for a lower variance of 31.0%. Thus, a second EFA was conducted by fixing the extraction to three factors. Table 2 presents the results of this analysis. All items, except #1, 2, and 4, had a factor loading of ≥0.32, with no cross-loading items. Compared to the original factor structure, items #8, 11, 13, 14, 16, and 23 loaded appropriately into the physical change factor; items #3, 6, 9, 12, 15, 17, 20, and 22 loaded appropriately into the psychosocial loss factor; and items #10, 18, 19, and 21 loaded appropriately into the psychological growth factor. However, three items did not load according to their original factors. Item #5 from the psychological growth factor loaded into the physical change factor, while items #7 and 24 from physical change loaded into psychological growth.

Item Selection and Internal Consistency

Based on the EFA results, item #1 "As people get older, they are better able to cope with life," item #2 "It is a privilege to grow old," and item #4 "Wisdom comes with age" showed poor factor loadings (<0.32) and were excluded. Subsequently, we conducted a third EFA using 21 items fixed into three factors. The total variance improved to 37.1%, and all but three items were loaded appropriately according to the original factors. Item #5 "There are many pleasant things about growing old," as in the second EFA, was supposed to load in psychological growth but instead loaded into the physical change factor. Content experts decided to retain this item because of its relevance to the new factor. However, item #7 "It is important to take exercise at any age" and item #24 "I keep myself as fit and active as possible by exercising," which loaded into the psychological growth factor, were removed as they were not conceptually appropriate for the new factor.

Subsequently, we performed a fourth EFA using 19 items. The results showed further improvement in total variance to 37.9% for a three-factor structure, namely physical change (Factor 1), psychosocial loss (Factor 2), and psychological growth (Factor 3)

Table 2. Three factor loadings for Attitude to Ageing Questionnaire in Malay version (AAQ-M) based on 24 items

Items	Factor 1	Factor 2	Factor 3
11. I don't feel old.	**0.574**	0.127	–0.042
13. My identity is not defined by my age.	**0.547**	0.112	0.067
5. There are many pleasant things about growing older.	**0.519**	–0.152	0.066
23. My health is better than I expected for my age.	**0.475**	0.009	–0.203
16. Problems with my physical health do not hold me back from doing what I want to.	**0.418**	0.030	–0.178
8. Growing older has been easier than I thought.	**0.417**	0.140	–0.152
14. I have more energy now than I expected for my age.	**0.399**	0.073	–0.202
2. It is a privilege to grow old.	0.272	–0.224	–0.022
4. Wisdom comes with age.	0.261	–0.241	–0.243
22. I feel excluded from things because of my age.	0.104	**0.720**	0.049
17. As I get older, I find it more difficult to make new friends.	0.045	**0.695**	–0.004
6. Old age is a depressing time of life.	–0.140	**0.670**	0.033
20. I don't feel involved in society now that I am older.	0.172	**0.589**	0.115
12. I see old age mainly as a time of loss.	0.081	**0.581**	0.106
15. I am losing my physical independence as I get older.	0.072	**0.565**	–0.238
9. I find it more difficult to talk about my feelings as I get older.	0.006	**0.553**	–0.144
3. Old age is a time of loneliness.	–0.183	**0.519**	–0.040
1. As people get older they are better able to cope with life.	0.209	–0.266	–0.169
21. I want to give a good example to younger people.	–0.081	–0.068	**–0.876**
18. It is very important to pass on the benefits of my experiences to younger people.	0.091	0.072	**–0.602**
24. I keep myself as fit and active as possible by exercising.	0.057	–0.047	**–0.561**
7. It is important to take exercise at any age.	–0.028	–0.005	**–0.488**
19. I believe my life has made a difference.	0.148	0.265	**–0.403**
10. I am more accepting of myself as I have grown older.	0.288	–0.086	**–0.374**
% of variance explained	17.3	14.0	3.3

Factor loadings with highest value are in bold.

(Table 3). The internal consistency (Cronbach's α) of the final version of the AAQ-M of 19 items was 0.79. The Cronbach α values of the physical change (seven items), psychosocial loss, (eight items), and psychological growth (four items) factors were 0.74, 0.82, and 0.71, respectively.

DISCUSSION

This study successfully translated and cross-culturally validated the AAQ. The original AAQ, translated into the Malay language (AAQ-M) through the standard translation process, then underwent assessments of its content and face validity. The content expert review deemed the AAQ to be important and relevant to the Malaysian older adult population. This was further supported by face validity, in which 10 older adults agreed that the AAQ-M was applicable and easy to understand.

The EFA of the AAQ-M was fixed at a three-factor structure, as suggested by the scree plot. This structure is similar to that of the original AAQ13) and represents physical change, psychosocial loss, and psychological growth factors. Other translated versions of the AAQ in various countries also showed three-factor structures similar to that of the original AAQ.[7,8,13-15] However, the final AAQ-M included only 19 items. Five items were removed: three for poor factor loading and two for incorrect loading and contextually inappropriate factors. Studies using the French and Spanish versions of the AAQ also reported that some items performed differently from their factor structures.[7,8] Older adults from different cultures may view aging differently. The living experiences of older adults may also differ individually, which may have influenced the results of our study. However, the re-analysis after removing the five items from the AAQ-M showed better psychometric properties. The finalized 19-item AAQ-M has been proven to be a valid and reliable questionnaire for assessing attitudes toward aging and can be used in future studies.

The first three items (#1, 2, and 4) were removed for poor factor loading (< 0.32). Originally, these items were intended to fall under psychological growth. Item #1 "As people get older, they are better able to cope with life" did not fit into any of the three factors. The older adults in this study might have had a different understanding of the phrase "cope with life," which would have influenced their response to this item. This phrase can be interpreted in the context of physical, psychological, social, and even spiritual endurance that corresponds to their life events, functional dependencies, poverty, health conditions, and spiritual or religious beliefs.[21,22] Notably, spirituality is a fundamental component of successful aging among Malaysian older adults[22] and thus may affect

Table 3. Three factor loadings for Attitude to Ageing Questionnaire in Malay version (AAQ-M) based on 19 items

Items	Factor 1 (physical change)	Factor 2 (psychosocial loss)	Factor 3 (psychological growth)
11. I don't feel old.	**0.678**	0.066	0.030
13. My identity is not defined by my age.	**0.570**	0.077	0.093
23. My health is better than I expected for my age.	**0.531**	–0.032	–0.133
16. Problems with my physical health do not hold me back from doing what I want to.	**0.442**	–0.007	–0.150
8. Growing older has been easier than I thought.	**0.410**	0.043	–0.176
14. I have more energy now than I expected for my age.	**0.410**	–0.152	–0.011
5. There are many pleasant things about growing older.	**0.399**	0.104	–0.182
22. I feel excluded from things because of my age.	0.070	**0.720**	0.043
6. Old age is a depressing time of life.	–0.172	**0.705**	0.046
17. As I get older, I find it more difficult to make new friends	0.050	**0.686**	0.024
20. I don't feel involved in society now that I am older.	0.115	**0.577**	0.067
9. I find it more difficult to talk about my feelings as I get older.	0.114	**0.561**	0.143
3. Old age is a time of loneliness.	–0.015	**0.556**	–0.136
12. I see old age mainly as a time of loss.	0.045	**0.555**	–0.257
15. I am losing my physical independence as I get older.	–0.217	**0.547**	–0.038
21. I want to give a good example to younger people.	–0.006	–0.115	**–0.820**
18. It is very important to pass on the benefits of my experiences to younger people.	0.118	0.026	**–0.600**
19. I believe my life has made a difference.	0.109	0.240	**–0.448**
10. I am more accepting of myself as I have grown older.	0.271	–0.112	**–0.392**
% of variance explained	18.9	15.4	3.6

Factor loadings with highest value are in bold.

their grappling with life events.

The poor loading in item #2 "It is a privilege to grow old" could be because of the word "privilege" that was translated as "*keistimewaan*" in the Malay language. The root word for "*keistimewaan*" is "*istimewa*," which means "special." Thus, those who did not really understand "*keistimewaan*" might have simplified the word using its root expression and misinterpreted the actual meaning of privilege. Nevertheless, the possibility of a double interpretation of "special" or "privilege" was not identified during the face validation. As aging involves multiple losses, older adults might have difficulty comprehending why getting older is special and an honor, especially if they have not yet experienced being special or have not received any privilege. The statement that growing old is a privilege requires evidence as people assume or judge based on evidence.[23]

The poor factor loading in item #4 "Wisdom comes with age," was related to the definition of "wisdom." In Asian culture, respect for older adults by younger people may reflect older adults' wisdom.[24] However, older Malaysian adults may view respect from the younger population as not entirely related to their wisdom but rather as more of a cultural expectation. The idea of becoming wiser as one grows older may be difficult for some people to accept because it is normal in Malaysia to consider aging as a time when one loses his/her cognitive function and develops dementia.[25] Older Malaysian adults who stay with their children may also feel they have lost their importance by becoming dependent[21,26] and thus lose their wisdom in decision-making and perhaps their role as the head of the family.

After removing the three items, the repeated EFA showed that items #5, 7, and 24 loaded into different factors from those loaded in the original AAQ. Item #5 "There are many pleasant things about growing old" that originally belonged to the psychological growth factor, was loaded into physical change instead. This placement was acceptable after examining the context of the sentences. Older adults may consider "many pleasant things" as something related to physical health and functioning. Although they might experience various physical limitations, they have a positive attitude about their life experience and feel grateful toward God as a result of contentment and acceptance.[27] Gratefulness is a desirable virtue in Asian culture and various religions. Thus, item #5 was retained in the physical change factor. However, item #7 "It is important to exercise at any age" and item #24 "I keep myself as fit and active as possible by exercising" were removed from the AAQ-M. Originally, these items were intended to measure the physical change factor but were loaded into the psychological growth factor instead. The incorrect loading of items could be because of possible connections between physical activity and psychological growth. The older adults in this study might have believed that physical activities could make them more independent and healthier and have good relationships with their friends or neighbors,[28] which is consistent with psychological growth.

The final AAQ-M, containing 19 items, showed good internal consistency, with a Cronbach's α of 0.79, comparable to the Norwegian ($\alpha = 0.82$) and French ($\alpha = 0.81$) versions of the AAQ.[8,14] The individual factors also showed good internal consistency, ranging from 0.71 to 0.82. As with other studies, the psychological growth factor showed the lowest reliability among all factors.[7,8,12,14] Cronbach's α values > 0.7 indicated good internal consistency.[20]

The strength of this study is that the participants were not limited to one ethnicity; rather, they were of different ethnicities, with Malays the predominant ethnic group, followed by Indians and Chinese. This study had several limitations. First, the AAQ-M did not undergo test-retest reliability assessments to assess its temporal stability. Second, the attitude regarding aging measured by the AAQ-M was restricted to three factors, namely physical change, psychosocial loss, and psychological growth, which accounted for 37.9% of the variance. Other aspects important in Asian cultures, such as spirituality, were not assessed.

In conclusion, this study produced a 19-item Malay version of the AAQ (AAQ-M) with a three-factor model similar to the original AAQ. Five items were removed for poor factor loadings (< 0.32) or loadings into factors deemed inappropriate. Our results demonstrated that the AAQ-M was a valid and reliable questionnaire for assessing the three aspects of attitude to aging, namely physical change, psychosocial loss, and psychological growth, among Malaysian older adults. Qualitative studies are needed to explore other aspects of attitude toward aging among older Malaysian adults.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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None.

AUTHOR CONTRIBUTION
Conceptualization, NAM, NR; Data collection, NR; Methodology, NAM; Data analysis, NAM, NR, HT, NMT, PWK, ID; Supervision, NAM; Writing–original draft, NAM, NR; Writing–review & editing, NAM, NR, HT, NMT.

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Potentially Inappropriate Medication Use among Nursing Home Residents: Medication Errors Associated with Pro re nata Medications and the Importance of Pill Burden

Fatma Özge Kayhan Koçak, Emin Taşkıran, Zehra Kosuva Öztürk, Sevnaz Şahin

Division of Geriatrics, Department of Internal Medicine, Faculty of Medicine, Ege University, Izmir, Turkey

Corresponding Author:
Fatma Özge Kayhan Koçak, MD
Division of Geriatrics, Department of Internal Medicine, Faculty of Medicine, Ege University, Izmir, Turkey
E-mail: drozgekayhankocak@gmail.com
ORCID:
https://orcid.org/0000-0002-6447-2352

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Background: The use of potentially inappropriate medications (PIM) has become more common among nursing home residents (NHR). This study focused on drugs initially prescribed as pro re nata (PRN) medications and pill burden in association with PIM among NHR. **Methods:** This observational cross-sectional study was conducted between March and April 2019 on 225 adult NHR aged ≥60 years. **Results:** The prevalence of PIM was 47.6% among NHR according to the Screening Tool of Older Persons' Prescriptions (STOPP) criteria version 2. The most frequent PIM was the use of any drug prescribed without evidence-based clinical indication; most medication errors were associated with PRN medications. The prevalence rates of PRN in non-PIM and PIM users were 12% and 62.4%, respectively. PRN medications that most commonly caused PIM were non-steroidal anti-inflammatory drugs and proton pump inhibitors. The cut-off value for both medications and pills to correctly identify participants with PIM was 5.5. Pill burden had a similar sensitivity to polypharmacy in identifying individuals with PIM. **Conclusion:** Medication errors associated with PRN medications were overlooked as factors that increased the risk of PIMs. The most common error related to PRN medications was the continued daily use despite symptom resolution.

Key Words: Potentially inappropriate medication list, Nursing homes, Aged, Medication errors

INTRODUCTION

The use of potentially inappropriate medication (PIM) has recently become more common among nursing home residents (NHR). Systematic reviews performed in long-term care facilities reported that up to 91% of NHR regularly took more than four medications and that the prevalence of PIM varied from 23.7% to 79.8%, according to the Screening Tool of Older Persons' Prescriptions (STOPP) criteria.[1,2] Not all treatments are prescribed by one physician, and NHR in Turkey often consult more than one hospital or physician. The number of prescribed medications had increased with increasing comorbidity. In addition, pro re nata (PRN) prescriptions contribute to an increase in the number of medications taken. PIM may be associated with medication errors related to PRN prescriptions.[3-5] In addition, the overall prevalence of PIM use and PRN prescriptions in nursing homes (NHs) increase with extended lengths of stay.[6,7] Therefore, PRN medication should be considered when determining inappropriate medication prescriptions in NHs.[5]

Pill burden (the number of pills taken per day) is an inconspicuous cause of PIM that influences adherence in the treatment of chronic diseases, especially HIV infection, cardiovascular disease, and renal disease.[8-10] The pill burden may be underestimated, especially in the presence of comorbidities. To our knowledge, no studies have compared the effects of pill burden and polypharmacy on the prevalence of PIM.

Two of the most commonly used criteria to define PIM are the Beers Criteria and the STOPP/Screening Tools to Alert Doctors

to Right Treatment (START) criteria.[11] The START criteria are one of the most frequently used tools for evaluating the use of PIM in older people. In contrast to the Beers criteria, the STOPP/START criteria do not include PRN medications. This study investigated the prevalence of PIM and the association of medications initially prescribed as PRN with PIM in NHR. This study focused on the association between pill burden, polypharmacy, and PIM in NHR.

MATERIALS AND METHODS

Setting and Participants

This observational cross-sectional study was conducted between March and April 2019 in an NH. The study participants were recruited among adults ≥ 60 years of age, with Katz activities of daily living (Katz-ADL) scores of 5 or higher, and institutionalized in NHs. No sampling was performed because this study planned to include all eligible NHRs who provided written informed consent.

Procedure

Nursing staff members were interviewed using a structured questionnaire. The functional status of NHRs was assessed as described below. NHR data on the number of chronic diseases and prescribed medications, falls (in the last 12 months), the presence of urinary and/or fecal incontinence, dizziness, visual impairment, hearing loss, walking disability (the use of a cane, crutches, or walking frame), nutritional support, amputation, having a pacemaker, and admission to a hospital in the last 6 months were obtained from their medical records. Information from the medical records was verified by interviewing the attending nurse.

Definitions

Functional status

We evaluated the functionality of the NHR using the KATZ-ADL score.[12] This score is used to measure the dependence of an individual regardless of their disability status. This index assesses six basic activities of daily living: eating, bathing, dressing, transferring, toileting, and continence. To prevent heterogeneity in disability status among the study population, NHRs with KATZ-ADL scores < 5 points were excluded.

Polypharmacy

Polypharmacy was defined as the daily use of five or more different medications.[13,14]

Pill burden

Pill burden was defined as the number of pills (tablets or capsules, oral solid dosage forms) that a patient regularly consumed. The number of pills taken in the last 30 days was included to calculate the pill burden.

PIM

We defined PIM as the use of more medication than clinically necessary or the use of potentially harmful medication for an individual. The START criteria are a medication assessment tool intended to identify drugs with a potentially higher risk when used in patients aged 65 years and over.[15] The START criteria were initially published in 2008 and revised in 2014.[15,16] We applied the STOPP criteria version 2 (STOPP-2) to evaluate the presence of PIM.[15,16] Each medical history was obtained from the medical records and daily medication lists in the nurse desks. The STOPP-2 criteria checklist was applied to all NHR medical histories of currently used medications.

PRN prescriptions

PRN prescription refers to the administration of prescribed medication "when required" or "as needed". PRN medication was determined through the examination of clinical records, including drug, dose, indications for use, and maximum daily dose. Each prescription was assessed with the attending nurse in terms of "is this medicine used as a PRN?" and "are there written instructions such as 'as needed'?" The US Food Drug Administration (FDA) defines medication error as "a preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer."[17] The daily administration of PRN prescriptions to patients with no symptoms was considered a medication error and PIM as "to use any drug prescribed without an evidence-based clinical indication." FÖKK and ET reviewed the medication lists of these NHRs.

Ethics Approval

The study was approved by the Human Research Ethics Committee of Ege University (No. 18-11T/16-99166796-050.06.04) and received approval from the Ministry of Family, Labor, and Social Services of the Republic. Informed consent was obtained from all the participants included in the study. This study was performed in accordance with the principles of the Declaration of Helsinki.

Also, this study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[18]

Statistical Analyses

Data analyses were performed using IBB SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Normality was assessed using Kolmogorov-Smirnov tests. Non-normally distributed quantitative variables were expressed as medians and minimum-maximum values. Qualitative variables were expressed as frequencies and percentages. Chi-squared (χ^2) and Fisher exact tests were used to analyze the qualitative variables. Mann-Whitney U tests were used to analyze quantitative variables. Multiple logistic regression analysis was performed for multivariate analysis. We applied a logistic regression model to variables that showed significant relationships in the univariate analysis. Multivariable logistic regression analysis was used to calculate the adjusted odds ratios (ORs) and 95% confidence intervals (CI) of variables for PIM in different models adjusted for potential confounders. For the multivariable logistic regression analyses, Model 1 was adjusted for medication number, pill number, and number of comorbidities, while Model 2 additionally adjusted for the presence of PRN. The optimal cut-off values for variables were determined using receiver operating characteristic (ROC) curve analysis. ROC curve analysis was also used to evaluate the ability of the number of pills (pill burden) and number of medications (polypharmacy) to predict PIM use. Differences with $p < 0.05$ were considered statistically significant.

RESULTS

We assessed the functional status of 268 NHR based on KATZ-ADL scores. Of these NHR, 225 had Katz-ADL scores of 5 or higher. To prevent heterogeneity in disability status among the study population, this cross-sectional study included data on the activities of daily living of 225 independent residents.

The median age of the study population was 76 years (range, 61–96 years), including 123 (54.7%) men and 102 (45.3%) women. Only 15 (6.7%) participants were married and had a living spouse. A total of 210 (93.8%) participants had been staying in the institution for >6 months. Among the NHRs, 19.4% had diabetes mellitus, 10.1% had arrhythmia, 27.2% had cardiovascular disease, 7.4% had heart failure, 58.5% had hypertension, and 6.9% had cerebrovascular disease. Various medications were used by the NHRs. Proton pump inhibitors (PPIs) were administered to one-third of NHRs. Moreover, almost half of the NHRs were taking antiplatelet medication. The most commonly used medication classifications are presented in Table 1.

In this study, 107 NHR were on PIM, corresponding to a PIM prevalence of 47.6% according to the STOPP-2 criteria. The most frequent PIM was the use of "any drug prescribed without an evidence-based clinical indication." Most occurred as medication errors associated with PRN medications. The detailed PIM subclasses are shown in Table 2.

PIM users had higher numbers of medications; numbers of pills; PRN use; polypharmacy prevalence; and comorbidity prevalence such as chronic obstructive pulmonary disease (COPD), constipation, muscle-skeletal disease, dizziness, visual impairment, and urinary incontinence compared to non-PIM users. We observed no significant differences in terms of the length of stay in the institu-

Table 1. The most used medication classes of all residents (n=225)

Medication classification	n (%)
Gastrointestinal system	
Proton pump inhibitors	81 (36)
Cardiovascular system	
Antiplatelet drugs	97 (43.1)
ACE inhibitor or ARB	99 (44)
Diuretic	91 (40.4)
Beta blocker	67 (29.8)
Calcium channel blocker	44 (19.6)
Vasodilator	41 (18.2)
Lipid lowering drugs	27 (12)
Piracetam	25 (11.1)
Anticoagulant drugs	14 (6.2)
Respiratory system	
Inhaler beta mimetic	43 (19.1)
Inhaler steroid	40 (17.8)
Inhaler ipratropium	31 (13.8)
Central nervous system & psychotropic drugs	
SSRI/SNRI	40 (17.8)
Antipsychotics	24 (10.7)
Atypical anti-depressant	15 (6.7)
Donepezil	15 (6.7)
Endocrine system	
Thyroid therapy	31 (13.8)
Metformin	24 (10.7)
DPP4 inhibitor	15 (6.7)
Musculoskeletal system	
NSAIDs	14 (6.2)
Calcium-vitamin D	11 (4.9)
Urogenital system	
Alpha blocker	40 (17.8)
Non-classified drugs	
Anticholinergic	39 (17.3)
Vitamin supplement	45 (20.1)

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; SSRI, selective serotonin reuptake inhibitors; SNRI, serotonin and norepinephrine reuptake inhibitors; DPP-4, dipeptidyl peptidase-4; NSAIDs, non-steroidal anti-inflammatory drugs.

Table 2. PIM prevalence according to drug classes described in STOPP criteria version 2

Drug classes	Number of residents
Any drug prescribed without an evidence-based clinical indication.	89
Any drug prescribed beyond the recommended duration, where treatment duration is well defined.	47
Any duplicate drug class prescription, e.g., two concurrent NSAIDs, SSRIs, loop diuretics, ACE inhibitors, anticoagulants (optimization of monotherapy within a single drug class should be observed prior to considering a new agent).	5
Beta-blocker in combination with verapamil or diltiazem (risk of heart block).	2
Loop diuretic as first-line treatment for hypertension (safer, more effective alternatives available).	3
Loop diuretic for treatment of hypertension with concurrent urinary incontinence (may exacerbate incontinence).	1
Aspirin plus clopidogrel as secondary stroke prevention, unless the patient has a coronary stent(s) inserted in the previous 12 months or concurrent acute coronary syndrome or has a high grade symptomatic carotid arterial stenosis (no evidence of added benefit over clopidogrel monotherapy).	2
Antiplatelet agents with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease (no added benefit from dual therapy).	1
NSAID with concurrent antiplatelet agent(s) without PPI prophylaxis (increased risk of peptic ulcer disease).	1
Anticholinergics/antimuscarinics in patients with delirium or dementia (risk of exacerbation of cognitive impairment).	5
Neuroleptics as hypnotics, unless sleep disorder is due to psychosis or dementia (risk of confusion, hypotension, extra-pyramidal side effects, falls).	3
First-generation antihistamines (safer, less toxic antihistamines now widely available).	9
Prochlorperazine or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonian symptoms).	1
PPI for uncomplicated peptic ulcer disease or erosive peptic esophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated).	23
Drugs likely to cause constipation (e.g., antimuscarinic/anticholinergic drugs, oral iron, opioids, verapamil, aluminum antacids) in patients with chronic constipation where non-constipating alternatives are available (risk of exacerbation of constipation).	2
Antimuscarinic drugs with dementia, or chronic cognitive impairment (risk of increased confusion, agitation) or narrow-angle glaucoma (risk of acute exacerbation of glaucoma), or chronic prostatism (risk of urinary retention).	6
Selective alpha-1 selective alpha blockers in those with symptomatic orthostatic hypotension or micturition syncope (risk of precipitating recurrent syncope).	3

PIM, potentially inappropriate medication; NSAIDs, non-steroidal anti-inflammatory drugs; SSRI, selective serotonin reuptake inhibitors; ACE, angiotensin-converting enzyme; PPI, proton pump inhibitor.

tion, cerebrovascular disease, peripheral vascular disease, walking disability, nutritional support, peptic ulcer disease, hypertension, malignancy, asthma, cardiovascular disease, arrhythmia, chronic prostatism, hearing loss, depression, diabetes mellitus, amputation, number of hospital admissions in the last 6 months, and having a pacemaker between the groups with and without PIM ($p > 0.05$). The p-values, numbers, and percentages for the descriptive statistics for the PIM users and non-PIM users are shown in Table 3.

The prevalence rates of PRN in non-PIM and PIM users were 12% and 62.4%, respectively. PRN medications that most commonly cause PIM are non-steroidal anti-inflammatory drugs (NSAIDs), PPIs, and betahistine dihydrochloride. Except for two residents, those NHR using piracetam were taking it as a PIM. Univariate analysis showed that PPIs, anticholinergic drugs, antiplatelet drugs, alpha-blockers, and inhaler beta mimetics were significantly associated with PIM prescription (Tables 4, 5). PPIs, betahistine dihydrochloride, and NSAIDs were initiated as PRN medications. However, there are no written instructions for the administration of PRN medication. These medica-

Table 3. Descriptives according to existence of PIM

	PIM users (n = 107)	Non-PIM users (n = 118)	p-value
Age (y)	77 (61–110)	75 (62–96)	0.240
Sex, male	59 (55.1)	64 (54.2)	0.892
Length of stay in institution (mo)			
0–6	6 (5.6)	8 (6.9)	0.730
> 6	100 (94.3)	110 (93.2)	
Medication number	7 (1–17)	4 (0–13)	< 0.001*
PRN	67 (62.6)	15 (12.7)	< 0.001*
Pill number	8 (0–25)	5 (0–17)	< 0.001*
Pill burden	83 (77.6)	62 (52.5)	< 0.001*
Polypharmacy	83 (77.6)	58 (49.2)	< 0.001*
Comorbidities	4 (1–8)	2 (0–7)	< 0.001*
COPD	29 (27.1)	14 (11.9)	0.004*
Urinary incontinence	21 (19.6)	7 (5.9)	0.002*
Dizziness	23 (21.5)	7 (5.9)	0.001*
Vision impairment	37 (34.6)	20 (16.9)	0.002*
Muscle-skeletal disease	20 (18.7)	7 (5.9)	0.003*
Constipation	10 (9.3)	2 (1.7)	0.011*

Values are presented as median (min-max) or number (%).
PIM, potentially inappropriate medication; PRN, pro re nata; COPD, chronic obstructive pulmonary disease.
*$p<0.05$.

tions were administered daily to NHRs as long-term medications without the knowledge of PRN. In multivariable logistic regression analysis, piracetam and anticholinergic medications were significant in both models, whereas PPI was significant in Model 1 only. The logistic regression results are presented in Tables 4 and 5.

The results of the univariate ROC analysis are presented in Table 6. ROC analysis of the pill numbers showed an AUC of 0.692 with a cutoff value of 5.5, above which PIM could be diagnosed.

DISCUSSION

This study investigated the association of medications initially prescribed as PRN with PIM in NHR patients who were independent according to KATZ-ADL scores. As this study did not include NHRs with a score Katz-ADL scores < 5, we excluded the effect of dependency. We found that PRN medications were administered daily to asymptomatic NHRs. Poor understanding of PRN administration also led to medication errors. PRN also refers to the use of a medication without an evidence-based clinical indication, which is a PIM. We found that the prevalence of PIM increased due to this medication error. Another important finding of this study was the observation that pill burden had similar sensitivity to polypharmacy for predicting PIM use.

The groups did not differ significantly in terms of the length of hospital stay. In addition, PIM users and non-PIM users did not differ significantly in terms of the rate of hospital admission. We noticed that PRN medications were administered daily to NHRs after nursing home transition. Dorks et al.[5] reported that 74.9% of the NHRs received at least one PRN medication. PRN medications can reduce the workload of nursing staff, and directions for use "as needed" should be noted on the prescription. Therefore, prescribers should regularly reconsider the need for each PRN medication.

The most common cause of PIM was the use of any medication prescribed without an evidence-based clinical indication. In this

Table 4. Effect of some variables on PIM for the whole group (logistic regression results from the univariate analysis)

Variable	Univariate		
	OR	%95 CI	p value
Medication number	1.264	1.151–1.388	0.000*
Pill number	1.156	1.080–1.237	0.000*
Comorbidities number	1.607	1.332–1.940	0.000*
Piracetam	15.881	3.644–69.204	0.000*
PPI	2.671	1.523–4.685	0.000*
Anticholinergic	5.609	2.445–12.867	0.000*
Antiplatelet	1.777	1.043–3.028	0.035*
Inhaler beta mimetic	2.434	1.218–4.863	0.012*

PIM, potentially inappropriate medication; OR, odds ratio; CI, confidence interval; PPI, proton pump inhibitor.
*p<0.05.

Table 5. Effect of some variables on PIM for the whole group (logistic regression results from the multivariate analysis)

Variable	Multivariate		
	OR	95% CI	p-value
Model 1			
Medication number	1.106	0.854–1.433	0.445
Pill number	0.943	0.793–1.122	0.508
Comorbidities number	1.249	0.947–1.648	0.115
Piracetam	19.304	4.160–89.586	0.000*
PPI	2.320	1.181–4.556	0.015*
Anticholinergic	5.196	2.112–12.786	0.000*
Antiplatelet	1.576	0.822–3.022	0.171
Inhaler beta mimetic	2.050	0.808–5.203	0.205
Model 2			
PRN	10.631	4.914–22.999	0.000*
Piracetam	31.310	6.355–154.266	0.000*
PPI	1.602	0.761–3.372	0.215
Anticholinergic	4.889	1.835–13.025	0.002*
Antiplatelet	2.118	1.049–4.279	0.036*
Inhaler beta mimetic	2.480	1.005–6.123	0.049*

PIM, potentially inappropriate medication; OR, odds ratio; CI, confidence interval; PPI, proton pump inhibitor; PRN, pro re nata.
*p<0.05.

Table 6. Receiver operating characteristic analysis for thresholds of pill burden and polypharmacy to predict PIM use

	Cut-off value	Sensitivity	Specificity	ROC AUC (95% CI)	Asymptotic significance (p)
Polypharmacy[a]	2.5	0.972	0.364	0.698	0.000
	5.5	0.673	0.619	(0.630–0.766)	
Pill burden[b]	2.5	0.925	0.347	0.67	0.000
	5.5	0.692	0.593	(0.601–0.740)	

PIM, potentially inappropriate medication; AUC, area under ROC curve; CI, confidence interval.
[a]Number of drugs.
[b]Number of pills.

study, 74% of PRN medications continued to be used regularly, despite symptom resolution. These findings demonstrated the misuse of PRN medications by nurses and NHR. In addition, the prescription cascade increased if PRN medication was used regularly rather than "as needed."

Medications for gastrointestinal problems are frequently used in the long-term care units.[2,19] The third most common cause of PIM was PPI use at full therapeutic dosage for >8 weeks for the treatment of uncomplicated peptic ulcer disease or erosive peptic esophagitis. Additionally, based on our observations, PPI was the most prescribed medication without an evidence-based clinical indication or beyond the recommended duration, where the treatment duration is well defined. PPI was prescribed as a PRN medication after receiving treatment for an adequate period. However, it was administered daily as a long-term scheduled medication despite the absence of symptoms and not as a PRN medication. Physicians and patients are generally afraid of symptom relapse after discontinuing PPI treatment, although on-demand therapy is recommended for gastroesophageal reflux disease and chronic gastritis. Therefore, PPI prescribed as a PRN medication but erroneously used daily was a common cause of PIM.[6,20,21]

We observed medication errors associated with the use of antipsychotics and anticholinergics. Although PRN antipsychotic medications are used for the acute control of agitation, the rescheduling of antipsychotic doses has been overlooked. Prescribers should record the indication and duration of use of PRN medication, especially to avoid misuse.[22] Although the use of anticholinergics has decreased significantly, it continues to increase in the presence of chronic diseases, such as dementia and depression, in long-term care settings.[23-25] Similarly, Kose et al.[26] reported significantly increased anticholinergic use during stroke rehabilitation. First-generation antihistamines may be used inappropriately as hypnotics in patients with behavioral and psychological symptoms of dementia or delirium.

Another notable medication among PIM users was piracetam. Piracetam is prescribed short-term to patients with peripheral vertigo.[27] However, piracetam was frequently used in this study for forgetfulness and vertigo of unknown origin. Most NHRs did not show a significant benefit from the use of piracetam. Furthermore, evidence supporting its effectiveness remains inadequate.

The most common definition of polypharmacy is the regular use of at least five medications. Polypharmacy has been associated with the risk of geriatric syndromes and the use of PIM, and lists of PIM are widely used to reduce the prevalence of geriatric syndromes.[28-32] The number of pills taken by an individual can increase, even if the number of medications used is lower, a situation that is oven overlooked. Therefore, we investigated the pill burden and threshold number of pills, which resulted in an increased risk of PIM similar to polypharmacy. In our study, the cutoff value for the number of pills to predict PIM use was similar to the number of medications used. The most sensitive cut-off value for the number of pills based on ROC analysis was 2.5. Pill burden had similar sensitivity and specificity to polypharmacy in identifying individuals with PIM. We found that neither definition was superior in identifying participants with PIM. Studies to date have demonstrated the association of a reduced pill burden and reduced PIM use with increased medication adherence. To our knowledge, this is the first study conducted in NHs to investigate the cut-off value for the number of pills taken to predict the presence of PIM. Finally, although the number of pills was insufficient to show the PIM arithmetically, it can still be used as an important risk factor for PIM.[33]

This study was conducted at a single center, thus resulting in a relatively small sample size. Some of the STOPP-2 criteria could not be applied owing to the requirement for laboratory assessment. As not all confounding factors, such as comorbidity and START criteria, were considered, medication error may not be associated solely with PRN or pill burden. We were unable to assess the medications that were necessary for use based on comorbidities according to the START criteria.

In conclusion, an improperly explained prescription of PRN can result in medication errors. Due to patient misunderstanding of the indication or duration of use, PRN may cause PIM as the use of "any drug prescribed without an evidence-based clinical indication." Older people who use PRN medications should be followed-up more closely. Ultimately, identifying the presence of PIM and PRN is important for identifying barriers to adherence and enhancing patient understanding of the indications and proper use of medications. To prevent the use of PIM caused by errors related to PRN medication, patients should be questioned at each visit regarding the use of each medication and prescribers should critically review the medication list.

An approach should be developed to reduce the pill burden, including reducing or stopping medications that are potentially harmful or no longer beneficial, using fixed-combination products, and reducing dose frequency. The number of pills taken is often not the same as the number of medications used and is usually more than the number of medications. Increasing the number of pills could reduce medication adherence, which, in turn, can lead to increased side effects, adverse drug reactions, or loss of efficacy. This indirectly leads to increased PIM use. Therefore, the numbers of pills and medications are important in terms of PIM use.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization: FÖKK and SS; Data curation and formal analysis: FÖKK, ET, and SS; Investigation and methodology: FÖKK, ET, ZKÖ, and SS; Project administration: FÖKK and SS; Supervision: FÖKK, ET, ZKÖ, and SS; Writing-original draft: FÖKK and ET; Writing-review & editing: FÖKK, ET, ZKÖ, and SS.

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Functional Constipation is Associated with a Decline in Word Recognition 2 Years Later in Community-Dwelling Older Adults: The Korean Frailty and Aging Cohort Study

Hoseok Jang[1], Sunyoung Kim[2], Byungsung Kim[2], Miji Kim[3], Jaehoon Jung[1], Chang Won Won[2]

[1]Department of Family Medicine, Kyung Hee University Medical Center, Seoul, Korea
[2]Department of Family Medicine, College of Medicine, Kyung Hee University, Seoul, Korea
[3]Department of Biomedical Science and Technology, College of Medicine/East-West Medical Research Institute, Kyung Hee University, Seoul, Korea

Corresponding Author:
Chang Won Won, MD, PhD
Elderly Frailty Research Center, Department of Family Medicine, College of Medicine, Kyung Hee University, Kyungheedaero 23, Dongdaemun-gu, Seoul, 02447, Korea
E-mail: chunwon62@naver.com
ORCID:
https://orcid.org/0000-0002-6429-4461

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Background: Consumption and cognitive impairment are the most common health problems among older adults. This study aimed to determine the effects of functional constipation on cognitive decline in community-dwelling older adults. **Methods:** This was a 2-year longitudinal analysis of Korean Frailty and Aging Cohort Study data, including 851 community-dwelling residents who participated in both the baseline and follow-up surveys. A neuropsychological test, the Consortium to Establish a Registry for Alzheimer's Disease Assessment Battery (CERAD-K), and the Korean version of the Frontal Assessment Battery (FAB) were used to evaluate cognitive function. Functional constipation was defined according to the ROME IV criteria. An analysis of covariance was used to identify the association between functional constipation and cognitive decline. **Results:** Among the 851 participants, 8.9% had functional constipation. The patients in the constipation group were more likely to have low physical activity (15.8% vs. 8.8%), polypharmacy (61.8% vs. 45.5%), and depression (30.3% vs. 17.4%) than the non-constipation group. After adjusting for potential confounding factors, including age, sex, education years, low physical activity, polypharmacy, type 2 diabetes mellitus, depression, and baseline Cognitive Function Test score, the mean changes in Word Recognition test scores from 2018 to 2020 were -0.07 and -0.54 in the non-constipation and constipation groups, respectively (p=0.007). Other cognitive function tests (Mini-Mental State Examination, word list memory, word list recall, digit span, trail-making test, and FAB) did not show any difference in decline between the two groups (p>0.05). **Conclusions:** Functional constipation at baseline was associated with a decline in word recognition after 2 years.

Key Words: Aged, Constipation, Cognition

INTRODUCTION

Constipation is an unsatisfactory defecation disorder characterized by infrequent stools, difficult stool passage, or both, and it is one of the most common health problems encountered in older adults.[1-3] Functional constipation was defined by the Rome Foundation to help standardize the diagnosis of chronic constipation without physiological abnormalities identified by routine diagnostic examinations, as deemed clinically appropriate.[4] The worldwide prevalence of functional constipation in adults is 10.1%,[5] and the prevalence of functional constipation increases with age. Functional constipation has been reported in 30%–40% of older adults worldwide[6] and 19.6% of Korean adults aged 72–86 years.[7]

Cognitive impairment is a major personal and public health problem in older adults. Therefore, identifying the risk factors for cognitive impairment is essential for preventing cognitive disor-

ders and can help promote successful cognitive aging.[8]

As an important manifestation of autonomic nerve dysfunction, constipation is well known to be the most common non-motor complication of Parkinson disease. Santos García et al.[9] found that constipation predicts cognitive decline in Parkinson disease. In a cross-sectional population-based cohort study, Wang et al.[10] showed that a higher prevalence of constipation is associated with dementia and non-amnestic mild cognitive impairment. However, no prospective cohort study has yet explored the predictive effects of functional constipation on cognitive decline. Therefore, we investigated the relationship between functional constipation and cognitive decline in community-dwelling older adults using the Korean Frailty and Aging Cohort Study (KFACS) longitudinal database.

MATERIALS AND METHODS

Study Population

The KFACS is a nationwide multicenter longitudinal study with a baseline survey conducted in 2016 and 2017 to identify factors contributing to frailty and aging in community-dwelling individuals aged 70–84 years. The baseline survey for the cohort study was conducted at 10 centers, with 1,559 participants in 2016 and 1,455 in 2017.[11] The participants were recruited from urban, suburban, and rural communities nationwide. To investigate the prevalence of frailty among the three age groups and consider the higher attrition rate in the oldest age group, the KFACS cohort adopted quota sampling stratified by age (70–74, 75–79, and 80–84 years, with a ratio of 6:5:4). This quota sampling is based on oversampling of the older group using population distribution data from the Korean Population and Housing Census conducted by Statistics Korea in 2015 (distributions of 43.5%, 33.8%, and 22.7% for adults aged 70–74, 75–79, and 80–84 years, respectively).[12]

Participants were recruited from diverse settings (local senior welfare centers, community health centers, apartments, housing complexes, and outpatient clinics) to minimize selection bias. All participants were ambulatory, with or without the use of walking aids. Follow-ups have been conducted at 2-year intervals. A questionnaire to evaluate functional constipation was included in a follow-up survey in 2018. Of the 1,292 participants aged 72–86 years who participated in the follow-up survey in 2018, 1,273 revisited the center after 2 years for the second follow-up survey in 2020.

Of the 1,273 participants, those without available prescription information (n = 356) and those who were diagnosed with dementia or cerebrovascular disease (n = 66) were excluded, and 851 subjects were enrolled in the analysis (Fig. 1).

The KFACS protocol was approved by the Institutional Review Board of the Clinical Research Ethics Committee of Kyung Hee University Medical Center (IRB No. 2015-12-103), and all participants provided written informed consent. Data anonymization was performed to protect participants' privacy. This study was conducted in accordance with the consensus ethical principles derived from the Declaration of Helsinki.

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

Assessment of Functional Constipation

Functional constipation is a functional bowel disorder that presents with obvious low-frequency or incomplete defecation.[4] Functional constipation was assessed based on the Rome IV criteria for functional constipation.

(1) Must include two or more of the following:
- Straining during more than one-fourth (25%) of defecations.
- Lumpy or hard stools (Bristol stool scale 1–2) in more than one-fourth (25%) of defecations.
- Sensation of incomplete evacuation in more than one-fourth (25%) of defecations.
- Sensation of anorectal obstruction or blockage in more than one-fourth (25%) of defecations.
- Manual maneuvers to facilitate more than one-fourth (25%) of defecation.

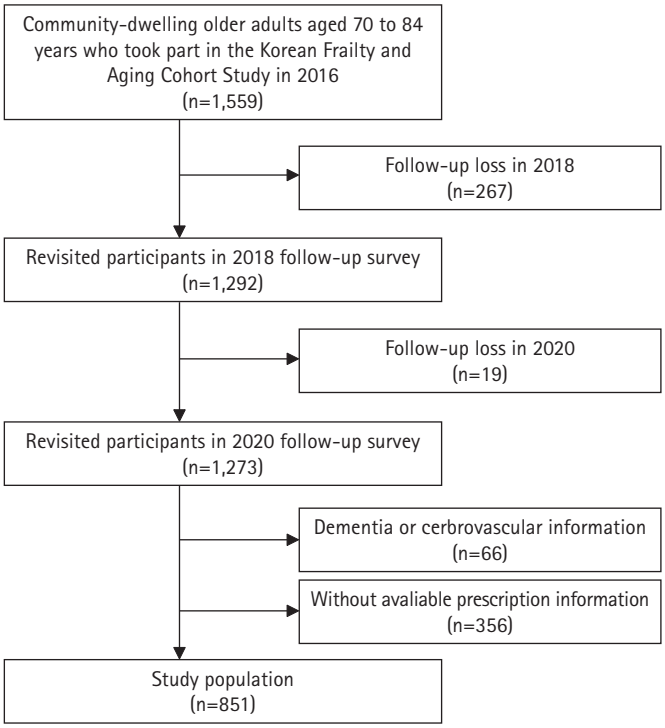

Fig. 1. Study population.

Fewer than three spontaneous bowel movements per week.

(2) Loose stools are rarely present without the use of laxatives.

(3) Insufficient criteria for irritable bowel syndrome.

In addition, those who had experienced an onset of symptoms more than 6 months prior were included for functional constipation according to the ROME IV criteria.

Assessment of Cognitive Function

A neuropsychological test, the Consortium to Establish a Registry for Alzheimer's Disease Assessment Battery (CERAD-K), and the Korean version of the Frontal Assessment Battery (FAB) were used to evaluate comprehensive cognitive function. The CERAD-K is a standardized clinical and neuropsychological assessment battery for evaluating patients with Alzheimer's.[14] The CERAD-K initially consisted of eight tests—verbal fluency, modified Boston naming, Korean version of the Mini-Mental State Examination (MMSE-KC), word list memory, constructional praxis, word list recall, word list recognition, and constructional praxis recall; however, in this study, word list memory, word list recall, word list recognition, digit span (forward and backward), trail-making test (TMT) A, and MMSE-KC were included.[14]

Word list memory is a test that assesses memory for new information learning. It is conducted by presenting 10 commonly used words at intervals of two seconds and reading the words aloud, followed by immediate recall of as many words as possible for 90 seconds. The maximum score was 30 points, with 10 points per session. The word list recall test evaluates the ability to recall the 10 words from the word list memory test. A maximum of 90 seconds was allowed, and the maximum score was 10. The word list recognition test measures recognition ability. The goal was to distinguish between the 10 words in the word list memory test and 10 new words. The maximum possible score was 10. TMT A assesses attention, ordering, executive function, time-space search, and mental motion velocity. Patients were asked to draw a line connecting numbers 1 to 25 in ascending order, and the time taken was recorded. Participants who did not complete this within 360 seconds were excluded. The digit span test assesses short-term memory, working memory, and attention by recalling the number sequence after hearing numbers forward and backward. Digit spans, forward and backward, were composed of seven digit questions and presented with two trials. One point was scored when each digit was correctly recalled, and the maximum score was 14 points for each digit span, forward and backward. The digit span total is the combined score of the forward and backward digit span.[14]

The FAB assesses executive functions, such as planning, working memory, mental flexibility, and inhibition. It consists of similarities (conceptualization), lexical-verbal fluency (mental flexibility), motor series (programming), conflicting instructions (sensitivity to interference), Go–No Go (inhibitory control), and prehension behavior (environmental autonomy), with a maximum score of 18; higher scores indicate better frontal lobe function.[15]

Other Measurements

Demographic information, including age, sex, independent living, marital status, years of education, medical aid, alcohol consumption, and smoking habits, was investigated through face-to-face interviews in 2018. Malnutrition was defined as a Mini Nutritional Assessment (MNA) score of < 17.[16] Physical activity was assessed using the metabolic equivalent of task minutes per week and kcal per week, calculated using the International Physical Activity Questionnaire.[11] Polypharmacy implies the use of five or more prescribed medications. The Geriatric Depression Scale (GDS) short form was used to define depression, and scores > 5 indicate depression. History of chronic diseases, including hypertension, type 2 diabetes mellitus, dyslipidemia, depressive disorder, dementia, cerebrovascular disease, other psychiatric disorders, renal disorders, thyroid disorders, and malignancies, was assessed in 2018 for analysis.

Statistical Analyses

Data are presented as mean ± standard deviation or percentages. Continuous variables were compared using the independent t-test, and categorical variables were compared using the chi-squared test. Univariate regression analysis was used to identify associations between each characteristic and decline in word list recognition over 2 years. Analysis of covariance (ANCOVA) was used to identify associations between functional constipation and cognitive decline, adjusted for age, sex, years of education, low physical activity, polypharmacy, type 2 diabetes mellitus, depression, and baseline cognitive function test scores. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, USA). The level of statistical significance was set at $p < 0.05$.

RESULTS

General Characteristics of the Study Population

The baseline characteristics of the participants are presented in Table 1. Among the 851 participants, 8.9% (n = 76) had functional constipation. The mean age of the functional constipation group (78.6 ± 3.9 years) was higher than that of the non-constipation group (77.5 ± 3.8 years). The functional constipation group was more likely to have a higher rate of low physical activity (15.8% vs.

Table 1. Baseline characteristics of study subjects according to functional constipation

	Total (n = 851)	No-constipation (n = 775)	Functional constipation (n = 76)	p-value
Age (y)	77.6 ± 3.8	77.5 ± 3.8	78.6 ± 3.9	0.012*
Sex, male	396 (46.5)	359 (42.2)	37 (49)	0.694
Independent living	747 (87.9)	682 (88.0)	65 (85.5)	0.510
Married	546 (64.2)	499 (64.5)	47 (61.8)	0.648
Education (y)	8.38 ± 4.93	8.36 ± 4.94	8.58 ± 4.83	0.716
Medical aid	49 (5.8)	45 (5.8)	4 (5.3)	0.844
Urban living	620 (73.0)	563 (72.8)	57 (75.0)	0.685
BMI (kg/m^2)	24.43 ± 3.07	24.44 ± 3.06	24.35 ± 3.17	0.799
Smoking	34 (4.0)	31 (4.0)	3 (3.9)	0.982
High-risk drinking	30 (3.5)	27 (3.5)	3 (3.9)	0.834
Low physical activity	80 (9.4)	68 (8.8)	12 (15.8)	0.046*
Polypharmacy	400 (47)	353 (45.5)	47 (61.8)	0.007*
Malnutrition	9 (1.1)	7 (0.9)	2 (2.7)	0.152
Type II DM	191 (22.4)	168 (21.7)	23 (30.2)	0.087
Hypertension	494 (58.0)	451 (58.2)	43 (56.6)	0.914
Dyslipidemia	347 (40.8)	323 (41.7)	24 (31.6)	0.213
Depression	158 (18.6)	135 (17.4)	23 (30.3)	0.006*
Other psychiatric disorder	34 (4.0)	29 (3.7)	5 (6.6)	0.228
Thyroid disorder	29 (3.4)	27 (3.5)	2 (2.6)	0.881
Renal disorder	5 (0.6)	5 (0.6)	0 (0.0)	0.098
MMSE score (/30)	25.81 ± 3.03	25.82 ± 3.03	25.75 ± 3.13	0.412
Word list memory score (/30)	17.93 ± 4.34	18.02 ± 4.33	17.05 ± 4.40	0.063
TMT score (/360 seconds)	85.93 ± 67.97	85.77 ± 67.79	87.63 ± 70.19	0.820
Word list recall score (/10)	5.96 ± 2.03	5.99 ± 2.03	5.74 ± 2.04	0.306
Word list recognition score (/10)	8.76 ± 1.64	8.77 ± 1.65	8.67 ± 1.55	0.615
Digit span score (/28)	9.75 ± 3.63	9.76 ± 3.62	9.61 ± 3.83	0.719
FAB score (/18)	13.28 ± 3.21	13.29 ± 3.12	13.22 ± 3.12	0.859

Values are presented as the mean±standard deviation or number (%).
Depression implies that the SGDS-K score is >5; smoking implies that currently smoking; independent living implies that people can live without help from others, and not in nursing homes or hospitals; low physical activity implies that IPAQ-based weekly physical activity (kcal/week) is less than 495.65 kcal/week in males, 283.5 kcal/week in females, and less than the 20% threshold in KFACS; polypharmacy implies taking five or more prescribed medications; malnutrition implies MNA score <17; High-risk drinking implies two or more alcoholic drinks weekly (once seven cups for males and five cups for females). MMSE, TMT (out of 360 seconds, increasingly worse), Span (digit span test, total score of 28), FAB (total score of 18), recall test (total score of 10), and recognition test (total score of 10).
SGDS-K, Korean version of the Short Form of the Geriatric Depression Scale; KFACS, Korean Frailty and Aging Cohort Study; MMSE, Mini-Mental State Examination; TMT, Trail-Making Test; MNA, Mini Nutritional Assessment; FAB, Frontal Assessment Battery; BMI, body mass index; DM, diabetes mellitus; IPAQ, International Physical Activity Questionnaires.
*p<0.05.

8.8%), polypharmacy (61.8% vs. 45.5%), and depression (30.3% vs. 17.4%) at baseline than the non-constipation group.

The characteristics of the participants 2 years after baseline are shown in Supplementary Table S1. Depression prevalence 2 years after baseline was 149 (19.2%) in the non-constipation group and 24 (31.6%) in the constipation group (p = 0.011). There was no statistically significant difference between the two groups in changes in depression over 2 years (p = 0.674). (Supplementary Table S2).

Changes in Cognitive Functions over 2 Years according to Constipation at Baseline

Changes in word list recognition over 2 years in the functional constipation group (-0.55 ± 0.23) were much higher than those in the non-constipation group (-0.07 ± 0.05). No statistically significant differences were found in the other cognitive function tests (MMSE, word list memory, word list recall, digit span, FAB, and TMT) between the constipation and non-constipation groups (Table 2).

Table 2. Changes of cognitive functions for 2 years according to constipation at baseline

	Change of cognitive function for 2 years			p-value
	Total (n = 851)	No-constipation (n = 775)	Functional constipation (n = 76)	
MMSE	-0.36 ± 2.22	-0.37 ± 0.08	-0.28 ± 0.28	0.736
Word list memory	-0.17 ± 3.43	-0.14 ± 0.12	-0.43 ± 0.38	0.481
TMT (s)	0.61 ± 35.76	0.04 ± 1.29	6.45 ± 3.75	0.136
Word list recall	-0.31 ± 1.63	-0.29 ± 0.06	-0.46 ± 0.19	0.386
Word list recognition	-0.11 ± 1.53	-0.07 ± 0.05	-0.55 ± 0.23	0.045*
Digit span	-0.26 ± 2.40	-0.24 ± 0.09	-0.42 ± 0.27	0.539
FAB	0.26 ± 2.38	0.29 ± 0.08	-0.07 ± 0.31	0.215

Values are presented as the mean±standard deviation.
MMSE, TMT (out of 360 seconds, increasingly worse), Span (digit span test, total score of 28), FAB (total score of 18), word list recall test (total score of 10), and word list recognition test (total score of 10).
MMSE, Mini-Mental State Examination; TMT, trail-making test; MNA, Mini Nutritional Assessment; FAB, Frontal Assessment Battery.
*p<0.05.

Univariate Regression Analysis of Characteristics for the Change in Word List Recognition over 2 Years

Table 3 shows the results of the univariate regression analysis of each baseline characteristic for the change in word list recognition test scores over 2 years. Age was only significantly associated with changes in word list recognition ($p < 0.05$).

Adjusted Mean Changes in Word Recognition

As shown in Table 4, we evaluated the association between functional constipation and decline in word recognition test scores over 2 years after controlling for confounders using the ANCOVA test. The confounding variables were selected from the statistically significant variables (age, low physical activity, polypharmacy, and depression) for functional constipation (Table 1) and decline in word list recognition test scores in univariate regression analysis (Table 3), and variables (sex, years of education, type 2 diabetes mellitus, and polypharmacy) already known to be related to functional constipation and declines in cognitive function.[17-19] The baseline measures of each cognitive function test in 2018 were also included as confounding variables.

In the ANCOVA, the word list recognition test scores declined more significantly in the constipation group (-0.53) than in the non-constipation group (-0.07) after adjusting for confounding factors ($p = 0.008$).

Table 3. Univariate regression analysis of each baseline characteristic for difference in word list recognition test scores

	B coefficient	p-value
Age (y)	-0.03	0.037*
Sex, male	0.05	0.614
Independent living	-0.08	0.600
Married	0.15	0.184
Education (y)	0.01	0.551
Medical aid	-0.17	0.454
Urban living	0.03	0.814
BMI (kg/m^2)	0.00	0.891
Smoking	-0.07	0.801
High-risk drinking	-0.06	0.841
Low physical activity	-0.03	0.874
Polypharmacy	-0.03	0.810
Malnutrition	0.23	0.657
Type II DM	0.10	0.441
Hypertension	-0.06	0.534
Dyslipidemia	-0.03	0.521
Depression	0.06	0.660
Other psychiatric disorder	-0.10	0.714
Thyroid disorder	0.06	0.695
Renal disorder	0.08	0.491

Univariate regression analysis was used to identify associations between each baseline characteristic and difference in word list recognition test scores.
Depression implies that the SGDS-K score is >5; smoking implies that currently smoking; independent living implies that people can live without help from others, and not in nursing homes or hospitals; low physical activity implies that IPAQ-based weekly physical activity (kcal/week) is less than 495.65 kcal/week in males, 283.5 kcal/week in females, and less than the 20% threshold in KFACS; polypharmacy implies taking five or more prescribed medications; malnutrition implies MNA score <17; high-risk drinking implies two or more alcoholic drinks weekly (once seven cups for males and five cups for females).
SGDS-K, Korean version of Short Form of Geriatric Depression Scale; KFACS, Korean Frailty and Aging Cohort Study; MNA, Mini Nutritional Assessment; BMI, body mass index; DM, diabetes mellitus; IPAQ, International Physical Activity Questionnaires.
*p<0.05.

DISCUSSION

Our study showed that functional constipation predicted a decline in word list recognition in community-dwelling older adults.

The proposed mechanism of the effect of constipation on cognitive decline is that constipation can indirectly affect cognitive status through irritability and aggression as well as pain and discom-

Table 4. Adjusted mean difference in word list recognition test scores between baseline and 2 years later

	Adjusted mean difference in word list recognition test scores	95% CI	p-value
No-constipation	-0.07	-0.17 to 0.03	0.007*
Constipation	-0.54	-0.86 to -0.21	

ANCOVA was used to identify associations between functional constipation and cognitive decline, adjusted for age, sex, education years, low physical activity, polypharmacy, type 2 DM, depression, and baseline cognitive function test scores in 2018.
DM, diabetes mellitus; CI, confidence intervals; ANCOVA, analysis of covariance.
*p<0.05.

fort.[20] Although antipsychotics may cause constipation and aggravate cognitive decline,[21] participants in this cohort study were not affected by dementia or psychosis. The brain-gut axis hypothesis may be another mechanism. According to the brain-gut axis theory, the gut is connected to the brain through the gut-brain axis[22]; that is, the central nervous system communicates with the enteric nervous system, intestinal mucosa, and muscle layer through two-sided (afferent and efferent) pathways. Pathological changes in any component of the gut-brain axis may affect intestinal activity and lead to constipation. Some pathological studies have demonstrated that α-synuclein deposits can originate from the intestinal plexus and develop along the vagus nerve, eventually reaching the brain and resulting in the development of dementia.[23] The last assumption is the dysfunction of the parietal lobe of the brain. The parietal lobe is suggested to be associated with constipation in children[24] and is known to be related to short-term memory[25] and recognition function.[26] Therefore, parietal lobe dysfunction may be associated with constipation and its recognition. However, there are no studies on this connection yet; therefore, further investigation is needed. The initial and most prominent cognitive deficits associated with aging are usually amnestic rather than non-amnestic, and the finding that constipation is associated with a decline in word list recognition seems reasonable.

This study had some limitations. First, our study participants were ambulatory community-dwelling older adults. Hospitalized, institutionalized, or bedridden older adults were excluded; therefore, our results may not be generalizable to other population settings. Second, the detailed medication history of the participants was not investigated in this study. Medications such as antipsychotics can be associated with both constipation and cognitive impairment. However, we excluded those who had been taking narcotics and those with a history of dementia. In addition, the prevalence of psychiatric disorders did not differ between the two groups at baseline. Third, there is a possibility that organic constipation, such as colorectal cancer, was included because colonoscopy results were not collected in our study. However, those who had cancer within 5 years before baseline were excluded; therefore, the possibility of colorectal cancer was low.

Nevertheless, this study has several strengths. First, our study is based on a 2-year longitudinal prospective cohort-based study, which allows a more appropriate temporal relationship than previous cross-sectional studies. To the best of our knowledge, this is the first longitudinal study to show an association between functional constipation and cognitive function decline. Second, we used the KFACS data, which included a relatively large number of community-dwelling older adults aged 72–86 from 10 nationwide centers, including urban and rural areas.

In conclusion, functional constipation at baseline was associated with a decline in word list recognition 2 years later.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, CWW, SK; Data curation, HSJ, SK; Funding acquisition, CWW; Investigation, CWW, SK; Methodology, CWW, SK, HSJ; Writing-original draft, HSJ, SK; Writing-review and editing, all.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.22.0092.

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Broken Toughness: Iranian Older Adults' Perceptions of Abuse

Esmaeili Maryam[1], Adib Masoomeh[2], Zakeri Moghadam Masomeh[3], Dehghan Nayeri Nahid[1], Mazaheri Monir[4,5]

[1]Department of Critical Care Nursing and Management, Nursing and Midwifery Care Research Center, School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran
[2]Department of Medical-Surgical Nursing, School of Nursing and Midwifery, Gilan University of Medical Sciences, Tehran, Iran
[3]Department of Medical-Surgical Nursing, School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran
[4]Division of Nursing, Department of Neurobiology, Sophiahemmet University, Stockholm, Sweden
[5]Department of Health Sciences, Care Sciences and Society, Karolinska Institutet, Huddinge, Sweden

Corresponding Author:
Zakeri Moghadam Masomeh, PhD
Medical Surgical Department, School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran 0098, Iran
E-mail: zakerimo@tums.ac.ir
ORCID:
https://orcid.org/0000-0002-9762-1887

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Background: Older people abuse includes intentional or unintentional conduct or omission of a specific behavior by a trusted person that causes injury or distress to older people. This study described older peoples' perceptions of abuse in Iranian society. **Methods:** This qualitative study applied a conventional content analysis method to understand the perceptions of abuse among older Iranian people. Twenty older residents were selected by purposeful sampling. Data were collected through in-depth, semi-structured, and face-to-face interviews. The six-step Graneheim and Lundman content analysis method guided data analysis. MAXQDA software version 10 was used to manage the data. **Results:** The data analysis led to the identification of three main themes: broken toughness, hidden abuse, and exploitation. The first theme had two sub-themes: domination and disturbed peace and tranquility. **Conclusion:** Abuse resulted from a combination of causes and factors. Abuse was hidden in many cases and was not limited to physical abuse. The other examples of abuse included disrespect, deprivation of authority, disturbed tranquility, and financial exploitation of older adults.

Key Words: Abuse, Older people, Perception, Qualitative study

INTRODUCTION

One of the most obvious demographic changes in the 21st century is the aging of the population, which affects all countries worldwide, including Iran.[1)] People live longer due to improvements in living conditions, increase in life expectancy, and advances in medicine.[2)] Old age in high-income countries is 65 years of age, while in low-income countries, people ≥60 years are considered older adults.[3)] In Iran, the retirement age is 60 years, which marks the beginning of old age.[4)] An aging population is defined as an increase in the ratio of older people compared to other age groups[5)]; if this ratio is ≥7%, the population is considered old.[6)] Accordingly, Iran became an old population in 2006, with more than 7.2% of the population ≥60 years of age.[7)]

The increase in the older adult population, followed by an increase in chronic diseases, often increases the dependence and disability of older people in society. These factors, along with risk factors such as cognitive disorders, poor health, functional disorders, and dependence on caregivers, make older adults vulnerable to abuse.[8)] Moreover, increasing numbers of older adults in families may negatively affect the physical and mental condition of family members, which may lead to economic pressure, emotional stress, irresponsibility, fatigue, and social isolation, which, in turn, may lead to antisocial behavior, violence, and abuse. Abuse of older adults is a type of domestic violence, which is considered a major health problem in today's society.[9)]

Abuse of older adults includes intentional or unintentional conduct or omission of a specific behavior by a trusted person that causes injury or distress to older adults. This behavior may be repeated only once or several times and may occur as physical, psy-

chological, sexual, and financial abuse or neglect.[10] With the increasing population of older adults in Iran, special social conditions such as urbanization, modernization, changes in traditional values, conflict between the value system of the current and old generations, and readiness to accept responsibility for the care of older adults have caused families to fail to fulfill their roles and responsibilities towards their older members, ultimately exposing older adults to abuse and its consequences.[11]

Statistics show that 3.2% to 27.5% of older adults have experienced abuse.[12] A systematic review reported the prevalence rates of abuse in different countries, from 2.6% in the United States to 4% in Canada, 18.4% in Israel, and 29.3% in Spain.[13] While accurate statistics on the prevalence of abuse in Iran are lacking, Heravi-Karimooi et al.[11] reported that 1.6%–19.3% of Iranian older people in Tehran had experienced various forms of abuse.

How older adults react to abuse varies between individuals and is influenced by a variety of factors, including the physical/mental abilities and dependency of these older adults, as well as cultural factors and the perception of older adults about abuse.[14] In one study, about half of the older adults exposed to abuse described it as a family conflict and denied any ill-treatment; moreover, some older adults believed that others had the right to treat them in that way.[15] Some victims stated that they only sought help when the abuse was so severe that it was no longer tolerable or when they were confident that resources were available to help them. Several older adults also ignored abuse for various reasons, including shame and embarrassment, dependence on family members, and fear of rejection or revenge.[16-18]

A review of the literature shows that, considering the culture of Asian countries and the level of available social support for older adults, there is a lack of knowledge concerning the perceptions of abuse among older adults. These perceptions may change under the influence of the sociocultural and family context of a society.[19] Since there is no published data in Iran regarding older adults' perception of abuse, this study was conducted to understand and describe this topic.

MATERIALS AND METHODS

This study was conducted in 2017 and employed a descriptive qualitative design and applied a content analysis method.

Study Participants

Twenty older people residing in Rasht Province were selected through purposeful sampling. The inclusion criteria were age ≥ 60 years, ability to speak, Abbreviated Mental Test (AMT) score > 7, and experience of abuse. To achieve maximum variation, this study included both women and men with different educational backgrounds. The participants were recruited from families, retirees, municipal health centers, public parks, religious associations, mosques, clinics, and workplaces.

Data Collection

Data were collected using in-depth, semi-structured, face-to-face interviews for 10 months between October 2016 and August 2017. The time and place of the interviews were chosen in agreement with the participants. The interviews lasted 30–60 minutes depending on the participants' circumstances. Participant recruitment continued until the data were saturated and no new data were obtained. Before the interview, the study aim and the participants' rights were explained to the participants and informed consent was obtained.

The interviews began with general questions about personal characteristics. The participants were then asked to share their experiences of abuse. They were also asked about their perceptions of abuse. During the interview, follow-up questions were posed to clarify ambiguities; for instance, "Can you give an example in this regard" or "Can you explain more about this?" The interviews ended with open-ended questions such as "Is there anything else you would like to add?"

Ethical Considerations

This study was approved by the Ethics Committee of the Research Council of Tehran University of Medical Sciences (Code No. IR.TUMS.FNM.REC.1396.4459). Written or oral informed consent was obtained from all participants. The participants received information about the study aim, their rights as participants, and how the research data were used and stored. They were informed that their study participation was voluntary and that they could withdraw from the study at any time without any consequences. The participants permitted the researchers to record the interviews after being reassured about the confidentiality of the data.

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

Data Analysis

A conventional content analysis method was used to analyze the data. The interviews were recorded and then transcribed using the Microsoft Word software at the first opportunity after the interviews. The transcribed text was read several times to obtain a general understanding. Then, the semantic units were identified according to the study objectives. Finally, initial codes were prepared. The codes were categorized in terms of similarities and differences, forming classes and subclasses. This process was continued until

the main themes were extracted. MAXQDA-10 software (VERBI GmbH, Berlin, Germany) was used to manage the large volume of data.

Trustworthiness

This study used various methods to increase the rigor of the results. The extracted codes were reviewed by the research team such that the data were independently coded and classified by the researchers. The extracted themes were then compared to each other. In cases of disagreement over the themes, the researchers met and discussed them until an agreement was reached. Member checks were also conducted by sharing the extracted codes with some participants and asking them to confirm the extracted codes or note their opinions about possible inconsistencies. A peer-review method was also performed. Several interviews were randomly selected and given to researchers familiar with the qualitative method and who were not part of the project. Attempts were made to recruit participants with maximum variation to ensure the broader transferability of the results.

RESULTS

The findings of this study were the result of interviews conducted with 18 older adults (14 women and 6 men), ranging in age from 61 to 92 years. The other demographic characteristics of the participants are presented in Table 1. Analysis of the data resulted in three themes: broken toughness, hidden abuse, and exploitation. The first theme had two sub-themes: domination and disturbed peace and tranquility.

Table 1. Participants' characteristics

Characteristic	n (%)
Mean age (y)	68.9
60–75	18 (90)
76–90	1 (5)
> 90	1 (5)
Sex	
Male	6 (30)
Female	14 (70)
Education	
Illiterate	2 (10)
Primary and junior high school	6 (30)
High school	2 (10)
University	5 (25)
Marital status	
Married	9 (45)
Widowed	7 (35)
Divorced	3 (15)
Single	1 (5)
Living arrangements	
Alone	5 (25)
With spouse	7 (35)
With children	6 (30)
With relatives	2 (10)
Place of residence	
Rural areas	7 (35)
Urban areas	13 (65)
Abuser	
Children	11 (55)
Spouse	5 (25)
Relatives	4 (20)

Broken Toughness

Broken toughness was described as unacceptable and inappropriate behaviors that emotionally harmed older people and damaged their identity, self-esteem, and self-worth. These behaviors include dominating older people and disturbing their peace and tranquility.

Under Domination

Older adults considered the dominating behaviors by those around them to be a form of abuse. They believed that these behaviors would limit their authority and deprive them of a peaceful life. Depriving older people of the right to choose and imposing other family members' opinions and decision-making on them deprives older adults of their authority.

Older adults were dissatisfied and annoyed with others making decisions. The participants did not feel weak or incapacitated to the extent that others viewed them as old or disabled. An older woman who was forced by her son to leave her free life in a villa and live in an apartment despite her wishes complained that she had no choice but to choose her place of residence. "Life in a cage," she said. (About her place …)

"I did not want to live in an apartment. I felt imprisoned and caged when my son sold my villa and forced me to live in an apartment." (P9)

The participants believed that, at this age, despite some physical problems, they had many experiences that made them independent of others who tried to make decisions about their lives. The findings of this study demonstrated that older people with higher levels of education suffered more from deprivation of their independence by their children and others.

One of the most distressing problems mentioned by the older adults in this study was the restriction imposed on them to com-

municate with other family members or social communication, which could lead to feelings of loneliness and cause psychological problems, including despair, depression, boredom, feelings of helplessness, and anxiety. One of the participants (P2) stated the following:

"I do not have independence in my house. One day my brother called and wanted to come over to see me. My son yelled and shouted why my brother should come now. He said go and make an excuse to prevent hip from coming over; why is my brother trying to come without notice? I had to get permission from him to see my brother, and that made me very angry." (P2)

Human beings are born with the need for communication and intimacy. Satisfying this need requires positive communication and interaction with others, especially with family members. Thus, by limiting communication, older adults experience deprivation, which can lead to feelings of loneliness. Attempts to eliminate this sense of loneliness in older adults can reduce the risk of complications such as depression.

Disturbed Peace and Tranquility

Older adults referred to the loss of peace and tranquility due to the negligence of family members as a form of abuse. These findings indicated that older adults showed depressive behaviors. They talked about the behaviors and actions that deprived them of a peaceful life. Harassment through noise, clutter, and indiscipline in tidying the house and bringing home strangers disturbed older people and stressed them mentally. Thus, after going through the ups and downs of life, older adults increasingly require mental and physical peace to be able to spend this stage of life with a sense of satisfaction.

In this study, noise was perceived as a serious threat to the peace and tranquility of older people. Noise can have an indirect impact on older people in the form of irritation, physical and mental fatigue, sleep disturbances, increased heart rate, and high blood pressure. An older woman who was suffering from the noise made by her young grandchildren said:

"The young people in this generation sleep until noon and stay awake until midnight. My grandchildren's room is next to mine. All nights, I hear the sound of laughter or talking over the phone to friend or listening to music. Sometimes in the middle of the night, he began eating while the sound of dishes and utensils is coming from the kitchen."

Hidden Abuse

The older adults in this study were exposed to hidden abuse, including psychological harassment. Behaviors such as neglect, constant blame, intimidation, disrespect, and disregard were some of the hidden abuses experienced by the study participants. These behaviors, while not having visible physical effects, were highly annoying and distressing to the participants. From the point of view of the older adults, these behaviors were a type of abuse.

One of the hidden abuses was blame, including reminders of shortcomings in a two-way relationship and behaviors with the intention of humiliating and exercising power over older adults. Blame distorts another person's personality and creates a feeling of worthlessness for older adults, leading to a loss of dignity and self-confidence. Blaming in front of others and the constant criticism of older adults by their children were perceived as tormenting. The older adults used the phrase "getting injured" to express the depth of their psychological distress:

"I always find myself exposed to his reproach and horrible criticism, which bothers me a lot and takes away my confidence. He blames me for everything I do. I feel I have been injured. Like a dagger that breaks everything to pieces, I am injured and broken into pieces by his constant rebukes." (P7)

Older adults have emotional, livelihood, security, and recreational needs and like to participate in social activities. Thus, family members and the community should be aware of these needs and strive to provide them. As people age, their emotional needs may increase. From the point of view of older adults, making them wait is emotional abuse. No matter how good the financial situation of the older adult, they still emotionally need others and society. The older adults stated that they expected love and affection, meeting loved ones, and quicker responses from their family members and community.

The older adults in the present study experienced negligence from their family members in meeting their health needs. Unkindness, lack of empathy and sympathy, not visiting, not answering their questions and lack of attention deprived the older people of their emotional needs, to the degree that they felt "abandoned". The older adults stated that their children did not visit them often because of work-life difficulties.

Lack of support by family members in matters such as cleaning, shopping, cooking, and financial and banking affairs were other experiences of abuse.

"With this disease, I have to do everything on my own. I am on

dialysis three times a week. None of my children would take me to the clinic. I go there alone. My wife died two years ago, this house needs cleaning, and no one does the cooking. The hospital staff, who know that I live alone, sometimes feel sorry for me and adjust my dialysis time close to lunch time, so that I can have a Hot Bite." (P19)

Ignoring their attachments was another psychological abuse experienced by older adults in this study. Belonging means loving something. Belonging is a psychological property. Older adults are particularly sensitive to their belongings, as they have sentimental value. Older adults should be allowed to maintain their belongings and their sense of ownership and belonging should be respected.

Exploitation

Exploitation of older adults was perceived by the participants as another form of abuse, which took advantage of older adults throughout their lives. The older adults in the present study were only physically and financially exploited. They did not refer to other forms of exploitation such as sexual exploitation. Most of the older adults who were exploited were women or older adults who were physically or financially dependent.

Exploitation was also experienced as a threat, fear, and violence. An older woman who was severely abused by her husband said:

"I went to bed a little early last night, I was not feeling well, but he called me seven times. At night, he woke me up for whatever he wanted, and I had to provide him. One time he wanted water, another time he wanted tea, or fruit or medication. I had to serve him like a servant. I am no longer comfortable with him." (P10)

Deception involves breaking interpersonal covenants. The participants talked about lying, cheating in marriage, cheating in business, and fraud. They stated that some market sellers took advantage of their age and sold goods at higher prices.

Fraud against older adults was another example of the exploitation of older adults by their children. Forcing older people to share their capital, misuse of properties and assets for personal gain, and claiming inheritance were examples of financial exploitation mentioned by the participants.

"My problem is my children. They expect financial help from me. I'm retired and do not have that much money. My salary provides for me and my wife, but they expect me to sell the house I live in and meet their financial needs. But I cannot do that now at this age." (P14)

DISCUSSION

The results of this study illustrated older adults' perception of abuse in Iran. The participants referred to abuse as a factor that disrupted their strength and tranquility in old age. They also referred to hidden abuse and exploitation of older adults.

According to the participants, psychological and verbal abuse were frustrating. The participants discussed psychological harassment, pain, and discomfort, which were no less than physical harassment. Physical abuse is not the only type of abuse that results in injury, as it includes a broader range such as threats, psychological and emotional violence, humiliation, ridicule, and obscenity. The impact of such behaviors is greater than that of physical abuse.[21] In another study, psychological abuse was the most common abuse mentioned by older adults. Approximately 68.8% of the study participants had experienced psychological abuse, 37% had experienced neglect, 6.3% had experienced financial abuse, and 3.8% had experienced physical abuse. None of the participants had been sexually abused. Another study in Iran demonstrated that psychological and financial abuses were the most prevalent abuse among older adults.[22] The reported rates of psychological abuse were 20.7% in Spain, 29.7% in Sweden, 27.1% in Germany, and 21.9% in Portugal.[23] Another study showed that the highest prevalence of abuse in the United States and the United Kingdom were physical and verbal violence, respectively.[9] Many studies have confirmed that psychological abuse is one of the most important types of domestic abuse among older people. For example, Filipska et al.,[24] Pi et al.,[10] Heravi-Karimooi et al.,[11] and Koosheshi and Valadvand[25] reported the importance of psychological abuse. The similarities and differences in the types of abuse in Western, Eastern, and American societies can be attributed to cultural differences. Psychological abuse is more prevalent in Eastern societies, including Iran. This can perhaps be attributed to the strong emotional bonds and attachments, especially emotional attachments between parents and children. This type of relationship leads to widespread interactions and, sometimes, excessive expectations of parents and children from each other such that some behaviors are considered abusive from their point of view. However, economic problems and rising inflation in recent years have deprived children of financial support, which, in the presence of severe economic pressures on children, may lead to the financial abuse of their parents.[8]

In the study of Heravi-Karimooi et al.,[11] the nature of abuse included "highly disturbing emotional behavior" and "disrespect." The participants stated that the abuse of older people was a distressing emotional behavior and an unpleasant, torturous, difficult, and painful inner experience. In the present study, almost all par-

ticipants identified disrespect as a form of abuse. Disrespect is a form of psychological abuse among older adults.[23] Disrespect includes behaviors and attitudes that violate cultural norms. In many Asian cultures, disrespect may be considered the most important form of abuse.[26] The older adults in the present study considered any behaviors that made them feel humiliated and ignored, especially in the public, to be disrespectful. A previous study reported that older Koreans considered their grandchildren's ignorance of them to be disrespectful. From their perspective, not speaking the mother tongue in conversation with parents, direct opposition to older people, or lack of attention and value of older people when entering the home were considered disrespectful behaviors.[27] Older Chinese adults also reported disrespect as the most serious form of abuse. In one study, Chinese seniors noted sharing responsibility among family members as a form of disrespect for them. They believed that, in this case, they would be exchanged like a ball among family members, which they perceived to be a kind of disrespect.[28,29] In Japanese culture, parental blame by children is a form of disrespect for parents and older adults.[30] Heravi-Karimooi et al.[11] reported that the participants stated that they needed respect more than water and food, and that disrespect was worse for them than thirst and hunger. Older people's description of disrespect in that study included rejection, neglect, lack of a dignified life, and violation of their rights. Another psychological abuse reported by older adults in the present study was a lack of communication with older adults. A study of Chinese and Korean older adults reported that failure to communicate with older adults was also considered a form of psychological humiliation and punishment.[31-33]

Financial expectations and pressure on older adults to sell their property and assets against their will, expropriation, fraud in transactions, and the prevention of older adults from making decisions regarding their own property and assets, use of older people's pensions, and unauthorized transfers of property were among the financial abuses experienced by older adults in the present study. A previous study reported that older adults spent their financial resources on educating their children and sacrificing their personal needs in favor of their children.[34] The older adults in our study experienced financial abuse such as pressure from family members to acquire land, property, and capital; in contrast, a study in Africa reported theft as the most common financial abuse. The unauthorized acquisition of property and assets belonging to older adults was also reported.[35]

The present study had several limitations, including the age of the participants and their fatigue during the interview, which might have affected their responses. Therefore, the researchers adjusted the interview times according to the participants' physical and mental conditions. The abuse of older adults is a hidden problem among many families and is a social taboo according to the prevailing culture in Iranian communities; hence, many abused older adults were not willing to be interviewed. Therefore, participant recruitment in this study was difficult and long. The process of dealing with abuse and its consequences is part of the education of medical students, as well as part of continuing educational programs for healthcare professionals. The results of the present study may help health workers to provide essential social, economic, welfare, and health support to older adults and their families. Health care providers can also benefit from employing specialized expert teams to design and implement support programs. Empowering older adults and their families plays an important role in preventing abuse. As the abuse of older adults is multidimensional and context-based, similar studies should be conducted in other contexts with diverse cultures and religions to gain a better understanding of the phenomenon.

In conclusion, the results of this study revealed that abuse may be hidden in many cases and was not limited to physical abuse. Other examples of abuse include disrespect, deprivation of authority, disturbed peace and tranquility, and financial exploitation of older adults. The results of this study can help increase knowledge in the field of abuse of older adults.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Study concept and design, ME, MA; Acquisition of subjects and/or data, ME, MA, MZ; Analysis and interpretation of the data, ME, MA, MZ, NN; Preparation of the manuscript, ME, MA, MZ, NN.

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Associations between Work-Related Factors and Happiness among Working Older Adults: A Cross-Sectional Study

Taiji Noguchi[1,2,3], Sadao Suzuki[2], Takeshi Nishiyama[2], Takahiro Otani[2], Hiroko Nakagawa-Senda[2], Miki Watanabe[2,4], Akihiro Hosono[2,5], Yuya Tamai[2], Tamaki Yamada[6]

[1]Department of Social Science, Center for Gerontology and Social Science, Research Institute, National Center for Geriatrics and Gerontology, Aichi, Japan
[2]Department of Public Health, Nagoya City University Graduate School of Medical Sciences, Aichi, Japan
[3]Japan Society for the Promotion of Science, Tokyo, Japan
[4]Faculty of Education, Aichi University of Education, Aichi, Japan
[5]Meito Public Health Center, City of Nagoya, Aichi, Japan
[6]Okazaki Public Health Center, Okazaki Medical Association, Aichi, Japan

Corresponding Author:
Taiji Noguchi, PhD, MSc
Department of Social Science, Center for Gerontology and Social Science, Research Institute, National Center for Geriatrics and Gerontology, 7-430 Morioka, Obu, 474-8511, Aichi, Japan
E-mail: noguchi.taiji0415@gmail.com
ORCID:
https://orcid.org/0000-0001-9165-5501

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Background: As the global population ages, the number of older adults working after retirement is increasing. However, knowledge regarding working conditions for health and happiness among this population is insufficient. Therefore, we examined the association between work-related factors (e.g., employment status, daily working time, work-related stress) and happiness among working older adults. **Methods:** This cross-sectional study recruited Japanese older adults, aged 65 years and older, who were engaged in paid work, during their annual health checkups. Self-administered questionnaires were used to assess happiness, employment status, daily working time, and work-related stress (i.e., job strain, job control, job suitability, and relationships at work). **Results:** The data of 520 men and 168 women were analyzed (mean ages, 68.5 years and 68.0 years, respectively). The results of the multivariable ordinal logistic regression analysis indicated that low job suitability was negatively associated with happiness in men (odds ratio [OR]=0.46; 95% confidence interval [CI], 0.28– 0.78; p=0.004). In women, long working hours and low job control were negatively associated with happiness—working >8 hours daily (OR=0.29; 95% CI, 0.12–0.71; p=0.008) and low job control (OR=0.29; 95% CI, 0.12–0.72; p=0.009). **Conclusion:** The results showed that low job suitability for men and long daily working time and low job control for women were negatively associated with happiness. These findings suggest the need to improve working conditions to enhance the well-being of working older adults.

Key Words: Happiness, Occupational stress, Job satisfaction

INTRODUCTION

With the continuously aging global population, achieving both health and longevity among older adults is an important public health challenge. In particular, maintaining social engagement during old age is crucial for ensuring healthy aging and enhancing peoples' well-being.[1,2] Continuing to engage in paid work is a particularly promising social commitment for this population group. In addition to the income earned, engaging in paid work provides multiple benefits for older adults, including greater social contributions, larger social networks, and more meaningful life goals, which lead to positive health benefits and overall improved well-being.[3]

Recently, particularly in Japan, where the aging rate is the highest worldwide, an increasing number of older adults either continue or intend to return to work after retirement, despite Japan's mandatory retirement age of 65 years.[4,5] In terms of working or not work-

ing post-retirement, a growing body of evidence has demonstrated the effects on the physical and mental health of older adults. From a traditional perspective, retirement due to old age does not necessarily have a negative effect. Some systematic reviews have suggested the positive impact of retirement on mental health.[6,7] Meanwhile, other studies have reported the positive health impacts of working post-retirement.[8] Thus, the results have been inconsistent.

Despite the contradictory results of these previous studies, the social environment of older adults is changing, such as an increasing number of individuals living alone and the weakening of their neighborhood relationships.[9,10] Thus, the meaning of post-retirement work may have changed. Therefore, further research is needed. In this context, the latest systematic review suggested the overall positive effects of people working in older age on physical and mental health.[11] Additionally, recent studies of a large sample of older Japanese adults reported that continuing to work during old age was associated with a lower risk of mortality,[12] greater activities in daily living,[13] higher functional capacity,[14] healthy cognitive functioning,[12] and better mental health maintenance.[12] Furthermore, working during older age also helped to prevent the incidence of long-term care.[15] Therefore, as the latest evidence suggests, continuing to work during older age may be a promising approach to increasing the social engagement of this population group, which could, in turn, maintain their overall health and well-being.

Despite the increasing number of older adults continuing to work post-retirement, limited research has focused on the personal impact of their job conditions, such as employment status or working environment. A previous systematic review suggested that working post-retirement had overall positive health effects, while poor working environments and high work-related stress had negative impacts,[11] including on physical and mental health.[16,17] Additionally, adverse health effects may occur depending on older adults' motivation to work.[18] These studies highlight the need for further research on positive work-related factors to support employed older adults' overall well-being. However, evidence is insufficient regarding these work-related factors that affect the health and well-being of working older adults. Further studies on this association are needed to promote healthy aging and maintain the well-being of older adults.

Therefore, this study examined the associations between work-related factors and happiness, a core concept of well-being, among working older adults.

MATERIALS AND METHODS

Study Participants

This cross-sectional study was conducted as part of the Japan Multi-Institutional Collaborative Cohort Study (J-MICC Study) in the Okazaki area.[19,20] We recruited community-dwelling Japanese adults aged 35–79 years from among the participants of regular health checkups at a public health center in Okazaki City, Aichi, Japan, between 2007 and 2011. During this period, a self-administered questionnaire was mailed to the participants before their health checkups. Subsequently, the questionnaire was collected at the health check-up site. A total of 7,580 individuals were recruited (response rate, 25.9%).[20] Responses from those < 65 years of age (n = 5,071), those not working (n = 1,820), and those with missing information on the work status question (n = 1) were excluded. Therefore, the final analysis included 688 older adults.

All participants provided written informed consent and the study protocol was approved by the ethics committee of affiliated institutions. This study was conducted in accordance with the latest guidelines of the Declaration of Helsinki.

Also, this study complied with the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[21]

Happiness

Based on a previous study, the participants' levels of happiness were assessed using the following single question concerning subjective happiness: "How would you score your current sense of happiness on a scale out of 100 points?"[22] Earlier research has suggested that happiness is an essential component of well-being[23]; therefore, we used this score as the outcome variable. We divided the score into four quartile ranges according to sex, as the data were not normally distributed—for men, 81.5 ± 12.9 (mean ± standard deviation), 80.0 (10.0) [median (interquartile range)], -1.38 (skewness), and 4.79 (kurtosis); for women, 82.6 ± 13.5 (mean ± standard deviation), 85.0 (10.0) [median (interquartile range)], -1.01 (skewness), and 4.28 (kurtosis).

Work-Related Factors

Regarding work-related factors, the participants' employment status, daily working hours, and work-related stress were assessed using a self-administered questionnaire. Employment status was categorized as "self-employed," "regular employment," and "non-regular employment." Daily working time was classified into three categories; " < 6 hours," "6–8 hours," and " > 8 hours." Work-related

stress was assessed using the simplified Brief Job Stress Questionnaire (BJSQ), which is a shortened version of the BJSQ with confirmed validity and reliability in assessing job stress.[24,25] Using these variables, we evaluated four areas of work-related stress: job strain, job control, job suitability, and relationships at work.[24] Job strain was defined as the psychological and physical workload. Job control was conceptualized as skill discretion and decision authority. Job suitability referred to the use of one's own skills and knowledge at work, as well as job satisfaction.

Relationships at work involved positive psychological relationships with colleagues. The participants answered 17 questions on work-related stress. Based on their responses, we assessed each type of stress and divided it into two categories (Supplementary Table S1).

Covariates

Based on a previous study,[17] we included participants' socioeconomic status, health status, and health-related behaviors as factors associated with job conditions and happiness. These included participants' age, living arrangements, educational attainment, present illnesses, body mass index (BMI), alcohol consumption status, smoking status, and exercise habits. Living arrangements were dichotomized as "living alone" and "living with others." Educational attainment was categorized as <9, 10–12, and ≥ 13 years. Present illnesses were categorized as "none" and "≥ 1" according to the number of diagnosed illnesses, including cancer, heart disease, stroke, hypertension, dyslipidemia, and diabetes. The BMI was dichotomized as <25.0 kg/m^2 and ≥ 25.0 kg/m^2. Alcohol consumption and smoking status were dichotomized as "never/past" and "current." Exercise habits were dichotomized as $<$once/week and $\geq$once/week.

Statistical Analysis

All analyses were conducted according to participants' sex, as men and women may have different priorities at work, particularly in the Japanese society, with different experiences and social meanings. First, we calculated the descriptive statistics collected from the participants' demographic characteristics. Second, we used a multivariable ordinal logistic regression analysis to calculate the odds ratio (OR) and 95% confidence interval (CI) of the studied work-related factors as association variables with participants' happiness scores in reference to the lowest quartile score category, based on the assumption of proportional odds.[26] Two models were then used: a crude model with no adjustments and an adjusted model for all covariates.

As a sensitivity analysis, we ran similar analysis models on absolute happiness scores every 10 points.

To mitigate potential bias due to missing information, a multiple imputation method was applied under the missing at random (MAR) assumption (i.e., the missing data mechanism depends only on the observed variables). We generated 20 imputed datasets using the multiple imputations by chained equations (MICE) procedure and pooled the results using standard Rubin's rule.[27]

The significance level was set at $p<0.05$. R software version 3.6.3 for Windows (R Foundation for Statistical Computing, Vienna, Austria) was used for all statistical analyses. The multiple imputation approach involved the use of the MICE function (mice package).

RESULTS

The final analysis included data from 520 men and 168 women. Tables 1 and 2 show the characteristics of the male and female participants, respectively. The mean ages were 68.5 ± 3.0 years for men and 68.0 ± 2.6 years for women. Among the participating men, those with a higher level of happiness were more likely to have higher educational attainment, higher BMI, regular exercise habits, non-regular employment, high job strain, high job suitability, and good relationships at work; not consume alcohol or smoke; and work <5 hours daily. Among the participating women, those with a higher level of happiness were more likely to consume alcohol, have regular exercise habits, work for no more than 8 hours daily, have a high sense of job control, and feel a high sense of job suitability.

Table 3 shows the results of the analysis of associations between the examined work-related factors and participant happiness, as identified by multivariable ordinal logistic regression analysis conducted separately for men and women. After adjusting for covariates, low job suitability was negatively associated with happiness in men (OR = 0.46; 95% CI, 0.28– 0.78; $p = 0.004$). In women, a daily working time of >8 hours and low job control were negatively associated with happiness (daily working time of <6 hours vs. >8 hours: OR = 0.29; 95% CI, 0.12–0.71; $p = 0.008$; low job control: OR = 0.29; 95% CI, 0.12– 0.72; $p = 0.009$). These results showed similar trends in the sensitivity analysis, for which the outcomes were divided into absolute ranges (Supplementary Table S2).

The results of the analysis results after excluding self-employed participants were nearly the same as the main results (Supplementary Table S3).

DISCUSSION

This cross-sectional study examined the association between work-related factors and happiness in older adults. Our results in-

Table 1. The characteristics of men participants

	Happiness score			
	Quartile 1 (lowest) (n = 130)	Quartile 2 (n = 130)	Quartile 3 (n = 130)	Quartile 4 (highest) (n = 129)
Age (y)	68.6 ± 3.0	68.4 ± 3.1	68.8 ± 3.1	68.1 ± 3.0
Living arrangement				
Living with others	119 (91.5)	125 (96.2)	126 (96.9)	124 (96.1)
Living alone	11 (8.5)	5 (3.8)	4 (3.1)	5 (3.9)
Educational attainment (y)				
< 10	36 (27.7)	51 (39.2)	40 (30.8)	35 (27.1)
≥ 10	94 (72.3)	79 (60.8)	90 (69.2)	94 (72.9)
Present illness				
None	56 (43.1)	66 (50.8)	72 (55.4)	57 (44.2)
One or more	74 (56.9)	62 (47.7)	58 (44.6)	71 (55.0)
BMI (kg/m^2)				
< 25.0	99 (76.2)	102 (78.5)	97 (74.6)	93 (72.1)
≥ 25.0	31 (23.8)	28 (21.5)	33 (25.4)	36 (27.9)
Alcohol consumption status				
Never/past	27 (20.8)	31 (23.8)	39 (30.0)	38 (29.5)
Current	103 (79.2)	99 (76.2)	91 (70.0)	91 (70.5)
Smoking status				
Never/past	107 (82.3)	111 (85.4)	112 (86.2)	103 (79.8)
Current	23 (17.7)	19 (14.6)	18 (13.8)	26 (20.2)
Exercise habits				
< once/week	32 (24.6)	35 (26.9)	27 (20.8)	28 (21.7)
≥ once/week	98 (75.4)	95 (73.1)	103 (79.2)	101 (78.3)
Employment status				
Regular-employed	10 (7.7)	9 (6.9)	10 (7.7)	16 (12.4)
Self-employed	44 (33.8)	54 (41.5)	54 (41.5)	55 (42.6)
Non-regular-employed	76 (58.5)	67 (51.5)	66 (50.8)	58 (45.0)
Daily working time (hr/day)				
< 6	31 (23.8)	33 (25.4)	39 (30.0)	42 (32.6)
6–8	44 (33.8)	50 (38.5)	40 (30.8)	32 (24.8)
≥ 8	55 (42.3)	45 (34.6)	51 (39.2)	55 (42.6)
Job strain				
Low	116 (89.2)	114 (87.7)	116 (89.2)	107 (82.9)
High	14 (10.8)	16 (12.3)	14 (10.8)	20 (15.5)
Job control				
High	104 (80.0)	111 (85.4)	112 (86.2)	105 (81.4)
Low	26 (20.0)	19 (14.6)	18 (13.8)	22 (17.1)
Job suitability				
High	103 (79.2)	114 (87.7)	116 (89.2)	117 (90.7)
Low	27 (20.8)	15 (11.5)	14 (10.8)	10 (7.8)
Relationships at work				
Good	110 (84.6)	116 (89.2)	120 (92.3)	117 (90.7)
Poor	12 (9.2)	10 (7.7)	6 (4.6)	7 (5.4)

Values are presented as mean±standard deviation or number (%).
Missing data: n=1 for happiness score, n=3 for present illness, n=2 for job strain, n=2 for job control, n=2 for job suitability, and n=2 for relationships at work.
BMI, body mass index.

Table 2. The characteristics of women participants

	Happiness score			
	Quartile 1 (lowest) (n = 42)	Quartile 2 (n = 42)	Quartile 3 (n = 42)	Quartile 4 (highest) (n = 42)
Age (y)	67.6 ± 2.6	68.4 ± 2.9	68.0 ± 2.6	67.9 ± 2.3
Living arrangement				
Living with others	37 (88.1)	33 (78.6)	33 (78.6)	37 (88.1)
Living alone	5 (11.9)	9 (21.4)	9 (21.4)	5 (11.9)
Educational attainment (y)				
< 10	15 (35.7)	11 (26.2)	9 (21.4)	18 (42.9)
≥ 10	27 (64.3)	31 (73.8)	33 (78.6)	24 (57.1)
Present illness				
None	19 (45.2)	24 (57.1)	21 (50.0)	20 (47.6)
One or more	23 (54.8)	18 (42.9)	21 (50.0)	22 (52.4)
BMI (kg/m^2)				
< 25.0	29 (69.0)	36 (85.7)	35 (83.3)	29 (69.0)
≥ 25.0	13 (31.0)	6 (14.3)	7 (16.7)	13 (31.0)
Alcohol consumption status				
Never/past	34 (81.0)	29 (69.0)	31 (73.8)	30 (71.4)
Current	8 (19.0)	13 (31.0)	11 (26.2)	12 (28.6)
Smoking status				
Never/past	40 (95.2)	42 (100)	40 (95.2)	39 (92.9)
Current	2 (4.8)	0 (0)	2 (4.8)	3 (7.1)
Exercise habits				
< once/week	14 (33.3)	12 (28.6)	12 (28.6)	9 (21.4)
≥ once/week	28 (66.7)	30 (71.4)	30 (71.4)	33 (71.4)
Employment status				
Regular-employed	5 (11.9)	6 (14.3)	4 (9.5)	4 (9.5)
Self-employed	10 (23.8)	12 (28.6)	17 (40.5)	9 (21.4)
Non-regular-employed	27 (64.3)	24 (57.1)	21 (50.0)	29 (69.0)
Daily working time (hr/day)				
< 6	8 (19.0)	4 (9.5)	7 (16.7)	12 (28.6)
6–8	6 (14.3)	15 (35.7)	8 (19.0)	9 (21.4)
≥ 8	28 (66.7)	23 (54.8)	27 (64.3)	21 (50.0)
Job strain				
Low	36 (85.7)	40 (95.2)	38 (90.5)	35 (83.3)
High	6 (14.3)	2 (4.8)	4 (9.5)	5 (11.9)
Job control				
High	32 (76.2)	35 (83.3)	38 (90.5)	39 (92.9)
Low	10 (23.8)	7 (16.7)	4 (9.5)	3 (7.1)
Job suitability				
High	34 (81.0)	39 (92.9)	37 (88.1)	41 (97.6)
Low	8 (19.0)	3 (7.1)	5 (11.9)	1 (2.4)
Relationships at work				
Good	37 (88.1)	40 (95.2)	37 (88.1)	40 (95.2)
Poor	1 (2.4)	1 (2.4)	3 (7.1)	1 (2.4)

Values are presented as mean±standard deviation or number (%).
Missing data: n=2 for job strain and n=8 for relationships at work.
BMI, body mass index.

Table 3. Associations between work-related factors and happiness among men and women, multivariable ordinal logistic regression analysis

	Male (n = 520)				Female (n = 168)			
	Crude model		Adjusted model		Crude model		Adjusted model	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Employment status (ref: regular-employed)								
Self-employed	0.78 (0.43–1.43)	0.424	0.81 (0.44–1.49)	0.493	2.06 (0.75–5.65)	0.163	1.96 (0.68–5.64)	0.212
Non-regular-employed	0.66 (0.36–1.21)	0.182	0.64 (0.35–1.17)	0.148	2.48 (0.90–6.80)	0.080	1.95 (0.67–5.68)	0.220
Daily working time (ref: < 6 hours)								
6–8 hours	0.68 (0.45–1.02)	0.062	0.68 (0.45–1.03)	0.072	0.48 (0.19–1.20)	0.116	0.39 (0.15–1.02)	0.058
≥ 8 hours	0.91 (0.61–1.34)	0.630	0.93 (0.62–1.40)	0.741	0.36 (0.15–0.86)	0.023	0.29 (0.12–0.71)	0.008
Job strain (ref: low)								
High	1.19 (0.73–1.94)	0.487	1.17 (0.72–1.92)	0.525	0.80 (0.29–2.25)	0.676	0.79 (0.27–2.31)	0.673
Job control (ref: high)								
Low	1.20 (0.75–1.92)	0.448	1.16 (0.72–1.86)	0.548	0.34 (0.14–0.82)	0.018	0.29 (0.12–0.72)	0.009
Job suitability (ref: high)								
Low	0.47 (0.28–0.79)	0.005	0.46 (0.28–0.78)	0.004	0.46 (0.17–1.23)	0.125	0.42 (0.16–1.13)	0.086
Relationships at work (ref: good)								
Poor	0.55 (0.29–1.04)	0.066	0.59 (0.31–1.12)	0.108	1.03 (0.24–4.47)	0.965	1.14 (0.24–5.39)	0.865

The adjusted model comprised participants' age, living arrangement, educational attainment, present illness, body mass index, alcohol consumption, smoking status, and exercise habits.
OR, odds ratio; CI, confidence interval.

dicated that low job suitability for men and long working hours and low job control for women were significantly and negatively associated with happiness. These findings underscore the conditions needed to promote beneficial working environments that enhance the well-being of working older adults.

Among older men, job suitability was associated with higher levels of happiness. The job suitability assessed in this study indicated that the use of work knowledge and skill sets in their work was associated with high levels of job satisfaction. In Japan, many older men regularly engage in single occupations until they reach the mandatory retirement age. Using their skills and knowledge in their older age during their retirement might increase their job satisfaction, potentially leading to higher life satisfaction. Additionally, men are more likely to seek a greater degree of professionalism and power in their workplace.[28] Therefore, even in their retirement work, having the expertise to use their skills and knowledge might lead to happiness.

Meanwhile, among older women, job control was associated with higher happiness, while long working hours was negatively associated with happiness. The interpretation of these results is speculative; however, there are possible reasons for these findings. Many older adult women in Japan do not engage in full-time employment. Therefore, they may be more likely to search for decision-making authority in their work, such as discretion and freedom of choice in operation, when they continue to work at an older age. Alternatively, in Japan, women may engage in many tasks related to household and community matters. Therefore, non-discretionary working conditions and long working hours may interfere with domestic tasks, which might negatively affect women's happiness.

A previous study reported the benefits of working in older age only for men, including preventing the onset of functional disability.[13] Additionally, productive activities in older age, such as paid work and volunteering, were beneficial only for men's mental health.[29] These findings imply the presence of sex differences in the impact of working status among older adults. In Japanese society, the role of paid work likely differs between men and women because the latter are relatively more likely to also have a social role outside their employment, such as housework or various community social involvements.

Meanwhile, the sex differences in work-related factors of happiness might be influenced by employment status between men and women. Unlike men, self-employed cases were relatively low in women participants. However, our preliminary analysis that excluded self-employed respondents showed results that were highly similar to those of the main analysis. We presume that the work-related factors associated with happiness differ by sex and not by employment type. Therefore, when promoting increased employment for older adults, a given social system needs to carefully consider the quality of working conditions, in addition to the different

job needs of men and women.

As the Japanese population ages, the number of older adults who continue to work after retirement will continue to increase.[6,8] Our results provide information on how to structure working environments for employed older adults to enhance their overall health and happiness. However, despite the growing evidence that working in later years can benefit overall health and happiness, it might also have negative consequences.[11,16,17] In addition to previous knowledge, our findings contribute to the promotion of the employment of older adults by identifying work-related factors that may be detrimental to happiness in this population group. The results of the present study highlight the need to consider the suitability of the job, create friendly working conditions, and make appropriate changes to the working environment when promoting increased employment of older adults. Further evidence is needed to promote the employment of older adults, including more detailed studies of working conditions and environments.

This study has certain limitations. First, the cross-sectional design prevented our determination of the causality of the investigated work-related factors on participants' happiness. Therefore, further investigation using longitudinal data is required. Second, we had no information about participants' economic status, such as income or overall wealth. These variables may have resulted in residual confounding factors. Third, we had no detailed information about the nature of the participants' jobs (for instance, employment in blue- or white-collar jobs). This information is important to note because the relationship between work-related factors and happiness may differ depending on the nature of the job. Fourth, we had no information on existing or potential mental illnesses, including depression. Mental illness is an important determinant of happiness, which may result in a bias in our results. Fifth, this study recruited only those individuals who had received annual health check-ups at a public health center. In addition, the response rate of the participants to the study recruitment was low (25.9%). Therefore, the backgrounds of the study participants may differ from those of typical older workers in this area. Our sample might have been more health-conscious and had a higher socioeconomic status compared to those of the average worker. This limitation may have resulted in a selection bias. Finally, we recruited participants from only one public health center in a suburban area of Japan. The types and conditions of work may have characteristics unique to this area. Therefore, the generalizability of our results may be limited and future studies using a nationwide sample are required.

In conclusion, the results of the present study showed that low job suitability in men, as well as long daily working time and low job control in women, were significantly and negatively associated with happiness among older working adults. These findings underscore the need to improve the working conditions of this population group to enhance their overall health and well-being.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, TNoguchi; Data curation, SS, TY; Formal analysis, TNoguchi; Supervision, SS; Writing_original draft, TNoguchi; Writing_review & editing, TNoguchi, SS, TNishiyama, TO, HNS, MW, AH, YT, TY.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.22.0048.

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Sexual Difference in Effect of Long Sleep Duration on Incident Sarcopenia after Two Years in Community-Dwelling Older Adults

Hyona Lee[1], Sunyoung Kim[2], Byung Sung Kim[2], Miji Kim[3], Jisoo Yang[2], Hanhee Bae[1], Chang Won Won[2]

[1]Department of Family Medicine, Kyung Hee University Medical Center, Seoul, Korea
[2]Department of Family Medicine, College of Medicine, Kyung Hee University, Seoul, Korea
[3]Department of Biomedical Science and Technology, Kyung Hee University, Seoul, Korea

Corresponding Author:
Chang Won Won, MD, PhD
Elderly Frailty Research Center,
Department of Family Medicine,
College of Medicine, Kyung Hee
University, Kyungheedaero 23,
Dongdaemun-gu, Seoul, 02447, Korea
E-mail: chunwon62@naver.com
ORCID:
https://orcid.org/0000-0002-6429-4461

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Background: Sarcopenia, a progressive and generalized skeletal muscle disorder involving an accelerated loss of muscle mass and muscle function, is a common condition in older individuals. This study aimed to determine whether sleep latency and duration were independently associated with incident sarcopenia and to explore sex differences in these associations. **Methods:** This 2-year longitudinal analysis of cohort study data included community-dwelling participants of the 2016–2017 Korea Frailty and Aging Cohort Study aged 70–84 years at baseline survey who completed the 2-year follow-up survey. Logistic regression was used to calculate the odds ratios (ORs) for sarcopenia and sarcopenia components. Sarcopenia was defined using the 2019 Asian Working Group for Sarcopenia guidelines. **Results:** Among 1,353 non-sarcopenic participants in the baseline survey, 1,160 (85.8%) and 193 (14.2%) were classified as non-sarcopenic and sarcopenic, respectively, after 2 years. Long sleep duration (>8 hours per night) was associated with incident sarcopenia in male—OR=2.41 (95% confidence interval [CI], 1.13–5.17) after adjusting for confounding factors. Long sleep duration was specifically associated with the development of low skeletal muscle mass and low muscle strength in male—adjusted OR=2.16 (95% CI, 1.02–4.61) and adjusted OR=2.70 (95% CI, 1.13–6.43), respectively. In female, compared to normal sleep duration, the adjusted ORs for long and short sleep duration for sarcopenia were 2.093 (95% CI, 0.753–5.812; p=0.157) and 0.852 (95% CI, 0.520–1.393; p=0.522), respectively, which were not significant. **Conclusion:** In male, long sleep duration was associated with incident sarcopenia, specifically the development of low muscle mass and low muscle strength, but not with low physical performance.

Key Words: Sleep, Sarcopenia, Sex characteristics, Aged, Cohort studies

INTRODUCTION

Aging is frequently accompanied by changes in sleep patterns, including increased sleep disturbances, which affect up to 50% of the population.[1] Sleep disturbances are associated with increased risks of coronary disease, hypertension, diabetes, and mortality.[2-5] Marked changes in sleep structure with aging have been reported, including decreased total sleep time and sleep efficiency and increased wake time after sleep onset.[6]

Sarcopenia, a progressive and generalized skeletal muscle disorder involving an accelerated loss of muscle mass and muscle function, is a common condition in older individuals.[7] The prevalence of sarcopenia ranges from 4% to 46.8% according to different diagnostic criteria.[8] Sarcopenia contributes significantly to morbidity, decreased quality of life, and increased health care costs in older adults.[9] In particular, sarcopenia is significantly correlated with cardiometabolic risk factors, especially diabetes, hypertension, and dyslipidemia.[10]

Several studies have indicated a relationship between sleep disturbances and sarcopenia.[11-13] Kwon et al.[12] showed that long

sleep duration (≥ 9 hours) was independently associated with sarcopenia in Korean adults, while Hu et al.[13] showed a U-shaped relationship between self-reported sleep duration and sarcopenia in Chinese community-dwelling older female. These previous studies were cross-sectional, a study design that did not allow the inference of causality between sleep disturbance and sarcopenia.[11-13] Recently, in a 4-year longitudinal study, Nakakubo et al.[14] showed an association between long sleep duration and the risk of progression to sarcopenia among older Japanese adults. However, this study did not explore the effect of sleep latency or sex differences on these associations. Related studies have reported conflicting findings regarding sex differences, which may be attributed to different daily sleep duration and/or requirements between sexes due to their different hormone levels.[15] Sex hormones also regulate muscle mass and function and differ between sexes.[16] Therefore, this study aimed to determine whether sleep latency and duration were independently associated with incident sarcopenia in community-dwelling older adults and to explore the sex differences in these associations.

MATERIALS AND METHODS

Participants

This study involved participants of the Korean Frailty and Aging Cohort Study (KFACS).[17] The KFACS is a national, multi-center, longitudinal cohort study. The baseline survey was conducted from 2016 to 2017, with a target number of 3,000 adults aged 70–84 years. The participants were recruited from 10 medical centers (8 hospitals and 2 public health centers) nationwide. For the 3,014 baseline survey participants, the first follow-up surveys (n = 2,864) were conducted from 2018 to 2019. Participants with missing data were excluded. The analysis in the present study included participants who did not have sarcopenia at baseline and who participated in the follow-up survey 2 years later (n = 1,353).

Sleep Parameters

Sleep parameters were reported by the participants using a questionnaire about their usual sleep patterns for the past 4 weeks. Two questions about subjective sleep quality were extracted from the Pittsburgh Sleep Quality Index (PSQI) questionnaire: (1) How long (in minutes) has it taken you to fall asleep each night? (2) How many hours of actual sleep did you get at night?[18] The sleep latency and sleep duration measures were based on the answers provided. A previous meta-analysis reported that sleep duration and the relative risk of sarcopenia showed a nonlinear U-shaped association, with nadirs at 6 hours and 8 hours of sleep per day.[19] Based on these findings, we categorized sleep duration as short (< 6 hours), average (6–8 hours), or long (> 8 hours). We defined prolonged sleep latency as taking more than 60 minutes to fall asleep.[20]

Definition of Sarcopenia

Sarcopenia was defined according to the 2019 Asian Working Group for Sarcopenia (AWGS) guidelines as low muscle mass plus low muscle strength or low physical performance.

The AWGS 2019 cutoffs for low muscle mass for sarcopenia diagnosis are height-adjusted appendicular skeletal muscle (ASM) < 7.0 kg/m^2 in male and < 5.4 kg/m^2 in female. Height-adjusted ASM was defined as ASM (kg)/height (m^2), as measured using dual-energy X-ray absorptiometry (DXA)—Lunar (GE Healthcare, Madison, WI, USA) and Hologic DXA (Hologic Inc., Bedford, MA, USA). ASM was calculated as the sum of the lean mass of the right and left arms and legs under the assumption that all non-fat and non-bone tissues were skeletal muscles. Handgrip strength, measured using a digital handgrip dynamometer (T.K.K.5401; Takei Scientific Instruments Co. Ltd., Tokyo, Japan), was used to indicate low muscle strength. The diagnostic cutoffs for handgrip strength were < 28.0 kg for male and < 18.0 kg for female. The participants were instructed to squeeze the handle with maximum effort for 3 seconds using each hand. Each hand was tested twice, and maximum handgrip strength was defined as the highest measurement for each hand, expressed in kilograms. Physical performance was evaluated using the usual gait speed, five-times sit-to-stand test, and the Short Physical Performance Battery (SPPB). The cutoff for low physical performance was usual gait speed < 1 m/s, five-time chair stand time ≥ 12 seconds, or SPPB score ≤ 9. Low physical performance was defined as obtaining values below the cutoff for any one of these three tests. The usual gait speed over a distance of 4 m was measured using an automatic gait speed meter (Dynamicphysiology, Daejeon, Korea) with acceleration and deceleration phases of 1.5 m each. The participants were asked to perform the test by walking at a normal pace. The five-times sit-to-stand test measures the time required to stand five times from a sitting position without using the arms from a straight-backed armchair as quickly as possible. The SPPB consists of three standing-balance measures, five chair-stand time measures, and an assessment of usual gait speed. Each test was assigned a score of 0–4, based on the normative scores obtained from the Established Population for Epidemiologic Studies of the Elderly, with a total score ranging from 0 to 12.[21,22]

Other Variables

The medical histories of participants were noted from a predefined list of chronic health conditions. Low physical activity levels were

defined as < 494.65 kcal/week for male and < 283.50 kcal/week for female, corresponding to the lowest 20% of the total energy consumed in a population-based Korean survey of older adults from among the general population.[17] Energy expenditure estimates (kcal/week) were calculated using the International Physical Activity Questionnaire (IPAQ), and metabolic equivalent scores were derived according to vigorous, moderate, and mild activity responses in the questionnaire. Nutritional status was rated using the Korean version of the Short Form of the Mini-Nutritional Assessment (MNA), and participants who scored ≤ 11 or less were considered as at risk for malnutrition or with malnutrition.[23] A 15-item Korean version of the Short Form Geriatric Depression Scale (GDS-K) was used to evaluate depression, with scores ≥ 6 defined as suggestive of depression.[24] Polypharmacy was defined as the use of five or more prescribed medicines for > 3 months. Muscle quality of the arms (MQIArm, kg/kg) was defined as the ratio between the dominant handgrip strength and dominant arm ASM.[25] We defined low MQIArm as -1 SD in our study population, which was 11.04 in male and 10.03 in female.[26]

Ethical Approval

The present study was submitted to and exempt from the requirement for Institutional Review Board approval by the Clinical Research Ethics Committee of Kyung Hee University Medical Center (IRB No. 2021-03-057) and complied with the ethical rules for human experimentation described in the Declaration of Helsinki. Informed consent was obtained from all participants or their proxy.

Also this study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[27]

Statistical Analysis

We compared characteristics according to sarcopenia category using independent-sample t-tests and chi-square tests for continuous and categorical data, respectively. After univariate analysis, we included factors with $p < 0.1$ as adjustment factors in multivariate logistic regression analyses. Statistical analysis was performed using IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA), and significance was defined as a p-value < 0.05.

RESULTS

General Characteristics of the Study Population

Among 1,353 non-sarcopenic participants at baseline, 1,160 (85.7%) were classified as non-sarcopenic and 193 (14.3%) as sarcopenic 2 years later, according to the 2019 AWGS guidelines (Table 1). The median ages of the non-sarcopenic and sarcopenic participants were 75.3 and 76.4 years in male and 74.9 and 76.4 years in female, respectively. The prevalence of cerebrovascular disease (CVD), angina, and depression was higher in men in the sarcopenic group than that in those in the non-sarcopenic group. The prevalence of CVD was higher than male in female with sarcopenia. The rates of low physical activity in non-sarcopenic and sarcopenic participants were 4.5% and 12.6% in male and 7.0% and 16.7% in female, respectively. The median sleep duration was 6.4 hours in both non-sarcopenic and sarcopenic male and 5.9 and 6.0 hours in non-sarcopenic and sarcopenic female, respectively. The rates of long sleep duration (total sleep time > 8 hours per night) in non-sarcopenic and sarcopenic participants were 5.7% and 11.7% in male and 3.5% and 6.7% in female, respectively (Table 1).

Sleep Patterns and Incident Sarcopenia in Male

Long sleep duration (> 8 hours) in male was associated with greater odds of incident sarcopenia after 2 years compared to the reference (6–8 hours). After adjusting for multiple factors including age, body mass index (BMI), smoking, polypharmacy, education, angina, CVD, depression, and physical activity, the association between long sleep duration and incident sarcopenia remained significant (odds ratio [OR] = 2.410; 95% confidence interval [CI], 1.125–5.166; p = 0.024). In comparison, short sleep duration (< 6 hours) was not associated with sarcopenia development in male (OR = 1.192; 95% CI, 0.725–1.960; p = 0.488). Prolonged sleep latency (≥ 60 minutes) was not associated with sarcopenia in male (OR = 1.014; 95% CI, 0.505–2.036; p = 0.969) (Tables 2, 3).

Sleep Patterns and Incident Sarcopenia in Female

Compared to normal sleep duration, the adjusted ORs for long and short sleep duration for sarcopenic female were 2.093 (95% CI, 0.753–5.812; p = 0.157) and 0.852 (95% CI, 0.520–1.393; p = 0.522), respectively, which were not significant. Prolonged sleep latency (≥ 60 minutes) was not associated with sarcopenia in female (OR = 0.674; 95% CI, 0.351–1.296; p = 0.237) (Tables 2, 3).

Effects of Sleep Duration on Sarcopenia Components in male

In male, after adjusting for multiple factors (including age, BMI, polypharmacy, alcohol, education, employment status, hypertension, osteoporosis, and depression), the association between long sleep duration and low muscle mass was significant (OR = 2.163; 95% CI, 1.016–4.605; p = 0.045) (Table 4). The association between long sleep duration and low muscle strength remained significant after adjusting for multiple correlates (OR = 2.695; 95% CI, 1.130–6.431; p = 0.025) (Table 5). However, long sleep duration was not associated with low physical performance (OR = 1.075; 95% CI, 0.546–2.117; p = 0.833) in male (Table 6). Short

Table 1. Characteristics of study participants, according to sarcopenia status at 2 years

	Male (n = 631)			Female (n = 722)		
	Non-sarcopenic (n = 528)	Sarcopenic (n = 103)	p-value	Non-sarcopenic (n = 632)	Sarcopenic (n = 90)	p-value
Age (y)	75.3 ± 3.6	76.4 ± 4.0	0.012	74.9 ± 3.6	76.4 ± 4.2	0.002
BMI (kg/m^2)	24.6 ± 2.9	24.1 ± 2.4	0.103	25.3 ± 2.9	23.9 ± 2.8	< 0.001
Polypharmacy[a)]	166 (31.4)	42 (40.8)	0.065	157 (24.8)	21 (23.3)	0.756
Smoking[b)]	405 (76.7)	71 (68.9)	0.094	14 (2.2)	2 (2.2)	0.997
Alcohol drinking[c)]	181 (34.3)	32 (31.1)	0.528	22 (3.5)	3 (3.3)	0.943
Married	346 (65.5)	62 (60.2)	0.3	446 (70.6)	56 (62.2)	0.107
Live alone	30 (5.7)	8 (7.8)	0.416	212 (33.5)	32 (35.6)	0.706
Education[d)]	423 (80.1)	74 (71.8)	0.061	322 (50.9)	39 (43.3)	0.176
Working	149 (28.2)	27 (26.2)	0.678	138 (21.8)	21 (23.3)	0.748
Low physical activity[e)]	24 (4.5)	13 (12.6)	0.001	44 (7.0)	15 (16.7)	0.002
MNA score	12.8 ± 1.6	12.9 ± 1.2	0.598	12.8 ± 1.4	12.8 ± 1.7	0.934
Risk of malnutrition[f)]	94 (17.3)	13 (14.9)	0.59	98 (16.3)	20 (16.3)	0.984
Hypertension	271 (51.3)	60 (58.3)	0.198	362 (57.3)	50 (55.6)	0.757
Diabetes	120 (22.7)	31 (30.1)	0.109	107 (16.9)	20 (22.2)	0.217
Dyslipidemia	142 (26.9)	27 (26.2)	0.887	267 (42.2)	31 (34.4)	0.16
Angina	31 (5.9)	13 (12.6)	0.014	30 (4.7)	8 (8.9)	0.1
CHF	4 (0.8)	0 (0.0)	0.376	2 (0.3)	1 (1.1)	0.273
CVD	24 (4.5)	14 (13.6)	< 0.001	19 (3.0)	7 (7.8)	0.023
Arthritis	56 (10.6)	14 (13.6)	0.377	204 (32.3)	31 (34.4)	0.682
Osteoporosis	81 (15.3)	15 (14.6)	0.841	92 (14.6)	15 (16.7)	0.598
Depression[g)]	43 (8.1)	16 (15.5)	0.018	160 (25.3)	22 (24.4)	0.859
HRT[h)]	-	-		143 (22.6)	14 (15.6)	0.128
Sleep duration (hr)	6.4 ± 1.3	6.4 ± 1.5	0.563	5.9 ± 1.4	6.0 ± 1.5	0.34
6–8	352 (66.7)	60 (58.3)	0.057	332 (52.5)	50 (55.6)	0.234
< 6	146 (27.7)	31 (30.1)		278 (44.0)	34 (37.8)	
> 8	30 (5.7)	12 (11.7)		22 (3.5)	6 (6.7)	
Sleep latency (min)	20.6 ± 24.8	21.3 ± 22.4	0.771	29.3 ± 30.0	24.7 ± 26.4	0.163
> 60	49 (9.3)	13 (12.6)	0.297	129 (20.4)	13 (14.4)	0.183

Values are presented as mean±standard deviation or number (%).
BMI, body mass index; MNA, Mini-Nutritional Assessment; CHF, chronic heart failure; CVD, cerebrovascular diseases; HRT, hormone replacement therapy.
[a)]Use of 5 or more drugs more than 3 months, [b)]≥5 pack-years per lifetime, [c)]≥2–3 times per week, [d)]≥7 years, [e)]<494.65 kcal for male and <283.50 kcal for female, [f)]MNA score ≤11, [g)]Geriatric Depression Scale score ≥6, [h)]≥1 month.

sleep duration (< 6 hours) was not associated with any sarcopenia component (low muscle mass, low muscle strength, or low physical performance) in unadjusted or adjusted analyses (Tables 4–6). Sleep duration was not associated with muscle quality after adjusting for multiple factors (Supplementary Table S2).

Effects of Sleep Duration on Sarcopenia Components in Female

In female, after adjusting for multiple factors, the ORs of long sleep duration for low height-adjusted ASM, low muscle strength, and low physical performance were 0.766 (95% CI, 0.278–2.105; p = 0.605), 1.997 (95% CI, 0.884–4.511; p = 0.096), and 1.885 (95% CI, 0.879–4.042; p = 0.103) (Tables 4–6, respectively). Short sleep duration (< 6 hours) was not associated with any sarcopenia component (low muscle mass, low muscle strength, or low physical performance) in the adjusted analyses. However, low gait speed and low SPPB score showed associations with short sleep duration (Tables 7, 8). Long 5 sit-to-stand test didn't showed association with sleep duration (Table 9).

DISCUSSION

The results of our study in community-dwelling older adults showed that long sleep duration, compared with normal sleep duration, increased the risk of incident sarcopenia after 2 years in male. Regarding sarcopenia components, long sleep duration was associated with low muscle mass and strength after 2 years in male.

Chronic inflammation and insulin resistance, and brain pituitary

Table 2. Odds ratio of sleep duration relationship to incident sarcopenia, by sex

	Sleep duration (hr)	Male				Female			
		OR	95% CI		p-value	OR	95% CI		p-value
Model1[a)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.246	0.775	2.002	0.364	0.812	0.511	1.291	0.379
	> 8	2.347	1.139	4.837	0.021	1.811	0.700	4.684	0.221
Model2[b)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.258	0.780	2.031	0.347	0.814	0.506	1.309	0.395
	> 8	2.409	1.158	5.012	0.019	2.085	0.778	5.582	0.144
Model3[c)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.217	0.744	1.992	0.434	0.821	0.504	1.339	0.43
	> 8	2.407	1.124	5.152	0.024	2.124	0.778	5.796	0.142
Model4[d)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.192	0.725	1.960	0.488	0.852	0.520	1.393	0.522
	> 8	2.41	1.125	5.166	0.024	2.093	0.753	5.812	0.157

OR, odds ratio; CI, confidence interval; BMI, body mass index; CVD, cerebrovascular disease.
[a)]Unadjusted, [b)]adjusted for age and BMI, [c)]adjusted for age, BMI, smoking, polypharmacy, education, angina, CVD, and depression, [d)]adjusted for age, BMI, smoking, polypharmacy, education, angina, CVD, depression, and low physical activity.
p-value was obtained by logistic regression analysis.

Table 3. Odds ratio of sleep latency relationship to incident sarcopenia, by sex

	Sleep latency > 60 min							
	Male				Female			
	OR	95% CI		p-value	OR	95% CI		p-value
Model1[a)]	1.412	0.736	2.709	0.299	0.658	0.355	1.222	0.185
Model2[b)]	1.355	0.702	2.614	0.366	0.621	0.329	1.174	0.143
Model3[c)]	1.001	0.5	2.004	0.997	0.636	0.332	1.219	0.173
Model4[d)]	1.014	0.505	2.036	0.969	0.674	0.351	1.296	0.237

OR, odds ratio; CI, confidence interval; BMI, body mass index; CVD, cerebrovascular disease.
[a)]Unadjusted, [b)]adjusted for age and BMI, [c)]adjusted for age, BMI, smoking, polypharmacy, education, angina, CVD, and depression, [d)]adjusted for age, BMI, smoking, polypharmacy, education, angina, CVD, depression, and low physical activity.
p-value was obtained by logistic regression analysis.

Table 4. Odds ratio of sleep duration relationship to low height-adjusted ASM index, 2-year follow-up, by sex

	Sleep duration (hr)	Male				Female			
		OR	95% CI		p-value	OR	95% CI		p-value
Model1[a)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.814	0.571	1.159	0.254	0.932	0.669	1.298	0.678
	> 8	1.818	0.939	3.517	0.076	0.657	0.260	1.665	0.376
Model2[b)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.808	0.542	1.205	0.296	0.928	0.650	1.326	0.682
	> 8	1.891	0.908	3.937	0.089	0.711	0.260	1.941	0.505
Model3[c)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.828	0.552	1.240	0.359	0.975	0.675	1.408	0.893
	> 8	2.163	1.016	4.605	0.045	0.766	0.278	2.105	0.605

ASM, appendicular skeletal muscle; OR, odds ratio; CI, confidence interval; BMI, body mass index; CVD, cerebrovascular disease; HTN, hypertension.
[a)]Unadjusted, [b)]adjusted for age and BMI, [c)]adjusted for age, BMI, polypharmacy, alcohol consumption, education, working, HTN, osteoporosis and depression.
p-value was obtained by logistic regression analysis.

Table 5. Odds ratio of sleep duration relationship to low muscle strength, 2-year follow-up, by sex

	Sleep duration (hr)	Male				Female			
		OR	95% CI		p-value	OR	95% CI		p-value
Model1[a)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.219	0.733	2.028	0.446	1.196	0.829	1.726	0.337
	> 8	2.212	1.026	4.769	0.043	2	0.921	4.342	0.080
Model2[b)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.199	0.716	2.009	0.491	1.231	0.845	1.793	0.278
	> 8	2.396	1.09	5.264	0.03	2.091	0.944	4.636	0.069
Model3[c)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.155	0.677	1.971	0.597	1.208	0.822	1.775	0.335
	> 8	2.637	1.105	6.296	0.029	1.943	0.862	4.382	0.109
Model4[d)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.137	0.664	1.947	0.639	1.223	0.831	1.801	0.307
	> 8	2.695	1.13	6.431	0.025	1.997	0.884	4.511	0.096

OR, odds ratio; CI, confidence interval; BMI, body mass index; CVD, cerebrovascular disease ; HTN, hypertension; DM, diabetes mellitus.
[a)]Unadjusted, [b)]adjusted for age and BMI, [c)]age, BMI, polypharmacy, smoking, HTN, DM, angina, CVD, arthritis, [d)]adjusted for age, BMI, polypharmacy, smoking, HTN, DM, angina, CVD, arthritis, and low physical activity.
p-value was obtained by logistic regression analysis.

Table 6. Odds ratio of sleep duration relationship to low physical performance, 2-year follow-up, by sex

	Sleep duration (hr)	Male				Female			
		OR	95% CI		p-value	OR	95% CI		p-value
Model1[a)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.923	0.638	1.336	0.672	0.882	0.675	1.152	0.357
	> 8	1.094	0.590	2.029	0.775	2.171	1.091	4.321	0.027
Model2[b)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.915	0.626	1.337	0.645	0.894	0.675	1.185	0.437
	> 8	1.212	0.641	2.294	0.554	2.080	1.011	4.282	0.047
Model3[c)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.842	0.563	1.258	0.401	0.781	0.580	1.051	0.102
	> 8	1.073	0.547	2.103	0.837	1.870	0.887	3.941	0.1
Model4[d)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.824	0.55	1.235	0.349	0.800	0.591	1.084	0.151
	> 8	1.075	0.546	2.117	0.833	1.885	0.879	4.042	0.103

OR, odds ratio; CI, confidence interval; BMI, body mass index; CVD, cerebrovascular disease ; HTN, hypertension; DM, diabetes mellitus.
[a)]Unadjusted, [b)]adjusted for age and BMI, [c)]age, BMI, education, living alone, polypharmacy, HTN, DM, CVD, dyslipidemia, arthritis, depression, [d)]age, BMI, education, living alone, polypharmacy, HTN, DM, CVD, dyslipidemia, arthritis, depression, low physical activity.
p-value was obtained by logistic regression analysis.

function are all important mechanisms explaining the relationship between long sleep duration and sarcopenia. Long sleep duration is also closely associated with increased insulin resistance.[28)] Insulin resistance contributes to decreased synthesis of skeletal mass protein, leading to sarcopenia in older adults.[29)] Another mechanism for the relationship between sleep duration and sarcopenia could be chronic inflammation. Long-duration sleepers have significantly higher levels of proinflammatory markers, such as C-reactive protein and interleukin-6 (IL-6),[30)] and inflammatory mediators play an important role in the development of sarcopenia by promoting muscle proteolysis. The results of a population-based study demonstrated significantly elevated circulating concentrations of IL-6 and tumor necrosis factor-α (TNF-α) in older adults with sarcopenia and showed that higher IL-6 and C-reactive protein (CRP) levels increased the risk of muscle strength loss.[31)] Chronic inflammation might affect the anabolic and catabolic metabolism of muscles, resulting in sarcopenia.[30)] The results of a recent meta-analysis revealed that higher IL-6 and CRP levels were signifi-

Table 7. Odds ratio of sleep duration relationship to low gait speed, 2-year follow-up, by sex

	Sleep duration (hr)	Male				Female			
		OR	95% CI		p-value	OR	95% CI		p-value
Model1[a)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.715	0.356	1.436	0.345	0.881	0.392	1.979	0.759
	> 8	0.740	0.353	1.551	0.425	0.750	0.331	1.696	0.489
Model2[b)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.052	0.631	1.753	0.845	0.746	0.519	1.072	0.113
	> 8	1.776	0.763	4.134	0.183	1.834	0.769	4.374	0.171
Model3[c)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.873	0.508	1.499	0.623	0.586	0.393	0.875	0.009
	> 8	1.920	0.799	4.614	0.145	1.969	0.769	5.039	0.158
Model4[d)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.851	0.492	1.472	0.564	0.596	0.398	0.893	0.012
	> 8	1.995	0.828	4.807	0.124	2.038	0.795	5.225	0.139

OR, odds ratio; CI, confidence interval; BMI, body mass index; CVD, cerebrovascular disease ; HTN, hypertension; DM, diabetes mellitus.
[a)]Unadjusted, [b)]adjusted for age and BMI, [c)]age, BMI, education, living alone, polypharmacy, HTN, DM, CVD, dyslipidemia, arthritis, depression, [d)]age, BMI, education, living alone, polypharmacy, HTN, DM, CVD, dyslipidemia, arthritis, depression, low physical activity.
p-value was obtained by logistic regression analysis.

Table 8. Odds ratio of sleep duration relationship to low SPPB test, 2-year follow-up, by sex

	Sleep duration (hr)	Male				Female			
		OR	95% CI		p-value	OR	95% CI		p-value
Model1[a)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.243	0.71	2.175	0.447	0.776	0.543	1.108	0.162
	> 8	1.983	0.824	4.774	0.127	0.74	0.27	2.024	0.557
Model2[b)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.204	0.677	2.14	0.527	0.777	0.537	1.122	0.178
	> 8	2.306	0.92	5.779	0.075	0.742	0.265	2.078	0.571
Model3[c)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.111	0.617	2.001	0.725	0.647	0.437	0.957	0.029
	> 8	2.188	0.847	5.65	0.106	0.669	0.229	1.954	0.463
Model4[d)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.088	0.601	1.971	0.78	0.656	0.442	0.972	0.036
	> 8	2.238	0.862	5.809	0.098	0.672	0.228	1.981	0.471

OR, odds ratio; CI, confidence interval; BMI, body mass index; CVD, cerebrovascular disease ; HTN, hypertension; DM, diabetes mellitus.
[a)]Unadjusted, [b)]adjusted for age and BMI, [c)]age, BMI, education, living alone, polypharmacy, HTN, DM, CVD, dyslipidemia, arthritis, depression, [d)]age, BMI, education, living alone, polypharmacy, HTN, DM, CVD, dyslipidemia, arthritis, depression, low physical activity.
p-value was obtained by logistic regression analysis.

cantly associated with long but not short sleep duration.[32)]

In addition, disrupted circadian rhythm, which is controlled by the brain, and hormonal changes associated with long sleep durations might also be a possible underlying mechanism explaining the link between long sleep duration and sarcopenia.[33)]

These findings might explain the association between long sleep duration and incident sarcopenia. In our study, CRP level was not associated with incident sarcopenia; however, insulin resistance showed an association in male (Supplementary Table S1), which may explain some of the association between long sleep duration and incident sarcopenia in male.

In female, short sleep duration was positively associated with low physical performance such as slow gait speed (OR = 0.564) and poor SPPB score (OR = 0.656). Older age is more strongly associated with poor subjectively reported sleep in female, and older female consistently report shorter and poorer sleep compared to older male.[34)] However, actigraphic sleep measures showed poorer sleep in male.[35,36)] The results of the Health ABC cohort study

Table 9. Odds ratio of sleep duration relationship to long 5 sit-to-stand test, 2-year follow-up, by sex

	Sleep duration (hr)	Male				Female			
		OR	95% CI		p-value	OR	95% CI		p-value
Model1[a)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.088	0.686	1.727	0.719	1.003	0.727	1.384	0.986
	> 8	1.452	0.662	3.185	0.353	1.256	0.54	2.923	0.597
Model2[b)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	1.058	0.662	1.692	0.813	1.024	0.731	1.434	0.89
	> 8	1.596	0.714	3.568	0.255	1.306	0.545	3.131	0.549
Model3[c)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.948	0.581	1.546	0.831	0.884	0.618	1.265	0.499
	> 8	1.407	0.607	3.262	0.426	1.217	0.482	3.071	0.678
Model4[d)]	6–8	1	Ref		Ref	1	Ref		Ref
	< 6	0.934	0.571	1.529	0.787	0.898	0.627	1.288	0.559
	> 8	1.432	0.617	3.325	0.403	1.239	0.489	3.136	0.651

OR, odds ratio; CI, confidence interval; BMI, body mass index; CVD, cerebrovascular disease ; HTN, hypertension; DM, diabetes mellitus.
[a)]Unadjusted, [b)]adjusted for age and BMI, [c)]age, BMI, education, living alone, polypharmacy, HTN, DM, CVD, dyslipidemia, arthritis, depression, [d)]age, BMI, education, living alone, polypharmacy, HTN, DM, CVD, dyslipidemia, arthritis, depression, low physical activity.
p-value was obtained by logistic regression analysis.

showed that thigh muscle mass was not associated with gait speed changes in female. However, all fat composition variables were associated with gait speed decline after 4 years.[37)] Furthermore, female are generally at a higher risk of osteoarthritis incidence and disease severity than male.[38)] These factors might explain the association of short sleep duration with slow gait speed and poor SPPB score. However, low physical performance was not associated with short sleep duration in female.

Sleep latency was not a significant predictor of sarcopenia in our study. In the previous two related publications, one study reported higher scores for sleep latency in sarcopenic subjects compared with those in non-sarcopenic subjects ($p = 0.03$) after adjusting for confounders[39)]; however, the other study did not find that sleep latency was associated with sarcopenia in middle-aged individuals.[40)] Yet another study[20)] postulated that depression was an intermediating factor between long sleep latency and frailty in older Korean male; therefore, sleep latency was not directly associated with frailty. However, these papers were cross-sectional designs; therefore, the results of our prospective study demonstrate the cause-effect relationship.

To our knowledge, no other longitudinal study has reported the sex-specific effects of sleep duration on incident sarcopenia in older adults. Nakakubo et al.[14)] reported that long sleep duration was associated with an increased risk of progression to sarcopenia among older adults but did not show differences in the association according to sex. However, they did report that long sleep duration was associated with slow gait and lower grip strength but not with lower muscle mass, contrary to our findings. To evaluate ASM, Nakakubo et al.[14)] used multi-frequency bioelectrical impedance analysis, which can overestimate ASM compared to DXA,[41)] which could explain the divergent results. Additionally, unlike the association of long sleep duration with slow gait and low grip strength after 4 years reported by Nakakubo et al.,[14)] we observed a relationship between sleep duration and muscle mass and strength but not physical performance in male only. However, 2 years may have been too short a duration to observe decreased physical performance.

In this study, we observed sex differences in the association between long sleep duration and incident sarcopenia. Unlike previous cross-sectional studies that reported the association of sleep duration with sarcopenia in female[13)] and both sexes,[19)] we observed an association only in male. However, both previous studies were cross-sectional and only two studies have reported on the longitudinal effect of long sleep duration on sarcopenia,[14,42)] neither of which investigated sex differences in this relationship. Therefore, our findings demonstrate the difference in the cause-effect relationships of long sleep duration on incident sarcopenia. We observed this relationship only in male; thus, the relationship reported in female in cross-sectional studies may have been coincidental findings. The sex difference in the effects of long sleep duration on sarcopenia may occur due to the different requirements for sleep duration between the sexes owing to their different hormone levels.[15)] Furthermore, female are more resilient to environmental stressors. Another explanation for the differential association according to sex may be that muscle mass declines more slowly in female than in male. A previous study reported a steeper decline in

relative skeletal muscle mass (kg/m^2) in male (15.2 − 0.07 × age; $p < 0.001$) compared with that in female (8.9 − 0.02 × age; $p < 0.001$).[43] Therefore, a 2-year follow-up may have been insufficient to determine the effect of sleep duration on incident sarcopenia in female.

This study had several limitations. First, the sleep variables were based on participant recall, which may lead to bias and differ from objective sleep measurements. One study reported that self-reported sleep latency was 10 minutes longer than objectively measured sleep latency and that the estimated total sleep duration was slightly shorter than the measured duration (median difference, -18.5 minutes) in adults with a mean age of 50 years.[20,44] Second, as the participants of this study were community-dwelling older adults, the results do not represent the entire population of older Korean adults as we did not include hospitalized, institutionalized, or bedridden older adults.

The study also has several strengths. We enrolled a relatively large number of community-dwelling older adults aged 70–84 years, and the cohort was gathered from 10 regions nationwide, including urban and rural areas of Korea. Therefore, the cohort was representative of the community-living age group across Korea. Previous studies have reported controversial associations between sleep duration and sarcopenia; however, no other studies have investigated sex differences in the effect of long sleep duration on incident sarcopenia. We observed that long sleep duration (>8 hours per night) was associated with high odds for incident sarcopenia after 2 years in male. Interventional studies are needed to investigate if the effect of a reduction in sleep time in these long sleepers can decrease their risk of sarcopenia.

In conclusion, after 2 years of follow-up, long sleep duration (>8 hours per night) was associated with high odds for incident sarcopenia, and the main correlates of incident sarcopenia due to long sleep duration were muscle mass loss and declining muscle strength in male. In contrast, long sleep duration in female was not associated with incident sarcopenia.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, CWW, HL; Data curation, HL, SK; Funding acquisition, CWW; Investigation, CWW, SK; Methodology, CWW, SK, HL; Project administration, CWW; Supervision, CWW; Writing-original draft, HL; Writing-review and editing, HL, SK, BSK, MK, JY, HB, CWW.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.22.0093.

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Atypical Presentation of Pill Aspiration in Older Adults with Dysphagia: A Picture Not To Be Forgotten

Stefano Cacciatore[1], Vincenzo Brandi[1], Camilla Cocchi[1], Daniele Elmi[1], Giordana Gava[1], Claudia Massaro[1], Celeste Ambra Murace[1], Carla Recupero[1], Matteo Tosato[1], Riccardo Calvani[2], Francesco Landi[1,2]

[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[2]Department of Geriatrics and Orthopaedics, Università Cattolica del Sacro Cuore, Rome, Italy

Corresponding Author:
Stefano Cacciatore, MD
Fondazione Policlinico Universitario Agostino Gemelli IRCCS, L.go A. Gemelli 8, Rome 00168, Italy
E-mail: stefanocacciatore@live.it
ORCID:
https://orcid.org/0000-0001-7504-3775

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Nonconventional clinical presentations of diseases are common in older adults. Even dramatic events, such as foreign body (FB) inhalation, can occur in a subtle and non-specific manner. Pill aspiration is a rare yet overlooked cause of airway injury. It accounts for approximately 7% of all FB aspirations. In contrast, oral dysphagia and polypharmacology, mainly administrated in solid oral dosage forms (SDOF), like tablets and pills, are common conditions in older adults. Herein, we present a case of SDOF aspiration in a 78-year-old man. FB inhalation developed with general clinical deterioration and neurological impairment (delirium) rather than overt respiratory symptoms. Bronchoscopy provided remarkable images of this unexpected finding. Caregivers and healthcare workers must be aware of the risk of SDOF aspiration and adopt proper safety measures. Early recognition and bronchoscopy for diagnostic and therapeutic purposes can be life-saving in such cases.

Key Words: Foreign bodies, Dysphagia, Delirium

INTRODUCTION

Pill aspiration is a rare yet overlooked cause of airway injury. It represents 7% of all foreign body (FB) aspirations in adults.[1)] In contrast, oral dysphagia and polypharmacology are common conditions in older adults. Drugs are mainly administered in solid oral dosage forms (SDOF), such as tablets and pills. Diagnosing pill aspirations presents many challenges. For example, clinical and radiological findings can be subtle and non-specific. Moreover, the suspicion of SDOF causing airway injury is often low-grade. Finally, pills may dissolve into the airways; thus, they are not observed during bronchoscopy.[2)] Herein, we present a case of pill aspiration in a 78-year-old man with an elusive clinical presentation. Pictures from the bronchoscopy of this patient raise a concern about the risks associated with the use of SDOF in older adults with oral dysphagia. Written informed consent was obtained from the patient for publication of this case report and accompanying image.

CASE REPORT

A 78-year-old man was admitted to our geriatric internal medicine ward with multiple spontaneous bone fractures due to metastasis of cancer of unknown primary origin, severe clinical deterioration, and delirium. The patient had a history of heavy smoking (approximately 80 pack-years). No other diseases were known, mainly because of poor medical supervision.

His relatives reported that he was quite well until approximately 20 days before hospitalization. Previously, he started presenting with widespread bone pain. An X-ray scan revealed multiple spontaneous pathological bone fractures. He had started taking painkillers (first paracetamol, then oxycodone and naloxone), and a computed tomography (CT) scan was scheduled. However, in the following days, he started presenting with clinical deterioration and sudden worsening of neurological signs. After a non-traumatic fall, relatives brought him to the emergency room (ER).

The patient presented with severe clinical deterioration upon ar-

rival. He was agitated, disoriented, and unable to maintain attention. He was eupnoeic in room air at a temperature of 36°C and had a blood pressure of 130/80 mmHg. Brain CT did not reveal intracranial hemorrhage. Chest radiography (Fig. 1) showed abnormal elevation of the left hemidiaphragm and reduced transparency of the corresponding lung due to possible atelectasis, with abundant pleural effusion on the left side. The levels of blood inflammation markers were elevated, likely due to current acute infection (leukocytes 21.33×10^9/L with 88.3% neutrophils, C-reactive protein 234.0 mg/L); therefore, antibiotic therapy was initiated.

On the following day, the patient was transferred to our hospital. He was eupnoeic in room air upon arrival. Physical examination of the lungs showed diminished breath sounds, especially on the left lung base, diffused rhonchi, and wheezing, mostly on the left side of the chest. The patient was heavily sarcopenic. Arterial blood gas showed hypoxemic respiratory failure (pH 7.48, $PaCO_2$ 45.7 mmHg, PaO_2 53.6 mmHg, sO_2 87.9%, lactates 1.7 mmol/L, HCO_3^- 33.1 mmol/L).

Chest CT showed that the left lung had collapsed due to airway occlusion. Bronchoscopy performed the next day unexpectedly showed a pill occluded the left mainstem bronchus (Fig. 2). Its size and appearance suggested an intact paracetamol pill. In addition, X-ray imaging performed on arrival showed lung atelectasis. For these reasons, we believed that aspiration had occurred several weeks before his hospitalization, at the beginning of his pain management therapy.

The FB was successfully removed during the procedure; however, the patient died due to pulmonary infection and respiratory failure the next day.

Fig. 1. Chest radiography showed abnormal elevation of the left hemidiaphragm and reduced transparency of the corresponding lung due to possible atelectasis, with abundant pleural effusion on the left side.

DISCUSSION

We report the case of a 78-year-old patient who experienced pill aspiration, characterized by atypical clinical manifestations. Unconventional clinical presentations are common in older adults. However, in this case, FB aspiration developed with general clinical deterioration and neurological signs and symptoms (delirium) rather than overt respiratory symptoms such as dyspnea.

Oral dysphagia is a common geriatric syndrome (10%–33%).[3] It is associated with a high burden of mortality and morbidity in older adults, mainly due to dehydration, malnutrition, and infection. The swallowing process has two important and complementary functions: ingestion of food and airway protection.[4,5] Swallowing problems are often comorbid with various conditions such as neurological diseases (e.g., Parkinson disease and Alzheimer disease), musculoskeletal conditions, cancer, and sarcopenia. They may also occur when stressors (i.e., infections, drugs, hospitalization) disrupt the delicate balance of frail older adults. Moreover, the aging population experiences a physiological reduction in swallowing function referred to as presbyphagia.[6]

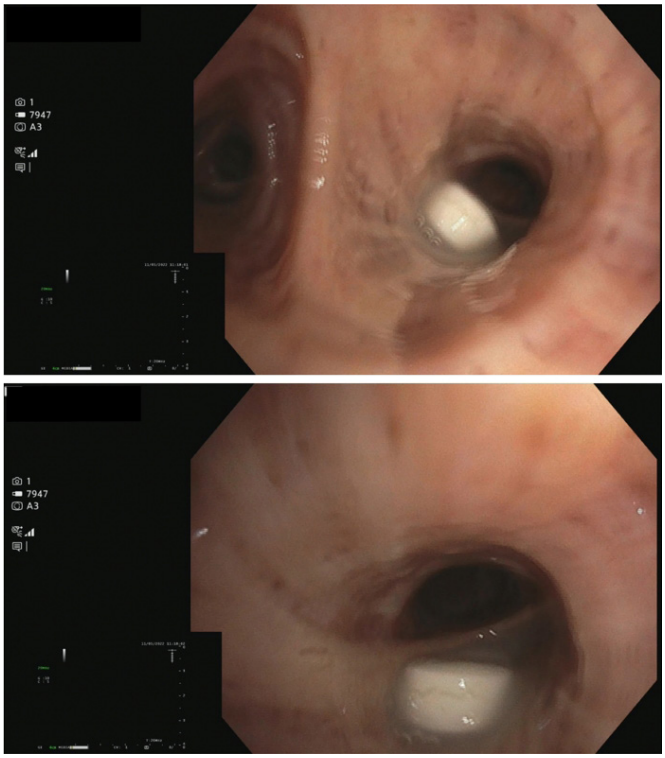

Fig. 2. Bronchoscopy showed a pill occluded the left mainstem bronchus.

In older adults, managing dysphagia is crucial when administering medical therapy. According to the SHELTER study, nearly 50% of older adults in nursing homes across Europe take 5–9 drugs, while 24.3% take ≥10 drugs.[7] Difficulties in swallowing SDOFs may affect not only older adults with overt dysphagia (45.5%) but also those with presbyphagia or even no dysphagia (12.3%).[8] FB aspiration can also occur "silently" without any clinical evidence of swallowing difficulty. Older age and common geriatric conditions (e.g., cerebrovascular impairment, diabetes, previous myocardial infarction, and chronic obstructive pulmonary disease) are risk factors associated with silent aspiration.[9] Although the relatives in the present case reported that the patient was independent in activities of daily living (ADL) and did not suffer from symptomatic oral dysphagia before the worsening of his clinical condition, he had risk factors that made his swallowing function highly vulnerable, such as age-related paraphysiological changes, sarcopenia, active cancer, and probable chronic obstructive pulmonary disease.[10]

SDOF can cause airway inflammation, obstruction, and systemic toxicity.[1] The time course of obstruction before an intervention can vary from days to months. Studies have highlighted the importance of early recognition and bronchoscopy for diagnosing and treating SDOF aspiration.[11]

Oral drugs are often administered in geriatric healthcare settings by crushing tablets or opening capsules and dispersing powders in water or gel. This represents the off-label use of the medication, which may negatively impact both efficacy and safety.[12] A possible solution to this problem is the implementation of alternative formulations, such as orally disintegrating tablets[13] or dispersible formulations. Some drugs are already available in "dysphagia-friendly" formulations. For many others, however, further investigation by geriatric pharmacology and investments are needed.

The risks associated with SDOF in older adults support calls to action for deprescribing, as this can help in two ways. First, some drugs are involved in swallowing disorders by causing esophageal injuries, xerostomia, and dysphagia.[8] Second, reducing the number of medications can also reduce the probability that tablets and capsules may "go down the wrong way."

Safety measures to prevent FB aspiration involve appropriate rest between swallows, adjusting posture, placing the pill or tablet in the patient's mouth according to the type of deficit, swallowing rehabilitation, and minimizing the use of hypnotics and sedatives.[14,15] In addition, managing and preventing sarcopenic dysphagia in hospitalized and bedridden patients may be useful.[16]

It is crucial for all caregivers and healthcare workers to be aware of the possible risks related to SDOF aspiration in older adults with dysphagia and to adopt appropriate safety measures. The consequences of FB inhalation can be fatal. However, when they occur, the ability to recognize them and proceed with proper management can be lifesaving.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, FL, VB, SC, CC; investigation, VB, CAM, SC, CC, CR, CM, GG; project administration FL; supervision, FL, MT, VB; visualization, SC; writing-original draft, SC; writing-review & editing, SC, MT, RC, DE. All authors read and approved the final version.

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Marked Cognitive and Activities of Daily Living Improvement by Shunt Embolization in a Very Old Man with Portosystemic Encephalopathy Mimicking Alzheimer Disease: A Case Report

Soichiro Kondo[1], Kazufumi Takada[1], Taro Kojima[1], Kosuke Tanaka[1], Mitsutaka Yakabe[1], Eisuke Shibata[2], Yumi Umeda-Kamayama[1], Hidemasa Takao[2], Sumito Ogawa[1], Masahiro Akishita[1]

[1]Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
[2]Department of Radiology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Corresponding Author:
Taro Kojima, MD, PhD
Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo, Taro Kojima, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan
E-mail: tkojima-tky@g.ecc.u-tokyo.ac.jp

ORCID:
https://orcid.org/0000-0003-3857-5267

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A 91-year-old man with chronic cognitive impairment underwent shunt embolization for portosystemic encephalopathy (PSE). He experienced intermittent episodes of impaired consciousness and decreased cognitive function and activities of daily living (ADL), for which Alzheimer disease was suspected. On admission, he was in a coma and PSE was diagnosed based on his high ammonia level and the computed tomography findings. After shunt embolization, the patient fully recovered from the impaired consciousness and experienced no recurrence. The patient's Revised Hasegawa Dementia Scale and Mini-Mental State Examination scores improved significantly from 12 and 17 to 30 and 29 points, respectively. The Barthel Index score also improved from 55/100 to 85/100, suggesting a marked improvement in ADL. PSE progresses slowly in very old patients and may mimic the clinical course of Alzheimer disease but without liver enzyme abnormalities. Therefore, it should be distinguished in every dementia case.

Key Words: Hepatic encephalopathy, Embolization, 80 and over aged, Dementia

INTRODUCTION

Portosystemic encephalopathy (PSE) is a noncirrhotic form of hepatic encephalopathy (HE) caused by a portosystemic shunt even in the absence of pre-existing liver disease.[1)] In general, PSE progression is associated with worsening cirrhosis. However, the clinical course of PSE in older patients has not been well documented. Thus, the efficacy of shunt embolization for older patients should be objectively evaluated using cognitive function tests and the activities of daily living (ADL) scale. While previous reports have described cases in which shunt embolization improved cognitive function and ADLs, none have reported this in patients >90 years of age or on the systematic evaluation using the Comprehensive Geriatric Assessment (CGA). Herein, we report a case of shunt embolization in an older adult with HE caused by an intrahepatic shunt and not by liver disease that resulted in marked improvement in cognitive function and ADL.

CASE REPORT

We experienced a case of a 91-year-old man whose cognitive function improved after shunt embolization for PSE. He had gradually talked less and less over a period of 1 year and 2 months and had experienced intermittent episodes of impaired consciousness for over 1 year before admission. His cognitive function and ADL declined, and he was unable to move. He was admitted to the University of Tokyo Hospital for pyelonephritis 1 year before his most recent hospitalization. Psychological assessment at that time showed disorientation and delayed recall, which led to a diagnosis of Alzheimer disease. A written informed consent was obtained from the patient and his wife.

The reason for admission to the University of Tokyo Hospital at

that time was that he was found unconscious on the floor at home. On arrival at the hospital, he was found to be in a coma (Japan Coma Scale III-100). His blood pressure was 161/83 mmHg, pulse was 68/min, respiratory rate was 23/min, oxygen saturation was 99% on a nasal cannula at 2 L/min, and body temperature was 36.8°C. Physical examination revealed normal pupil diameter and pupillary light reflexes. No involuntary movements or gross paralysis of the extremities were observed.

The patient had a history of hypertension, atrial fibrillation, chronic heart failure, left parietal lobe stroke, benign prostatic hyperplasia, and pyelonephritis and was taking an anticoagulant, a loop diuretic, and a histamine receptor antagonist. He had a history of smoking 40 cigarettes per day for 20 years. He drank alcohol occasionally but had no history of heavy drinking. Blood tests revealed an ammonia level of 232 μg/dL (normal range: 12–66 μg/dL), a white blood cell count of 6,800 cells/μL, C-reactive protein concentration of 0.40 mg/dL (0–0.30 mg/dL), a glucose level of 121 mg/dL (73–109 mg/dL), a sodium level of 147 mmol/L (138–145 mmoL/L), a potassium level of 4.3 mmol/L (3.6–4.8 mmol/L), a corrected calcium level of 9.4 mg/dL (8.8–10.1 mg/dL), an estimated glomerular filtration rate (eGFR) of 43.2 mL/min/1.73 m^2, and a total bilirubin level of 1.0 mg/dL (0.4–1.5 mg/dL). The patient's liver function was normal, and tests for hepatitis virus antigen were negative. The patient had no history of liver disease. Computed tomography (CT) of the head revealed no apparent acute infarction or hemorrhage. Electroencephalography revealed no obvious abnormalities related to the loss of consciousness. To clarify the cause of the increased ammonia level, abdominal contrast-enhanced CT was performed that revealed a high-density area (the same density as that of the portal vein) in S6 of the liver, suggesting a portosystemic shunt (Fig. 1A). Abdominal echography confirmed that the intrahepatic P6 line and right hepatic vein formed a portosystemic shunt. These results suggested that the coma was caused by hyperammonemia due to intrahepatic portosystemic shunts.

Following administration of extracellular fluid, the patient's consciousness improved the day after admission; therefore, conservative treatment was performed first. Oral administration of lactulose and branched-chain amino acid preparations was tested[2,3]; however, no improvement in hyperammonemia was observed. Thus, portosystemic shunt embolization was considered.

Shunt embolization was performed on the 22nd day after admission. The catheter was advanced from the right femoral vein into the inferior right hepatic vein (IRHV). Portosystemic shunts were confirmed by retrograde contrast imaging under balloon occlusion. Portal vein angiography showed that two P6 vessels supplied the bloodstream for the portosystemic shunt, and both vessels were successfully embolized with coils. No intraoperative complications, including bleeding, infection, pain, access site complications,[4,5] and displacement of the coil into the systemic circulation, occurred. Postoperatively, the patient's blood ammonia concentration improved and remained within the normal range (Fig. 2).

The abdominal CT images obtained before and after embolization are shown in Fig. 1. A portosystemic shunt leading from portal

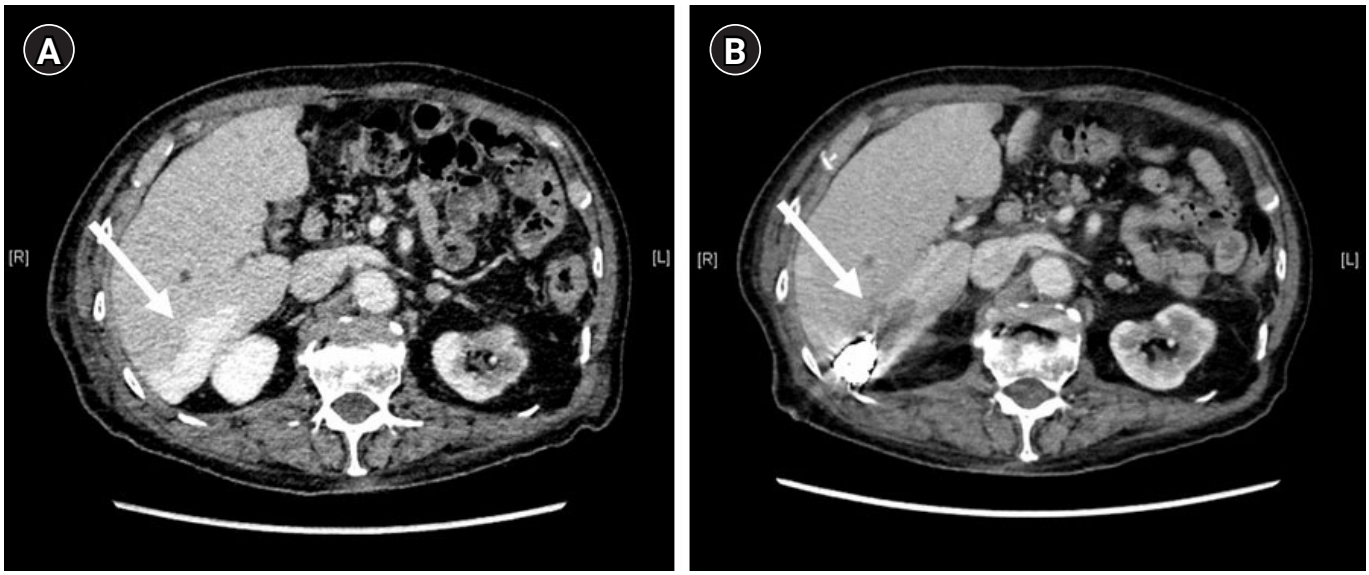

Fig. 1. Contrast-enhanced computed tomography before and after embolization. (A) Pre-embolization (the arrow indicates a potential portosystemic shunt leading from portal vein P6 to the inferior right hepatic vein). (B) Post-embolization (the arrow indicates a thrombus from the coil embolization site to the inferior right hepatic vein, suggesting successful embolization).

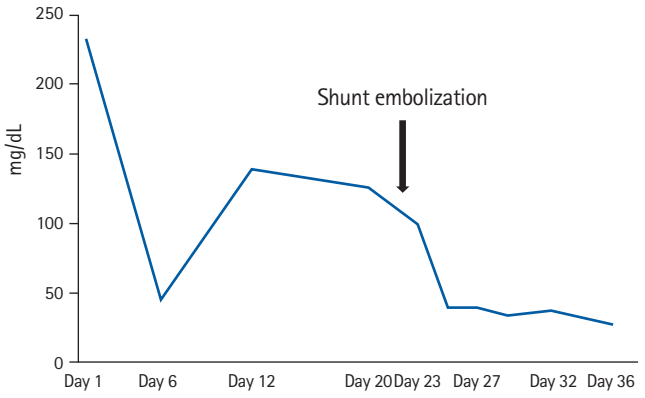

Fig. 2. Blood ammonia levels during hospitalization. Extracellular fluid was administered on days 1–4, lactulose and branched-chain amino acid preparations were administered on days 14–25, and shunt embolization was performed on day 22.

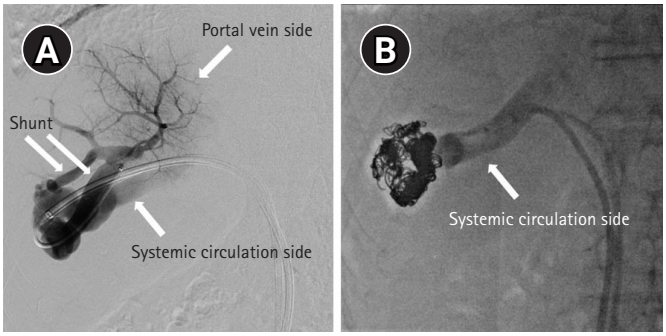

Fig. 3. Intraoperative findings of shunt embolization. (A) Pre-embolization: portal angiography showing that the two lines of P6 were the blood supply pathways for the portosystemic shunt. (B) Post-embolization: following the administration of contrast agent in the inferior right hepatic vein near the coil embolization, no blood flow is observed on the portal vein side, confirming that the shunt blood flow had disappeared.

vein P6 to the IRHV was observed before embolization (Fig. 3A). After the procedure, the position of the embolic coil was appropriately fixed and the shunt blood flow disappeared, confirming successful embolization (Fig. 3B).

Cognitive function tests were performed 1 year before admission, before and after the procedure, and as an outpatient (7 months after the procedure). One year before admission, the patient scored 18 on the Revised Hasegawa Dementia Scale (HDS-R) and 23 on the Mini-Mental State Examination (MMSE), with disorientation and loss of points on the delayed recall.

At this stage, the ADLs were preserved (Barthel Index, 70/100; Lawton IADL, 5/8), and a diagnosis of Alzheimer disease was not made. After admission, the HDS-R and MMSE scores were 12 and 17, respectively, lower than those 1 year prior. The patients' scores for temporal disorientation, immediate and delayed recall, item recall, and verbal fluency worsened. At this point, the ADLs were significantly poorer than they had been 1 year earlier (Barthel Index, 55/100). Based on the results of the cognitive function tests, complications of Alzheimer disease were suspected. However, after shunt embolization, the HDS-R and MMSE scores improved significantly to 20 and 28 points, respectively. In an outpatient setting, the HDS-R and MMSE scores were 30 and 29 points, respectively, and the Barthel Index also markedly improved to 85/100. No recurrence of impaired consciousness was observed during the 6 months after discharge.

DISCUSSION

HE often occurs in the terminal stages of cirrhosis but can also occur due to shunt formation in patients without a history of liver disease. PSE accounts for approximately 10% of all cases, is relatively rare, and is characterized by (1) high blood ammonia levels without abnormal liver function, (2) repeated episodes of psychiatric symptoms, and (3) abnormal vascular shadowing in conjunction with the portal vein on contrast-enhanced CT.[6] Because patients usually have no evidence of liver enzyme elevation or jaundice and the symptoms mimic those of dementia, this type of HE can be overlooked.[7,8] A report in 2000[6] noted an average age of nine patients with the same disease type as that of the current patient as 56.9 years, suggesting that PSE develops in middle age or later. With the development of technologies such as CT and ultrasound and the increased recognition of PSE, a recent case report described a higher average age, ranging from 65 to 82 years.[9] Therefore, the age range of patients with PSE could be older than that currently assumed.

While congenital malformations, complications after abdominal surgery, trauma, and liver biopsy can cause shunt formation, in many cases the cause of shunt formation is unknown.[6] In the present case, there was no obvious acquired cause of intrahepatic shunt formation, and it was assumed that the condition was congenital. The patient would have been in a state of covert encephalopathy before the onset of cognitive decline and inappropriate behavior. He had experienced an episode of suspected cognitive decline and inappropriate behavior approximately 1 year and 2 months before admission, at which point the HE became overt. The onset of PSE is more common in older people, suggesting that congenital shunts may develop gradually due to blood vessel fragility and hemodynamic changes with aging.[9] The function of the blood-brain barrier (BBB) also gradually declines in older patients, making it easier for toxic substances to reach the brain.[10] Recent studies have shown that high levels of ammonia in the brain accelerate damage to the BBB structure.[11] Muscles are also a major metabolizing or-

gan of ammonia, and the presence of sarcopenia increases the risk for HE.[12,13] Therefore, older age increases the likelihood of developing overt HE or manifesting psychiatric symptoms of HE.

In this case, the deficits in cognitive function tests resembled those of Alzheimer disease, and the patient's gradual cognitive decline led to the suspicion of complications of Alzheimer disease at the time of admission. However, since the deficits disappeared after shunt embolization, the course of pure HE is believed to have mimicked that of Alzheimer disease. Cognitive decline in HE is characterized by attention deficits, problems with working memory, and deficits in executive function.[14] Some reports show that hyperammonemia impairs long-term potentiation (LTP), a synaptic model of learning, in the hippocampus, a brain region involved in memory acquisition.[15,16] Therefore, the clinical course of cognitive decline in HE is similar to that of Alzheimer disease. Some patients suspected of having Alzheimer disease may also have HE; thus, the measurement of blood ammonia levels should be considered when cognitive decline is exacerbated even in the absence of a history of liver disease.

Shunt embolization helps prevent the recurrence of attacks of disturbance of consciousness and improves consciousness level and physical function.[4,5,7,17] However, there have been no reports of successful shunt embolization in patients > 90 years of age. This case was also unique in that the Barthel Index was used to assess basic ADLs.

In conclusion, we report a case in which cognitive function and ADL improved after intrahepatic shunt embolization in a patient with HE caused by intrahepatic portosystemic shunt without liver disease. It is important to properly diagnose and treat PSE in very old patients.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, SK, KaT, TK; Patient treatment and care, SK, KaT, KoT, MY, ES, YUK, HT. Writing-original draft: SK, Writing-review & editing: KaT, TK; Supervision SO, MA.

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

Contact Us

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

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

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

Statement of Informed Consent and Institutional Approval

Copies of written informed consent should be kept for studies on human subjects. Clinical studies with human subjects should provide a certificate, an agreement, or the approval by the Institutional Review Board (IRB) of the author's affiliated institution. For research with animal subjects, studies should be approved by an Institutional Animal Care and Use Committee (IACUC). If necessary, the editor or reviewers may request copies of these documents to resolve questions regarding IRB/IACUC approval and study conduct.

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The corresponding author of an article is asked to inform the Editor of the authors' potential conflicts of interest possibly influencing their interpretation of data. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. A potential conflict of interest should be disclosed in the manuscript even when the authors are confident that their judgments have not been influenced in preparing the manuscript. The disclosure form should be the same as the ICMJE Form for Disclosure of Potential Conflicts of Interest (http://www.icmje.org/conflicts-ofinterest/).

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- Description of co-first authors or co-corresponding authors is also accepted if corresponding author believes that their roles are equally contributed.
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When the journal faces suspected cases of research and publication misconduct, such as redundant (duplicate) publication, plagiarism, fraudulent or fabricated data, changes in authorship, undisclosed conflict of interest, ethical problems with a submitted manuscript, appropriation by a reviewer of an author's idea or data, and complaints against editors, the resolution process will follow the flowchart provided by COPE (http://publicationethics.org/

resources/flowcharts). The discussion and decision on the suspected cases are carried out by the Editorial Board.

Editorial Responsibilities

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

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

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

Archiving and Posting Policy

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

Correction

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

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

SUBMISSION & PEER REVIEW PROCESS

Submission

All manuscripts should be submitted online via the journal's website (http://submit.e-agmr.org/submission/) by the corresponding author. Once you have logged into your account, the online

system will lead you through the submission process in a stepwise orderly process. Submission instructions are available at the website. All articles submitted to the journal must comply with these instructions. Failure to do so will result in the return of the manuscript and possible delay in publication.

Peer-Review Process

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

Appeals of Decisions

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

MANUSCRIPT PREPARATION

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

General Requirements

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

All authors of a manuscript must have agreed to its submission and are responsible for its content, including appropriate citations and acknowledgements; they must also have agreed that the corresponding author has the authority to act on their behalf on all matters pertaining to the publication of the paper. By publishing in this journal, the authors agree that the Korean Geriatrics Society

has the right to protect the manuscript from misappropriation. Illustrations in published articles will not be returned to the authors.

Reporting Guidelines for Specific Study Designs

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

Composition of Manuscripts

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

Table 1. Recommended maximums for articles submitted to AGMR

Type of article	Abstract (word)	Text (word)[a]	Reference	Table & figure
Original article	Structured[b], 250	3,500	50	7
Review	150	6,000	unlimited	7
Case report	150	1,500	20	7
Editorial	No	1,200	15	7
Letter to the editor	No	1,200	15	1

AGMR, Annals of Geriatric Medicine and Research.

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

[b]Background, methods, results, and conclusion.

Title Page

The Title Page should include only the following information:

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

    Sample:

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

  - ORCID: We recommend that the open researcher and contributor ID (ORCID) of all authors be provided. In order to obtain an ORCID, authors should register in the ORCID website: http://orcid.org/. Registration is free to every researcher in the world.
  - Additional Contributions: All persons who have made substantial contributions, but who have not met the criteria for authorship, are acknowledged here.
  - Previous Presentation: Please inform any previous presentation of the material. Provide the exact data and location of the meeting.

Abstract & Keywords

A concise and factual abstract is required. The abstract should not be more than 250 words (150 words for case reports and reviews). Abstracts should include the following headings: Background, Methods, Results, and Conclusion. Author(s) should specify the number of study participants. The abstract's conclusion should emphasize clinical relevance. Do not use vague phrases such as "We believe that …" or "We suppose that …". Non-standard or uncommon abbreviations should be avoided, but if essential, must be defined the first time they are mentioned in the abstract. After the abstract, list 3-5 keywords to be used for indexing. The keywords are from medical subject headings (MeSH; https://www.ncbi.nlm.nih.gov/mesh). Editorials and Letters to the editor do not require an abstract. An abstract is often presented separately from the article, and therefore must be able to stand alone.

Guidelines for the Main Body

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

References

The citation of references in the text should be made using consecutive numbers in parentheses (Vancouver style). They should be listed in the text in the order of citation, with consecutive numbering in this separate section. The style for papers in periodicals is as follows: the name and initials of all authors, the full title of article, the journal name abbreviated in accordance with Index Medicus, the year and volume, and the first and last page numbers. If there are more than 7 authors, write the names of the first 6 authors, followed by "et al." The style for a book chapter is as follows: author and title of the chapter, editor of the book, title of the book, edition, volume, place, publisher, year, and first and last page numbers. The style for a book is as follows: author, title of the book, edition, place of publication, publisher, and year of publication. The style for a website is as follows: title of the website, place of publication, publisher, year of copyright, and Internet address. Other types of references not described below should follow ICMJE Recommendations (https://www.nlm.nih.gov/bsd/uniform_requirements.html). Authors are responsible for the accuracy and completeness of their references and for ensuring that their text citations are correct. Papers still in press may be listed among the references using the journal name and a tentative year of publication. Unpublished data and personal communications may be listed only with the author's written permission.

Reference Style

- Journal article:

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

- Book:

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

- Book chapter:

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

JH, Brenner BM, editors. Hypertension pathophysiology, diagnosis, and management. 2nd ed. New York, NY: Raven Press; 1995. p. 465-78.

- Website:

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

Tables and Figures

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

- Table: Please submit tables as editable text and not as images. Avoid using vertical rules. Tables should be simple and should not duplicate information already presented in figures. Title all tables and number them using Arabic numerals in the order of their citation. Tables should be double-spaced, with each table on a separate sheet. Describe all abbreviations using footnotes. Footnotes are followed by the source notes, other general notes, abbreviation, notes on specific parts of the table (a), b), c), d)…), and notes on level of probability (*, **, *** for p-values). Each column and row should have an appropriate heading. The first letter of the first word in each column and row should be capitalized. Use Arabic numerals after "Table" in accordance with the order of citation, with a space between "Table" and the Arabic number. Mean and standard deviation (mean ± SD) and numbers of subjects are included and the significance of results is indicated through appropriate statistical analysis. The p-value should be provided to 3 decimal places and the letter "p" in "p-value" written in lower case. Table footnotes should be indicated with superscript markings. All units of measurement and concentration should be designated. Exponential terminology is discouraged. The table should be drawn in MS word and not as an image file (JPG, GIF, TIFF, etc.).
- Figure: Electronic art should be created/scanned and saved and submitted as either a TIFF (tagged image file format) or an EPS (encapsulated postscript) file. Figures must be cited in the text and numbered in order of first mention. Make sure to mark the figure number clearly on the figure or part of the electronic file name (i.e., Figure 1.tif). Line art must have a resolution of at least 1,200 dpi (dots per inch), and electronic photographs, radiographs, CT scans, and scanned images must have a resolution of at least 300 dpi. Images should be supplied at a size that approximates the final figure size in the print journal. If fonts are used in the artwork, they must be converted to paths or outlines, or embedded in the files. Color images must be created/scanned, saved, and then submitted as CMYK files. Please note that artwork generated using office suite programs such as Corel Draw or MS Word, as well as artwork downloaded from the Internet (JPEG or GIFF files), cannot be used. Color photographs will be published if the editor considers them absolutely necessary. The expense of reproducing color photographs/ designs will be passed on to the author. The author is responsible for submitting prints that are of sufficient quality to permit accurate reproduction, and for approving the final color galley proof.
- Figure legend: All of the figure legends should be typewritten and double-spaced. Use a separate sheet for each legend. Figure legends should describe briefly the data shown, explain any abbreviations or reference points in the photographs, and identify all units, mathematical expressions, abscissas, ordinates, and symbols.

Other Manuscript Formats

General guidelines are same as for original articles.

- Review Articles: The text is structured in the following order: Title page, Introduction, Main text, Conclusion, and References, which should not exceed 100. Unstructured abstracts should contain no more than 150 words. Review article does not necessarily need to be reviewed by an Institutional Review Board.
- Case Reports
  - Case reports are considered for publication only if they report rare conditions, atypical symptoms and signs, or novel diagnostic or therapeutic approaches. The manuscript is structured in the following order: Title Page, Abstract, Introduction, Case Report, Discussion, References, Tables, and Figures. The abstract should be unstructured and should be no more than 150 words, with no more than 3 keywords attached. The introduction should briefly state the background and significance of the case. The actual case report should describe the clinical presentation and the diagnostic and therapeutic measures taken. The discussion should focus on the uniqueness of the case and should not contain an extensive review of the disease or disorder. The number of references is limited to 20. The maximum word count is 1,500 words, except references, figure legends, and tables.
  - A case report is an academic/educational activity that does not meet the definition of "research", which is: "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." Therefore, the activity does not necessarily need to be reviewed by an Institutional Review Board. However, patients have a right to privacy that should not be infringed without an informed consent. Identifying information, including patients' names, initials, or hospital numbers, should

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

Supplemental Data

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

FINAL PREPARATION FOR PUBLICATION

Final Version

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

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

Gallery Proof

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

Errata and Corrigenda

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