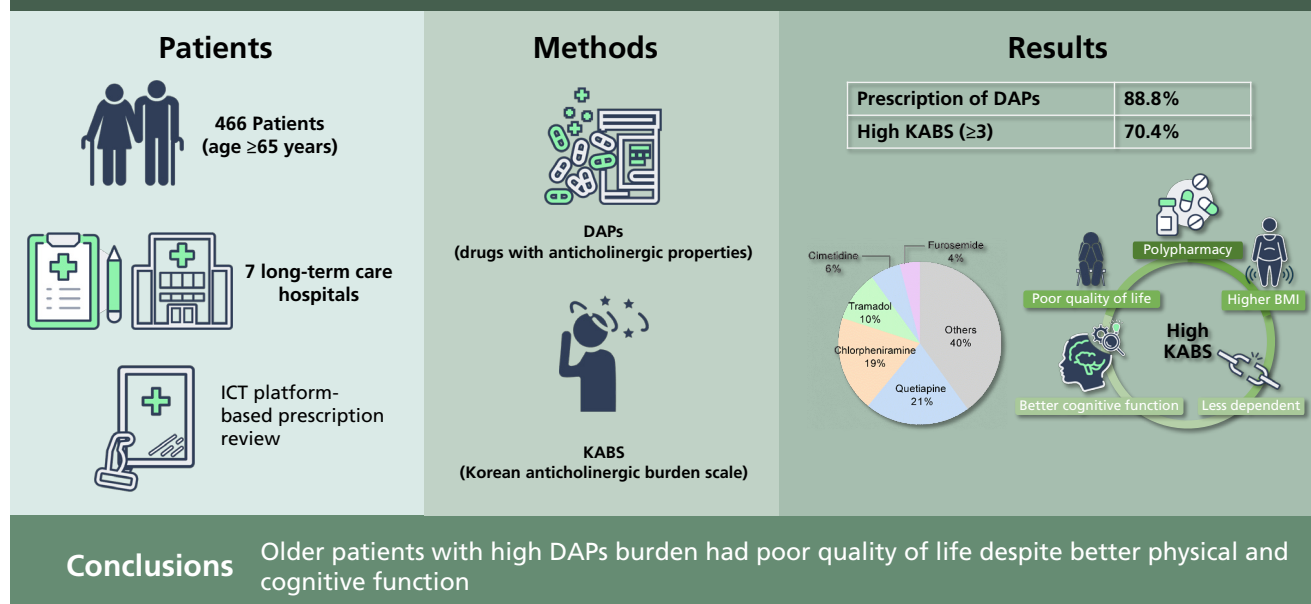KJIM

Factors associated with anticholinergic burden among older patients in long-term care hospitals in Korea

Jung-Yeon Choi[1], Hongsoo Kim[2,3,4], Young-il Jung[5], Seungyeon Chun[2], Sooyoung Yoo[6], Jae-Young Lim[4,7,8], Jin Young Ko[7], Kayoung Park[9], and Kwang-il Kim[1,10]

[1]Division of Geriatrics, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam; [2]Department of Public Health Sciences, Graduate School of Public Health, [3]Institute of Health and Environment, [4]Institute on Aging, Seoul National University, Seoul; [5]Department of Environmental Health, Korea National Open University, Seoul; [6]Office of eHealth Research and Businesses, Seoul National University Bundang Hospital, Seongnam; [7]Department of Rehabilitation Medicine, Seoul National University Bundang Hospital, Seongnam; [8]Department of Rehabilitation Medicine, Seoul National University College of Medicine, Seoul; [9]Department of Pharmacy, Seoul National University Bundang Hospital, Seongnam; [10]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea

Factors associated with anticholinergic burden among older patients in long-term care hospitals in Korea

Patients

466 Patients (age ≥65 years)

7 long-term care hospitals

ICT platform-based prescription review

Methods

DAPs (drugs with anticholinergic properties)

KABS (Korean anticholinergic burden scale)

Results

| Prescription of DAPs | 88.8% |
| High KABS (≥3) | 70.4% |

Cimetidine 6%
Furosemide 4%
Tramadol 10%
Others 40%
Chlorpheniramine 19%
Quetiapine 21%

Polypharmacy
Poor quality of life
Higher BMI
High KABS
Better cognitive function
Less dependent

Conclusions Older patients with high DAPs burden had poor quality of life despite better physical and cognitive function

Correspondence to Kwang-il Kim, M.D.
Department of Internal Medicine, Seoul National University Bundang Hospital, 82 Gumi-ro 173beon-gil, Bundang-gu, Seongnam 13620, Korea
Tel: +82-31-787-7032, Fax: +82-31-787-4052, E-mail: kikim907@snu.ac.kr
https://orcid.org/0000-0002-6658-047X

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Background/Aims: Drugs with anticholinergic properties (DAPs) are associated with adverse health outcomes in older patients. The objective of this study was to evaluate the factors that determine the prescribing of more DAPs in long-term care hospitals (LTCHs) in Korea. In addition, the current patterns of DAP prescription were explored using a novel platform, which can collect data from LTCHs.

Methods: This was a Health-RESPECT (integrated caRE Systems for elderly PatiEnts using iCT) sub-study, which is a pragmatic, cluster-randomized, controlled trial. The Health-RESPECT platform was used to collect prescribed medication data of 466 patients (aged ≥ 65 years) from seven LTCHs. DAPs were identified using the Korean Anticholinergic Burden Scale (KABS). Physical frailty, cognitive function, functional status, and quality of life were evaluated.

Results: Among 466 LTCH patients, 88.8% (n = 414) were prescribed DAPs, and the prevalence of high KABS (≥ 3) was 70.4% (n = 328). The drugs that contributed most to the total KABS were quetiapine (20.7%), chlorpheniramine (19.5%), tramadol (9.8%), cimetidine (5.8%), and furosemide (3.6%). Polypharmacy, higher body mass index, less dependence, better communication and cognitive functions, and poorer quality of life were associated with high KABS.

Conclusions: Although the patients with a high burden of DAPs were less dependent and had better cognitive and communication functions, they had poorer quality of life. DAP use in LTCH patients should be monitored carefully, and the risk/benefit relationship for their use should be considered.

Keywords: Cholinergic antagonists; Korean Anticholinergic Burden Scale; Long-term care; Polypharmacy; Medication review

INTRODUCTION

In Korea, the proportion of older adults, defined as those aged 65 or older, has doubled in only 17 years from 7% (an aging society) in 2000 to 14% (an aged society) in 2017 and is expected to grow to 21% (a super-aged society society) by 2026 [1]. Consequently, the prevalence of chronic diseases, non-specific symptoms caused by ageing, and functional impairment is expected to increase. Accordingly, the number of older people who require the services of a long-term care hospital (LTCH) in Korea has increased drastically due to the growth of the population in need of medical services for chronic multi-morbidity and personal care [2,3]. Frail older patients are hospitalized at LTCHs in Korea for extended durations because of the decrease in family support for older parents and easy access to inpatient care financed by the National Health Insurance Program [4].

Given the comorbidities in older adults, polypharmacy is common, thus raising the risk of using potentially inappropriate medications (PIMs), defined as medications with more risks than benefits. Polypharmacy and PIMs are growing concerns for older patients because of increased healthcare costs, adverse drug events, drug interactions, medication non-adherence, functional decline, and multiple geriatric syndromes [5,6]. Most drugs with anticholinergic properties (DAPs) are classified as PIMs, and their use in older patients is discouraged. DAPs are associated with dry mouth, dry eye, constipation, dizziness, falls, cognitive decline, and physical impairment [7-9]. Older patients with multi-morbidities, who are independent or frail, tend to complain of symptoms related to diseases or geriatric syndromes and are more likely to experience polypharmacy or take PIMs due to the prescribing cascade, resulting in adverse drug events [10-12]. Since the clinical and demographic characteristics of hospitalized patients at LTCHs are expected to differ from those of community-dwelling older patients, DAPs are likely to be prescribed more frequently for the older patients living in LTCHs. However, no study has identified the clinical characteristics of patients with a high DAP burden or the prescription pattern of DAPs in LTCHs in Korea.

The anticholinergic drug burden of an individual is defined by the cumulative effect of taking one or more DAPs. Several anticholinergic drug burden indices have been validated, and a higher anticholinergic drug index strongly correlates with poor cognitive and functional outcomes [13]. Due to differences in prescribing patterns and medication availability across countries, country-specific anticholinergic burden scales have been developed. In Korea, the Korean Anticholinergic Burden Scale (KABS) was developed and validated based on literature evaluation and a modified Delphi process [14,15]. KABS was validated in a claim-based case-control study on the dose-response relationship between KABS

burden and incident dementia [15].

We aimed to investigate the clinical and demographic factors associated with the prescribing of more DAPs according to the KABS data in older patients. In addition, we explored the prevalence of DAPs and DAP burden, current status of polypharmacy, and patterns of DAP prescription in LTCH residents in Korea.

METHODS

Study population
Data from participants of the Health-RESPECT (integrated caRE Systems for elderly PatiEnts using iCT) study, a cluster-randomized controlled trial conducted in long-term care institutions, were analysed. The study was conducted in seven LTCHs and five nursing homes in Korea. The study involved cluster randomization, after which patients who provided informed consent were recruited. During the study period, after the initial assessment, the intervention group underwent a 3-month intervention, while the observation group underwent a 3-month observation period with no intervention. A specific time point (initial assessment) was defined as the date when the intervention was started in the intervention group and was defined as the date of assessment visit in the observation group. Patients aged 65 years or older with chronic diseases and who had stayed in the facility for at least 2 weeks before enrolment were included in this study. However, patients that were comatose, expected to expire, or to be discharged within 3 months were excluded. Specific inclusion and exclusion criteria and services provided were described previously [16,17]. We analysed the data of patients recruited from LTCHs only to maintain the homogeneity of the accuracy of the data because nursing homes do not use electronic medication record systems, and the prescriptions were received from multiple medical institutions. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Patients or legal guardians provided written informed consent.

Health–RESPECT platform and data acquisition
The Health-RESPECT platform provides comprehensive geriatric assessment, individualized care plans for chronic diseases, medication and rehabilitation management through the service platform, periodic videoconference, and in-system assessment. The Health-RESPECT platform evaluates adverse events and generates warning alarms that are delivered via message to the attending physician of the LTCH. Data including patients' vital signs, laboratory findings, and prescribed medication were retrieved from the electronic medication records of the LTCH via a health information exchange network system, which was previously developed and used for the patient referral service between institutions [18]. Medication prescription data were extracted from the Health-RESPECT platform.

Measurements
A trained nurse conducted an independent assessment of frailty status, demographic data, cognitive function, functional ambulatory capacity, overall functional status, and quality of life. Frailty status was evaluated using the Korean version of the FRAIL (K-FRAIL) scale. Scores of ≥ 3, 1 to 2, and 0 were classified as frail, pre-frail, and robust, respectively [19]. Functional status of older participants was measured using an interRAI long-term care facilities (LTCF) tool and comprehensive geriatric assessment [20]. From the items in the interRAI LTCF tool, several functional scales can be generated, including activities of daily living (ADL), cognition, depression, communication, and pain [21]. The ADL hierarchy (ADLH) scale is a seven-level tool of functional performance based on four items: personal hygiene, locomotion, toilet use, and eating [22]. Using an algorithm, severity patterns of the variables categorized people from 0 (independent) to 6 (total dependence). The depression rating scale measured the mood of an individual, and its score ranges from 0 to 14 [23]. The communication (COMM) scale encompasses two four-point items: self-understanding and the ability to understand others [24]. The COMM scale ranges from 0 to 8, with higher scores reflecting poorer communication. The pain scale quantifies pain frequency and intensity; a higher pain score indicates more severe pain (ranges from 0 to 3) [25]. EuroQol-5 Dimension (EQ-5D), the Korean version of the Mini-Mental State Examination (MMSE), and functional ambulatory category were used to evaluate the quality of life, cognitive function, and functional ambulatory category, respectively [26,27].

The data collected at initial assessment, which was initially surveyed by the assessment team or medical records collected from the Health-RESPECT platform, were analysed. The copies of written informed consent and study protocol were reviewed and approved by the Seoul National University Bundang Hospital Institutional Review Board (IRB number:

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Polypharmacy, potentially inappropriate medications, and Korean anticholinergic burden index

To investigate the current status and characteristics of the prescription pattern in LTCHs in Korea, the medication list at initial assessment was used for analysis. The medication list was defined for oral medications prescribed from 21 days before initial assessment to initial assessment. Although prescribing intervals differ across LTCHs, the time window was defined as 21 days because most LTCHs enter a prescription every 1 to 2 weeks. Polypharmacy and KABS were evaluated in the defined drug list. The numerical definition of polypharmacy was indicated as the simultaneous prescription of 5 or more drugs. Excessive polypharmacy was defined as the simultaneous prescription of 10 or more drugs [28]. A list of 89 PIMs was developed based on the Beers criteria and the 2016 Seoul National University Bundang Hospital Inappropriate Medication for Elderly criteria and adjusted for their clinical significance and frequencies in long term care facilities (Supplementary Table 1) [6,29]. Anticholinergic burden was evaluated using the KABS, and a KABS score of 3 and above was defined as a strong anticholinergic effect or high anticholinergic burden [14].

Statistical analysis

Descriptive statistics, including mean and standard deviation for continuous variables and frequency and percentages for categorical variables, are provided. The independent t test and chi-squared test were used for continuous and categorical variables, respectively, to compare the patients' baseline characteristics according to the anticholinergic burden. The relationship between frailty status, multi-morbidity, demographic data, ADL, cognition, depression, communication, and pain, EQ-5D, polypharmacy, or other confounding factors and KABS was determined using logistic regression. We used logistic regression analysis to evaluate the clinical factors associated with the high anticholinergic burden among LTCH patients while adjusting for demographic variables (age, sex, body mass index [BMI], medical aid beneficiary, and length of hospital stay). Adjusted odds ratios (aORs) with 95% confidence intervals (CI) are reported.

All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and $p < 0.05$ was considered significant with two-tailed analysis. All data from the participants were de-identified and analysed anonymously.

RESULTS

From September 5, 2019 to January 31, 2020, 508 patients were enrolled from LTCHs. After excluding 42 patients who did not complete an initial assessment because of unexpected death (n = 4), transfer to another institution or hospital (n = 16), discharge before assessment (n = 5), refusal for assessment (n = 16), or withdrawal of consent (n =1), 466 patients were included in the final analysis. The mean age of the participants was 81.8 ± 7.1 years and women accounted for 73.4% (n = 342). Hypertension was the most common comorbid condition (75.3%) followed by dementia (68.7%), diabetes (49.8%), cerebrovascular disease (36.5%), Parkinson's disease (12.9%), heart failure (8.2%), and atrial fibrillation (7.9%). The mean number of medications and PIMs were 11.0 ± 4.6 and 1.14 ± 1.14, respectively, and 88.8% (n = 414) of patients were prescribed DAPs according to the KABS. The study found that 93.1% and 62% of the participants had polypharmacy and excessive polypharmacy, respectively. The mean KABS was 4.55 ± 3.34, and the proportion of patients with high KABS was 70.4% (n = 328) (Table 1).

The top 10 frequently prescribed DAPs were quetiapine (47.0%), chlorpheniramine (29.6%), tramadol (22.3%), clonazepam (17.0%), furosemide (16.5%), escitalopram (14.4%), cimetidine (13.1%), alprazolam (12.4%), trazodone (10.5%), and guaifenesin (5.6%). Drugs with a KABS score of 1, 2, and 3 contributed to 27.0%, 37.9%, and 35.1% of the cumulative KABS score, respectively. Quetiapine (KABS 2, 20.7%), chlorpheniramine (KABS 3, 19.5%), tramadol (KABS 2, 9.8%), cimetidine (KABS 2, 5.8%), and furosemide (KABS 1, 3.6%) had the highest contribution to the total KABS score (Fig. 1). According to drug category, the most frequently prescribed DAPs were antipsychotics (49.4%), antihistamines (36.1%), anxiolytics (32.2%), antidepressants (31.3%), and analgesics (23.0%).

Patients with a greater BMI had high KABS scores. Additionally, lower ADLH scale, communication scale, and EQ-5D scores and a higher MMSE score were associated with high KABS, as were polypharmacy, excessive polypharmacy, and the number of PIMs (Table 2). Logistic regression analysis adjusted for age, sex, BMI, medical aid beneficiary status, and length of hospital stay revealed a significant association between high KABS and a higher MMSE score (aOR, 1.028; 95% CI, 1.001 to 1.056), lower EQ-5D score (aOR, 0.385; 95% CI, 0.182 to 0.815), polypharmacy (aOR, 3.71;

Table 1. Baseline characteristics of the study population

Characteristic	Value
Demographic	
Age, yr	81.8 ± 7.1
Women	342 (73.4)
Body mass index, kg/m^2	20.1 ± 4.1
Medical aid beneficiary	47 (10.1)
Length of hospital stay, day	515.7 ± 518.3
Functional	
MMSE[a]	13.1 ± 8.3
Functional ambulatory class	0.9 ±1.4
EQ-5D score	0.531 ± 0.276
ADL hierarchy scale	3.86 ± 1.77
Communication scale	3.39 ± 2.53
Depression rating scale	1.83 ± 2.45
Frailty[b]	204 (43.8)
Medication	
Number of medications	11.0 ± 4.6
Polypharmacy	434 (93.1)
Excessive polypharmacy	289 (62.0)
Number of PIMs	1.14 ± 1.14
High KABS (≥ 3)	328 (70.4)
Comorbidity	
Hypertension	351 (75.3)
Diabetes	232 (49.8)
Heart failure	38 (8.2)
Cerebrovascular disease	170 (36.5)
Atrial fibrillation	37 (7.9)
Dementia	320 (68.7)
Parkinson's disease	60 (12.9)

Values are presented as mean ± standard deviation or number (%). MMSE, Korean version of the Mini-Mental State Examination; EQ-5D, EuroQol-5 Dimension; ADL, activities of daily living; PIM, potentially inappropriate medication; KABS, Korean Anticholinergic Burden Scale.
[a]Data were missing for 36 patients.
[b]Data were missing for 2 patients.

95% CI, 1.691 to 8.144), excessive polypharmacy (aOR, 12.403; 95% CI, 5.541 to 27.760), moderate ADL dependence (ADLH ≥ 5, aOR, 0.489; 95% CI, 0.322 to 0.744), and moderate impairment of communication (COMM ≥ 4, aOR, 0.611; 95% CI, 0.400 to 0.933) (Table 3).
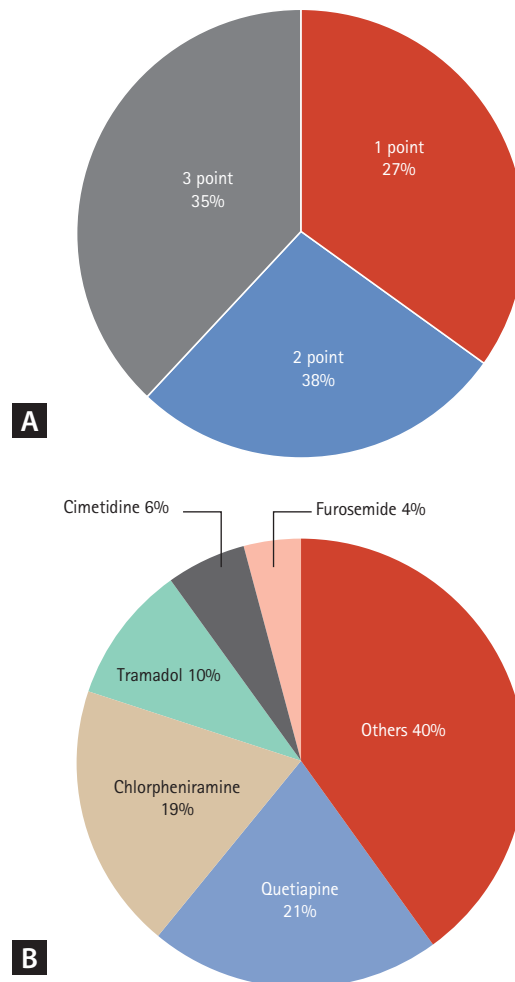

Figure 1. Distribution of (A) Korean Anticholinergic Burden Scale (KABS) score of medications and (B) specific medications that contributed to the total KABS burden of the study population. Medications of KABS scores 1, 2, and 3 contributed 27%, 38%, and 35%, respectively, to the total KABS burden. The top five medications with the highest contribution to the total KABS burden were quetiapine (21%), chlorpheniramine (19%), tramadol (10%), cimetidine (6%), and furosemide (4%).

DISCUSSION

The study results revealed a higher administration of DAPs to LTCH patients who are less dependent and have better communication and cognitive functions. This trend was maintained even after adjusting for age, sex, BMI, status of medical aid beneficiary, and length of hospital stay. Patients with a high burden of DAPs had a poorer quality of life and tended to use more drugs (7.93 vs. 12.32, respectively; $p <$ 0.001). This pattern was similar to that observed in previous

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Table 2. Comparison of demographic, functional, medical, and comorbidity components by low and high KABS prescription

Variable	Low KABS (n = 138)	High KABS (n = 328)	p value
Demographic			
Age, yr	81.5 ± 7.0	81.8 ± 7.1	0.562
Women	95 (68.8)	242 (73.8)	0.277
Body mass index, kg/m^2	20.2 ± 4.0	21.5 ± 4.1	0.003
Medical aid beneficiary	14 (10.1)	27 (8.2)	0.506
Length of hospital stay	455.0 ± 535.5	541.2 ± 509.5	0.101
Functional			
MMSE[a]	11.5 ± 8.6	13.7 ± 8.2	0.014
Functional ambulatory class	0.78 ± 1.42	0.89 ± 1.41	0.440
EQ-5D score	0.581 ± 0.291	0.510 ± 0.267	0.014
ADL hierarchy scale	4.3 ± 1.7	3.7 ± 1.8	0.002
Communication scale	3.95 ± 2.69	3.16 ± 2.43	0.002
Depression rating scale	1.65 ± 2.32	1.90 ± 2.50	0.314
Frailty[b]	60 (44.1)	144 (43.8)	0.966
Medication			
Number of medications	7.93 ± 4.18	12.32 ± 4.17	< 0.001
Polypharmacy	113 (81.9)	321 (97.9)	< 0.001
Excessive polypharmacy	43 (31.2)	246 (75.0)	< 0.001
Number of PIMs	0.55 ± 0.85	1.38 ± 1.16	< 0.001
Comorbidity			
Hypertension	106 (76.8)	245 (74.7)	0.629
Diabetes	74 (53.6)	158 (48.2)	0.282
Heart failure	11 (8.0)	27 (8.2)	0.925
Cerebrovascular disease	55 (39.9)	115 (35.1)	0.326
Atrial fibrillation	6 (4.3)	31 (9.5)	0.063
Dementia	92 (66.7)	228 (69.5)	0.545
Parkinson's disease	15 (10.9)	45 (13.7)	0.402

Values are presented as mean ± standard deviation or number (%).
KABS, Korean Anticholinergic Burden Scale; MMSE, Korean version of the Mini-Mental State Examination; EQ-5D, EuroQol-5 Dimension; ADL, activities of daily living; PIM, potentially inappropriate medication.
[a]Data were missing for 36 patients.
[b]Data were missing for 2 patients.

studies conducted in LTCF in Helsinki [30]. The drugs with the highest contribution to the total KABS score were quetiapine (KABS 2, 20.7%), chlorpheniramine (KABS 3, 19.5%), tramadol (KABS 2, 9.8%), cimetidine (KABS 2, 5.8%), and furosemide (KABS 1, 3.6%).

The prevalence of DAP prescription in LTCHs was 88.8% (n = 414), and this was higher than in previous research conducted in LTCF, which ranged from 30% to 77% [31,32]. This difference in DAP prevalence is likely due to the varied drug list used to define DAPs and the different population characteristics. Possibly, the patients in Korean LTCHs had excellent access to prescriptions, and the proportion of severe dementia was relatively small compared to those in nursing homes (mean cognitive performance score: 2.7 vs. 3.2); thus, more complaints of pain or non-specific symptoms for various geriatric diseases, such as urinary incontinence, dermatitis, insomnia, or allergy, could be expected [32]. Contrary to other countries where most long-term

Table 3. Factors associated with a high anticholinergic burden: univariate analysis with adjustment

Characteristic	Odds ratio (95% CI)	p value
Functional		
MMSE[a]	1.028 (1.001–1.056)	0.043
Functional ambulatory class	1.031 (0.889–1.197)	0.686
EQ-5D score	0.385 (0.182–0.815)	0.013
Frailty[b]	1.044 (0.684–1.593)	0.841
ADL hierarchy scale	0.841 (0.739–0.957)	0.009
Communication scale	0.900 (0.828–0.977)	0.012
Depression rating scale	1.043 (0.956–1.138)	0.347
Polypharmacy		
< 5	1.00	
5–9	3.710 (1.691–8.144)	0.001
> 10	12.403 (5.541–27.760)	< 0.001
Comorbidity		
Hypertension	0.817 (0.504–1.327)	0.414
Diabetes	0.755 (0.498–1.145)	0.186
Heart failure	1.027 (0.481–2.194)	0.944
Cerebrovascular disease	0.805 (0.525–1.233)	0.318
Atrial fibrillation	2.422 (0.967–6.067)	0.059
Dementia	1.169 (0.749–1.824)	0.492
Parkinson's disease	1.343 (0.710–2.539)	0.364

CI, confidence interval; MMSE, Korean version of the Mini-Mental Status Examination; EQ-5D, EuroQol-5 Dimension; ADL, activities of daily living.
[a]Data were missing for 36 patients.
[b]Data were missing for 2 patients.

Figure 2. Quality of life score according to the anticholinergic burden: no anticholinergic medication (Korean Anticholinergic Burden Scale [KABS] 0), intermediate burden of anticholinergic medications (KABS 1–2), and high burden of anticholinergic medications (KABS 3 or more). There was a significant difference in the quality of life score according to the anticholinergic burden (KABS 0 vs. 3 or more, p = 0.01).

care institutions are nursing homes, in Korea, various medical services, including subacute, palliative, and rehabilitation care, are provided in LTCHs. Patients pay only 10% to 20% of the total medical fees because most of the citizens are eligible for coverage under the National Health Insurance Program. The prescription pattern observed in this study is characterized by frequent use of central nervous system active drugs (antipsychotics, 49.4%; anxiolytics, 32.2%; and antidepressants, 31.3%), antihistamines (36.1%), and analgesics (23.0%), which is consistent with that observed in a previous study conducted in LTCF [33].

In previous observational and retrospective cohort studies, a high burden of DAPs was associated with adverse cognitive impact or incident dementia [15,34]. However, in an-
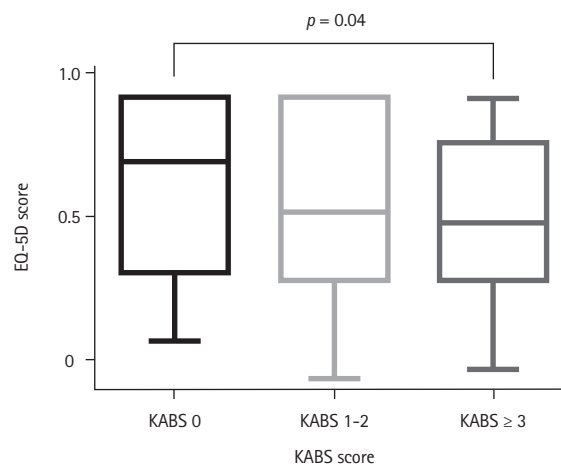
other study, similar to the current study, the use of DAPs was associated with better cognition and functioning [9,30]. This finding may be related to several medical and non-medical factors. First, since the priority of medical treatment in LTCHs is improving quality of life rather than improving survival or guideline-based chronic disease management, patients with poor cognitive or communication function are likely to have been prescribed a lower number of DAPs because their symptom complaints are not frequent or clear. Second, previous studies have emphasized the avoidance of DAPs, which may impact cognition, delirium, or behavioural symptoms [35,36]. Therefore, patients with low cognitive function may have possibly tried adjusting medications or reducing the unnecessary DAPs to improve delirium. An increase in the number of DAPs according to the KABS, from 0 to more than 3 (p = 0.28 in Kruskal-Wallis test), was associated with a stepwise decrease in the quality of life (Fig. 2). Although further study is needed to investigate causality between DAP use and cognitive function, physical function, or quality of life, we showed a dose-response relationship between the DAP burden and quality of life of LTCH patients.

DAPs have central and peripheral antagonist effects on muscarinic receptors, leading to delirium, falls, cognitive impairments, constipation, and dry mouth [31,33]. In a previous study, DAPs were widely prescribed for various diseases

in older adults, including Parkinson's disease, depression, cardiovascular disease, urinary incontinence, asthma, and allergies [37]. Older patients in LTCHs were more likely to be exposed to polypharmacy, PIMs, and DAPs because of their disease patterns, frailty, pain, and non-specific symptoms. In this study, although there was no difference in the number of PIMs (1.20 vs. 1.12, $p = 0.571$) and anticholinergic burden (KABS, 4.65 vs. 4.53, $p = 0.746$) according to disease burden (number of comorbidities ≥ 4), more medications (11.98 vs. 10.77, $p = 0.022$) were prescribed to the group of patients with high disease burden. As the use of DAPs in LTCHs is inevitable, a periodic automatic monitoring system is needed for proper management of the patients. The medical staff in LTCHs also need an appropriate consultation system to facilitate the control of symptoms and to prevent disease aggravation without the need to transfer the patients to regional acute care hospitals. To solve these unmet needs for patients and medical staff in LTCHs, access to information on PIMs could be provided by linking the electronic medication record of the LTCH to the Health-RESPECT platform, along with periodic videoconferencing with the geriatrician of the regional acute care hospital, to ensure timely care of acute conditions [17]. In addition, linking the Health-RESPECT system to the health information exchange network system can ensure real-time monitoring and adjustment of PIMs and DAPs.

Our study had several methodological strengths. In contrast to previous research that used claim data, we used cross-sectional drug exposure data, which can be considered more reliable because the data were extracted directly from each electronic medication record of the LTCH. In addition, the Health-RESPECT program, a system to share and cooperate with regional acute care hospitals, was established to access PIMs or DAPs and facilitate intervention in further practice. However, our study was limited by the cross-sectional design, which cannot determine causality. Further observational studies are needed to identify the prevalence of adverse outcomes related to DAP administration.

In conclusion, the prevalence of DAP administration in this study was 88.8% (n = 414), and 70.4% (n = 328) of the patients had a high burden of DAPs. Patients with a prescription of many DAPs (high KABS) tended to have higher BMI, less dependence, better communication and cognitive functions, and poorer quality of life. The long-term relationship between DAP administration and adverse clinical outcomes in older LTCH patients should be investigated in further ob-

servational or cohort studies.

KEY MESSAGE

1. Over 70% of long-term care hospital (LTCH) patients experienced high anticholinergic burden, and quetiapine (20.7%), chlorpheniramine (19.5%), tramadol (9.8%), cimetidine (5.8%), and furosemide (3.6%) mostly contributed.
2. High anticholinergic burden in LTCHs is associated with polypharmacy, less dependence, better cognitive function, and poor quality of life.
3. It is necessary to develop and apply a medication management program considering the high prevalence, adverse impact, and characteristics of LTCH patients.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Supplementary Table 1. List of potentially inappropriate medications

Organ system/ therapeutic category	Medications
Anticholinergics	First-generation antihistamines
	Chlorpheniramine
	Clemastine
	Cyproheptadine
	Cinnarizine
	Diphenhydramine
	Hydroxyzine
	Triprolidine
	Anti-Parkinson agents
	Benztropine
	Trihexyphenidyl
	Antispasmodics
	Atropine
	Belladonnaalkaloids
	Clidinium-chlordiazepoxide
	Scopolamine
Antithrombotics	Dipyridamole, oral short acting
	Ticlopidine
Cardiovascular	Peripheral alpha-1 blockers
	Doxazosin
	Prazosin
	Terazosin
	Anti-arrhythmic agents
	Amiodarone
	Dronedarone
	Digoxin
	Central alpha blockers
	Clonidine
	Methyldopa
	Moxonidine
	Calcium channel blocker
	Short acting nifedipine

Supplementary Table 1. Continued

Organ system/ therapeutic category	Medications
CNS	Antidepressants
	Amitriptyline
	Amoxapine
	Clomipramine
	Doxepin > 6 mg/day
	Imipramine
	Nortriptyline
	Paroxetine
	Barbiturates
	Phenobarbital
	Pentobarbital
	Antipsychotics
	1st (conventional)generation
	Sulpiride
	Chlorpromazine
	2nd (atypical)generation
	Amisulpride,
	Ziprasidone
	Clozapine
	Olanzapine
	Aripiprazole
	Zotepine
	Paliperidone
	Lithium
	Benzodiazepines
	Short and intermediate acting
	Alprazolam
	Clotiazepam
	Etizolam
	Lorazepam
	Triazolam
	Tofisopam
	Long acting
	Chlordiazepoxide
	Clonazepam
	Diazepam
	Clobazam
	Pinazepam
	Flurazepam
	Nonbenzodiazepine, hypnotics
	Zolpidem
	Ergoloid mesylates
Genitourinary	Desmopressin
Endocrine	Megestrol

Supplementary Table 1. Continued

Organ system/ therapeutic category	Medications
Gastrointestinal	Metoclopramide
	Levosulpiride
	Proton-pump inhibitors (PPIs)
	Esomeprazole
	Lansoprazole
	Omeprazole
	Pantoprazole
	Rabeprazole
Pain	Meperidine
	Non-steroidal anti-inflammatory drug (NSAID)
	Indomethacin
	Ketorolac, includes parenteral
	Non–COX-selective NSAIDs, oral
	Aceclofenac
	Dexibuprofen
	Diclofenac
	Dexketoprofen
	Fenoprofen
	Ibuprofen
	Ketoprofen
	Meloxicam
	Nabumetone
	Naproxen
	Piroxicam
	Sulindac
	Skeletal muscle relaxants
	Chlorzoxazone
	Cyclobenzaprine
	Methocarbamol
	Orphenadrine
	Systemic steroid
	Methylprednisolone
	Prednisolone
	Triamcinolone