J Korean Med Sci. 2024 Mar 18;39(10):e84
https://doi.org/10.3346/jkms.2024.39.e84
eISSN 1598-6357·pISSN 1011-8934

JKMS

Original Article
Public Health & Preventive Medicine

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Characteristics According to Frailty Status Among Older Korean Patients With Hypertension

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OPEN ACCESS

Received: Nov 4, 2023
Accepted: Jan 17, 2024
Published online: Feb 21, 2024

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ABSTRACT

Background: As the prevalence of hypertension increases with age and the proportion of the older population is also on the rise, research on the characteristics of older hypertensive patients and the importance of frailty is necessary. This study aimed to identify clinical characteristics of older hypertension in Korea and to investigate these characteristics based on frailty status.
Methods: The HOW to Optimize eLDerly systolic BP (HOWOLD-BP) is a prospective, multicenter, open-label, randomized clinical trial that aims to compare intensive (target systolic blood pressure [SBP] ≤ 130 mmHg) with standard (target SBP ≤ 140 mmHg) treatment to reduce cardiovascular events in older hypertensive Korean patients aged ≥ 65 years. Data were analyzed through a screening assessment of 2,085 patients recruited from 11 university

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Trial Registration
Clinical Research Information Service Identifier: KCT0003787

Funding
This study was supported by a research grant from Korea National Institute of Health (grant number: 2021-ER0901, 2021–2023).

Disclosure
The authors have no potential conflicts of interest to disclose.

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hospitals. Demographic, functional (physical and cognitive), medical history, laboratory data, quality of life, and medication history of antihypertensive drugs were assessed.
Results: The mean age was 73.2 years (standard deviation ± 5.60), and 48.0% (n = 1,001) were male. Prevalent conditions included dyslipidemia (66.5%), obesity (body mass index ≥ 25 kg/m^2, 53.6%), and diabetes (28.9%). Dizziness and orthostatic hypotension were self-reported by 1.6% (n = 33) and 1.2% (n = 24), respectively. The majority of patients were on two antihypertensive drugs (48.4%), while 27.5% (n = 574) and 20.8% (n = 433) were on 1 and 3 antihypertensive medications, respectively. Frail to pre-frail patients were older and also tended to have dependent instrumental activities of daily living, slower gait speed, weaker grip strength, lower quality of life, and lower cognitive function. The frail to pre-frail group reported more dizziness (2.6% vs. 1.2%, $P < 0.001$) and had concerning clinical factors, including lower glomerular filtration rate, more comorbidities such as diabetes, stroke, and a history of admission. Frail to pre-frail older hypertensive patients used slightly more antihypertensive medications than robust older hypertensive patients (1.95 vs. 2.06, $P = 0.003$). Pre-frail to frail patients often chose beta-blockers as a third medication over diuretics.
Conclusion: This study described the general clinical characteristics of older hypertensive patients in Korea. Frail hypertensive patients face challenges in achieving positive clinical outcomes because of multifactorial causes: they are older, have more morbidities, decreased function, lower quality of life and cognitive function, and take more antihypertensive medications. Therefore, it is essential to comprehensively evaluate and monitor disease-related or drug-related adverse events more frequently during regular check-ups, which is necessary for pre-frail to frail older patients with hypertension.

Trial Registration: Clinical Research Information Service Identifier: KCT0003787

Keywords: Frailty; Hypertension; Older; Elderly

INTRODUCTION

A rapid aging population, characterized by a significant increase in the proportion of older adults in a country or population, is a global challenge faced by many countries, including Korea.[1] Korea is on track to become a super-aged society by 2025, with the proportion of people aged 65 years reaching 20% of the total population.[2] With the aging of society and the increase in life expectancy, the impact of these conditions on the health and well-being of older individuals has significant implications for both individuals and the healthcare system. Hypertension is a major cause of premature death and functional decline worldwide, being one of the most prevalent chronic diseases among older people. It is a well-known major risk factor for cardiovascular diseases such as heart disease, stroke, and kidney disease, affecting a substantial portion of the global population, particularly older adults.[3,4] In 2020, 29.4% of the adult population suffered from hypertension, and 5.0 million (40% of total hypertension patients) aged 65 years or older had hypertension in Korea. Due to population aging, the number of people with hypertension aged 65 or older is increasing rapidly compared to those aged 20–64.[5]

Frailty could be defined as a reduction in functional capacity, an increased vulnerability to adverse health outcomes, and a diminished ability to cope with stressors.[6,7] It is a multidimensional syndrome encompassing factors such as muscle weakness, fatigue, slowed movement, weight loss, and low physical activity.[6] Frailty is associated with an elevated risk of

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falls, hospitalization, disability, and mortality.[8] Previous studies have identified the potential benefits of intensive treatment for hypertension in reducing the incidence of cardiovascular events and mortality, even in the older population.[9,10] However, the optimal target blood pressure (BP) for older hypertensive patients varies from under 130 to 140 mmHg according to guidelines.[11-13] The HOW to Optimize eLDerly systolic BP (HOWOLD-BP) trial, comparing the incidence of cardiovascular events in older Korean patients with hypertension based on two target systolic blood pressure (SBP) levels (≤ 130 and ≤ 140 mmHg) is currently ongoing.

This study aimed to evaluate baseline characteristics of older hypertensive patients and patterns of antihypertensive medications in participants enrolled in the HOWOLD-BP study up to December 31, 2022. We will also identify clinical differences and antihypertensive medication use patterns according to frailty status.

METHODS

The HOWOLD-BP trial is designed as a prospective, multicenter, open-label randomized clinical trial planned to follow-up each participant for three years. The HOWOLD-BP trial aims to compare intensive SBP-lowering treatment (target SBP ≤ 130 mmHg) with standard treatment (target SBP ≤ 140 mmHg) to reduce cardiovascular events in older hypertensive Korean patients over 65 years. The subjects have been recruited from 11 university hospitals in Korea since January 15, 2019.

The inclusion criteria were 1) patients aged ≥ 65 years, 2) patients diagnosed with hypertension who were already taking antihypertensive medications or treatment-naïve patients with a clinic SBP of 140 to 180 mmHg, 3) patients with independent activity of daily living (ADL) and 4) patients who provided written informed consent. Participants were excluded if they met any of the following criteria: 1) a past medical history of secondary hypertension, 2) resistant hypertension, 3) orthostatic hypotension with symptoms during screening, 4) a recent experience of acute coronary syndrome, cardiac surgery, or urgent percutaneous coronary intervention within the recent 3 months, 5) heart failure with left ventricular ejection fraction < 40%, 6) hypertrophic obstructive cardiomyopathy, aortic stenosis, moderate to severe valve disease, or congenital heart disease, 7) diagnosis of acute cerebral infarction within the last 3 months, 8) uncontrolled diabetes mellitus at screening (HbA1c ≥ 10%), 9) end-stage renal disease (on hemodialysis or estimated glomerular filtration rate [eGFR] less than 15 mL/min/1.73 m^2), 10) diagnosis of moderate to severe retinopathy (retinal hemorrhage, visual impairment, microaneurysm) within the last 6 months, 11) clinically significant liver disease or an aspartate transaminase/alanine transferase level greater than 3 times the upper normal range, 12) uncontrolled thyroid dysfunction, 13) enrollment in other clinical trials within the last 4 months or plans to participant other clinical trials during our study, and 14) other reasons that may limit participation or the progress of the study, as determined by the investigators.

We utilized data collected during the screening assessment to identify baseline clinical characteristics. Physical measurements included clinic BP, heart rate, weight, height, and orthostatic hypotension. Blood tests and urine analyses were also performed. Family history, medical history, sociodemographic history, smoking history, and alcohol-drinking history were assessed. ADLs were evaluated using the modified Barthel index (range, 0 to 100; lower numbers indicate worse activity and daily living function).[14] Instrumental ADLs (IADLs) were

measured using the Lawton and Brody index (range, 0–5 for males; 0–8 for females; lower numbers indicate worse IADL function).[15] Frailty was assessed using the Korean version of the fatigue, resistance, ambulation, illnesses, and weight loss (K-FRAIL) questionnaire, with a score of 1–2, ≥ three defined as having pre-frail and frailty, respectively.[16] Gait speed was measured based on the time it took to transverse a 4-m course, including 1 m for acceleration and deceleration. The handgrip strength was measured twice in both arms using a TKK-5401 GRIPD (Takei, Niigata, Japan), and maximum handgrip strength was used for analysis. Cognitive function was assessed using the Korean version of the Montreal Cognitive Assessment (MoCA-K; range, 0 to 30, with lower numbers indicating worse function).[17] Health-related quality of life was evaluated using the Korean version of the EQ-5D.[18] Detailed descriptions for assessment and primary and secondary outcomes were presented in the protocol paper.[19] BP and heart rate were measured at the heart level in the seated position using a professional digital BP monitor (HEM7080-IC, Omron Healthcare, Lake Forest, IL, USA). BP was measured in a quiet room after 5 minutes of rest and was repeated three times after another 2 minutes of rest under the supervision of the research coordinator. The mean systolic and diastolic blood pressure (DBP) from the second and third measurements were used. Control of hypertension was defined as meeting both systolic BP of less than 140 mmHg and DBP of less than 90 mmHg. Orthostatic hypotension was defined as a decrease in systolic BP of at least 20 mmHg or a reduction in DBP of at least 10 mmHg within 3 minutes of standing.

Continuous variables were expressed as the mean ± standard deviation (SD), while percentages and numbers were used for categorical data. The baseline characteristics of the robust and pre-frail to frail groups were compared using the Student's *t*-test for continuous data and Pearson's χ^2 test for categorical data. All statistical analyses used a significance level of 0.05 and were performed using the PASW Statistics software (SPSS version 25.0; IBM Corp., Armonk, NY, USA). The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics statement

The study protocol has been approved by the ethics committee of each participating center, including the Seoul National University Bundang Hospital (approval No. B-1811-504-006). Informed consent was submitted by all subjects when they were enrolled. This study was registered with the Clinical Research Information Service (Internet) in 2019 (KCT0003787, available from: https://cris.nih.go.kr/).

RESULTS

Patients were enrolled in the HOWOLD-BP study from January 15, 2019, to December 31, 2022. A total of 2,093 patients were registered, but one patient dropped out before the eligibility assessment, two patients dropped out after randomization, and five patients dropped out due to screening failure. Finally, 2,085 patients were analyzed, including 1,044 patients in the intensive treatment group and 1,041 patients in the standard treatment group (**Fig. 1**).
The mean age of participants was 73.2 years (SD, 5.60), and 48.0% (n = 1,001) were male. Over half were obese (53.6%, n = 1,118), and 20.75% were overweight. Mean BP was 136.5 (± 15.23)/74.7 (± 9.71) mmHg, and mean pulse pressure was 69.3 (± 12.87) per minute. About 60.4% (n = 1,260) of patients had well controlled BP. More than two-thirds (66.5%, n = 1,387) had dyslipidemia, and about one-third (28.9%, n = 603) had diabetes with comorbidity.

https://doi.org/10.3346/jkms.2024.39.e84

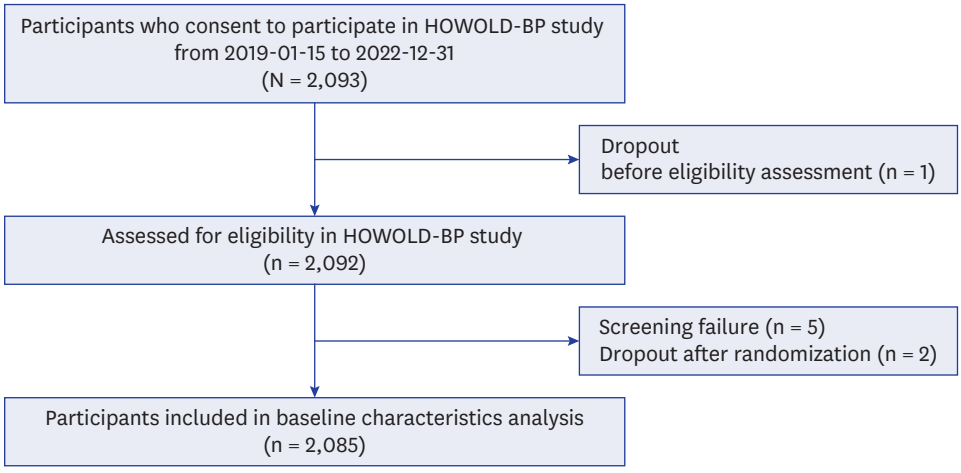

Fig. 1. Flow chart of inclusion of study participants.
n = number of patients, HOWOLD-BP = HOW to Optimize eLDerly systolic BP.

Among the participants, 63.0% (n = 1,314), 49.8% (n = 1,039), and 19.7% (n = 410) had experience of admission, surgery, and coronary revascularization, respectively. Only a small proportion of patients were current smokers (6.5%, n = 136), consumed drinking alcohol more than twice per week (14.0%, n = 290). More than half of the participants exercised regularly (52.5%, n = 1,095), while 12.0% (n = 251) maintained an active lifestyle without exercise, and 21.9% (n = 456) did not exercise at all. About 4.9% (n = 103) reported at least one episode of syncope, acute kidney injury, electrolyte imbalance, falls, and hypotension. Dizziness was also self-reported among 1.6% (n = 33), and orthostatic hypotension was measured among 1.2% (n = 24). Most participants were independent in IADL (97.0%, n = 2,023). Regarding physical performance, 27.7% (n = 577) of patients had a slow gait speed (≤ 0.8 m/sec), and 29.2% (n = 609) had low grip strength (men: ≤ 28 kg; women: ≤ 18 kg). Participants had a mean MoCA-K score was 24.4 (± 4.59), and 25.0% (n = 521) participants were categorized for cognitive impairment (MoCa-K score < 23) (**Table 1**).

The majority of older Korean hypertensive patients received two antihypertensive drugs (48.4%, n = 1,009), while 27.5% (n = 574) and 20.8% (n = 433) received 1 and 3 antihypertensive medications, respectively. Among hypertensive patients taking only one drug, 52.1% (n = 299), 36.2% (n = 208), 10.8% (n = 62) and 0.9% (n = 5) were prescribed an angiotensin receptor blocker (ARB)/angiotensin-converting-enzyme inhibitor (A), calcium channel blocker (CCB) (C), beta-blocker (B) and thiazide-like diuretics (D), respectively. The most frequently prescribed two-drug combination was A + C (55.2%, n = 557), followed by A + B (23.8%, n = 240) and A + D (10.8%, n = 109). Among patients taking three medications, A + C + D combination (45.0%, n = 195) and A + B + C (44.3%, n = 192) were the most frequent combinations (**Table 2**).

The control rate of hypertension was similar in robust (61.2%, n = 917) vs. prefrail to frail (58.3%, n = 341) patients (P = 0.220). Frail hypertensive patients tended to be older, have lower hemoglobin, lower serum sodium, higher serum potassium, lower eGFR, and a lower percentage of males. In terms of comorbidity, frail patients are more likely to have diabetes, a history of stroke, and admission. Regarding lifestyle, frail patients were less likely to have a history of past or current smoking and less likely to exercise regularly. Interestingly, robust patients were less likely to report dizziness, but the actual rate of orthostatic hypotension

https://doi.org/10.3346/jkms.2024.39.e84

Table 1. Baseline characteristics of 2,085 participants recruited from the HOWOLD-BP study

Characteristics	Values (N = 2,085)
Age, yr	73.2 ± 5.60
Male	1,001 (48.0)
Body mass index, m/kg^2	25.4 ± 3.17
Underweight (BMI ≤ 18.5 kg/m^2)	24 (1.2)
Normal (18.5 kg/m^2 < BMI < 23 kg/m^2)	512 (24.6)
Overweight (23 kg/m^2 ≤ BMI < 25 kg/m^2)	431 (20.7)
Obesity (25 kg/m^2 ≤ BMI)	1,118 (53.6)
Systolic blood pressure, mmHg	136.5 ± 15.23
Diastolic blood pressure, mmHg	74.7 ± 9.71
Control of HTN (SBP < 140 & DBP < 90)	1,260 (60.4)
Pulse (/min)	69.3 ± 12.87
WBC,[a] ×10^3/μL	6.44 ± 1.70
Hemoglobin,[b] g/dL	13.5 ± 1.46
Platelet,[c] ×10^3/μL	217.4 ± 55.18
Na[d]	140.9 ± 2.38
K[d]	4.4 ± 0.40
Creatinine,[e] mg/dL	0.88 ± 0.285
BUN[f]	17.9 ± 7.12
eGFR[e]	81.43 ± 16.33
Past medical history	
Diabetes	603 (28.9)
Dyslipidemia	1,387 (66.5)
Stroke	126 (6.0)
Myocardial infarction	164 (7.9)
Admission	1,314 (63.0)
Surgery	1,039 (49.8)
Coronary revascularization	410 (19.7)
Cigarette smoking status	
Non-smoker	1,337 (64.1)
Past smoker	612 (29.4)
Current smoker	136 (6.5)
Alcohol drinking (time/wk)	
Never	1,458 (69.9)
1	337 (16.2)
2–3	193 (9.3)
4+	97 (4.7)
Physical activity	
None	251 (12.0)
Active lifestyle with no exercise	456 (21.9)
Irregular exercise	283 (13.6)
Regular exercise	1,095 (52.5)
Dizziness (yes)	33 (1.6)
Orthostatic hypotension (yes)	24 (1.2)
Syncope/AKI/electrolyte imbalance/falls/hypotension (yes)	103 (4.9)
Dependent IADL	62 (3.0)
Gait speed (m/sec)[g]	1.0 ± 0.266
Slow gait speed (≤ 0.8 m/sec)[g]	577 (27.7)
Grip strength[g]	25.94 ± 8.63
Low grip strength[g] (men: ≤ 28 kg; women: ≤ 18 kg)	609 (29.2)
Frailty (Robust/Prefrail/Frail)[h]	1,498 (71.8)/503 (24.1)/82 (3.9)
Eq-5D-5L[e]	0.9377 ± 0.08921
MoCA-K[i]	24.4 ± 4.59
Cognitive decline (MoCA-K < 23)	521 (25.0)

Values are presented as number (%) or mean ± standard deviation.
HOWOLD-BP = HOW to Optimize eLDerly systolic BP, BMI = body mass index, HTN = hypertension, SBP = systolic blood pressure, DBP = diastolic blood pressure, WBC = white blood cell, BUN = blood urea nitrogen, eGFR = estimated glomerular filtration rate, AKI = acute kidney injury, IADL = instrumental activities of daily living.
[a]11 patients were missing, [b]9 patients were missing, [c]12 patients were missing, [d]22 patients were missing, [e]3 patients were missing, [f]4 patients were missing, [g]7 patients were missing, [h]2 patients were missing, [i]10 patients were missing.

https://doi.org/10.3346/jkms.2024.39.e84

Table 2. The medication history of 2,085 participants recruited from the HOWOLD-BP study

Medication	Values (N = 2,085)
Mean antihypertensive medication	1.98 ± 0.784
No. of medications	
0	10 (0.5)
1	574 (27.5)
2	1,009 (48.4)
3	433 (20.8)
4	59 (2.8)
Types of medications	
One agent	
ACE inhibitor/ARB (A)	299 (52.1)
Beta blocker (B)	62 (10.8)
Calcium channel blocker (C)	208 (36.2)
Thiazide (D)	5 (0.9)
Two agents	
A + B	240 (23.8)
A + C	557 (55.2)
A + D	109 (10.8)
B + C	83 (8.2)
B + D	8 (0.8)
C + D	12 (1.2)
Three agents	
A + B + C	192 (44.3)
A + B + D	41 (9.5)
A + C + D	195 (45.0)
B + C + D	5 (1.2)

Values are presented as number (%) or mean ± standard deviation.
HOWOLD-BP = HOW to Optimize eLDerly systolic BP, ACE = angiotensin-converting-enzyme, ARB = angiotensin receptor blocker.

was similar to frail to pre-frail patients. The composite incidence of syncope, acute kidney injury, electrolyte imbalance, falls, and hypotension was higher than the pre-frail to frail group than the robust group (5.7% vs. 3.65%, $P < 0.001$). Pre-frail to frail patients tended to have dependent IADL, slower gait speed, lower grip strength, lower quality of life score, and cognitive function (**Table 3**).

Table 3. Baseline characteristics according to frailty status from the HOWOLD-BP study

Characteristics	Robust (n = 1,498)	Prefrail/frail (n = 585)	*P* value
Age, yr	72.7 ± 5.36	74.6 ± 5.98	< 0.001
Male	811 (54.1)	190 (32.5)	< 0.001
Body mass index, m/kg^2	25.4 ± 2.99	25.4 ± 3.59	0.867
Body mass index (category)			0.171
Underweight (BMI ≤ 18.5 kg/m^2)	8 (0.5)	16 (2.7)	
Normal (18.5 kg/m^2 < BMI < 23 kg/m^2)	365 (24.4)	147 (25.1)	
Overweight (23 kg/m^2 ≤ BMI < 25 kg/m^2)	319 (21.3)	111 (19.0)	
Obesity (25 kg/m^2 ≤ BMI)	806 (53.8)	311 (53.2)	
Systolic blood pressure, mmHg	136.9 ± 14.93	137.8 ± 15.37	0.269
Diastolic blood pressure, mmHg	75.3 ± 9.38	74.7 ± 10.43	0.198
Control of HTN (SBP < 140 & DBP < 90)	917 (61.2)	341 (58.3)	0.220
Supine SBP, mmHg	137.4 ± 18.81	138.1 ± 16.01	0.402
Supine DBP, mmHg	76.1 ± 10.42	74.8 ± 10.86	0.010
Standing 1 min SBP, mmHg	137.9 ± 17.95	138.6 ± 19.09	0.367
Standing 1 min DBP, mmHg	78.7 ± 10.02	78.7 ± 10.02	0.096
Standing 3 min SBP, mmHg	138.7 ± 17.35	140.6 ± 17.34	0.024

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https://doi.org/10.3346/jkms.2024.39.e84

Table 3. (Continued) Baseline characteristics according to frailty status from the HOWOLD-BP study

Characteristics	Robust (n = 1,498)	Prefrail/frail (n = 585)	*P* value
Standing 3 min DBP, mmHg	78.8 ± 9.99	78.0 ± 11.11	0.147
Pulse (/min)	69.2 ± 13.99	70.5 ± 12.10	0.043
WBC,[a] $\times 10^3/\mu L$	6.4 ± 1.62	6.5 ± 1.889	0.358
Hemoglobin,[b] g/dL	13.7 ± 1.41	13.0 ± 1.46	< 0.001
Platelet,[c] $\times 10^3/\mu L$	215.9 ± 53.78	221.2 ± 58.53	0.056
Na[d]	141.0 ± 2.35	140.7 ± 2.46	0.012
K[d]	4.4 ± 0.38	4.5 ± 0.44	0.003
Creatinine,[e] mg/dL	0.88 ± 0.276	0.87 ± 0.308	0.562
BUN[f]	17.7 ± 5.87	18.6 ± 9.5	0.036
eGFR[e]	82.4 ± 15.58	78.9 ± 17.87	< 0.001
Past medical history			
Diabetes	384 (25.6)	219 (37.4)	< 0.001
Dyslipidemia	1,012 (67.6)	373 (63.8)	0.099
Stroke	62 (4.1)	64 (10.9)	< 0.001
Myocardial infarction	112 (7.5)	52 (8.9)	0.282
Admission	889 (59.3)	424 (72.5)	< 0.001
Surgery	729 (48.7)	310 (53.0)	0.076
Coronary revascularization	287 (19.2)	123 (21.0)	0.336
Cigarette smoking status			< 0.001
Non-smoker	875 (58.4)	460 (78.6)	
Past smoker	512 (34.2)	100 (17.1)	
Current smoker	111 (7.4)	25 (4.3)	
Alcohol drinking (time/wk)			< 0.001
Never	977 (65.2)	479 (81.9)	
1	265 (17.7)	72 (12.3)	
2–3	172 (11.5)	21 (3.6)	
4+	84 (5.6)	13 (2.2)	
Physical activity			0.001
None	95 (6.3)	155 (22.5)	
Active lifestyle with no exercise	325 (21.7)	130 (22.2)	
Irregular exercise	205 (13.7)	78 (13.3)	
Regular exercise	873 (58.3)	222 (37.9)	
Dizziness (yes)	18 (1.2)	15 (2.6)	0.025
Orthostatic hypotension (yes)	17 (1.1)	7 (1.2)	0.906
Syncope/AKI/electrolyte imbalance/falls/ hypotension (yes)	59 (3.9)	44 (7.5)	< 0.001
Dependent IADL	18 (1.2)	44 (7.5)	< 0.001
Gait speed (m/sec)[g]	1.05 ± 0.246	0.88 ± 0.280	< 0.001
Slow gait speed (≤ 0.8 m/sec)[g]	295 (19.8)	282 (48.2)	< 0.001
Grip strength[g]	27.2 ± 8.54	22.6 ± 7.98	< 0.001
Low grip strength[g]	372 (24.9)	237 (40.5)	< 0.001
Eq-5D-5L[e]	0.959 ± 0.0643	0.884 ± 0.1172	< 0.001
MoCA-K[h]	25.3 ± 3.65	21.9 ± 5.70	< 0.001
Cognitive decline (MoCA-K < 23)	256 (17.2)	265 (45.5)	< 0.001

Values are presented as number (%) or mean ± standard deviation.
HOWOLD-BP = HOW to Optimize eLDerly systolic BP, BMI = body mass index, HTN = hypertension, SBP = systolic blood pressure, DBP = diastolic blood pressure, WBC = white blood cell, BUN = blood urea nitrogen, eGFR = estimated glomerular filtration rate, AKI = acute kidney injury, IADL = instrumental activities of daily living.
[a]11 patients were missing, [b]9 patients were missing, [c]12 patients were missing, [d]22 patients were missing, [e]3 patients were missing, [f]4 patients were missing, [g]7 patients were missing, [h]10 patients were missing.

Frail to pre-frail older hypertensive patients used more antihypertensive medications than robust older hypertensive patients (1.95 vs. 2.06, $P = 0.003$). Most pre-frail to frail patients used two medications (48.9%) or three medications (23.4%) to control hypertension, whereas robust patients used two medications (48.2%) or one medication (29.4%). For three-drug combinations, frail to pre-frail patients preferred beta blockers, while robust patients preferred diuretics after ACE inhibitor/ARB and CCB combination (**Table 4**).

https://doi.org/10.3346/jkms.2024.39.e84

Table 4. The hypertension medication history according to frailty status from the HOWOLD-BP study

Medication	Robust (n = 1,498)	Prefrail/frail (n = 585)	*P* value
Mean ± SD	1.95 ± 0.773	2.06 ± 0.81	0.003
No. of medications			0.003
0	4 (0.3)	6 (1.0)	
1	440 (29.4)	134 (22.9)	
2	722 (48.2)	286 (48.9)	
3	295 (19.7)	137 (23.4)	
4	37 (2.5)	22 (3.8)	
Types of medications			
One agent			0.572
ACE inhibitor/ARB (A)	236 (53.6)	63 (47.0)	
Beta blocker (B)	45 (10.2)	17 (12.7)	
Calcium channel blocker (C)	155 (35.2)	53 (39.6)	
Thiazide (D)	4 (0.9)	1 (0.7)	
Two agents			0.025
A + B	151 (20.9)	89 (31.1)	
A + C	409 (56.6)	147 (51.4)	
A + D	84 (11.6)	25 (8.7)	
B + C	62 (8.6)	21 (7.3)	
B + D	6 (0.8)	2 (0.7)	
C + D	10 (1.4)	2 (0.7)	
Three agents			< 0.0001
A + B + C	107 (36.3)	85 (62.0)	
A + B + D	29 (9.8)	12 (8.8)	
A + C + D	155 (52.5)	39 (28.5)	
B + C + D	4 (1.4)	1 (0.7)	

HOWOLD-BP = HOW to Optimize eLDerly systolic BP, SD = standard deviation, ACE = angiotensin-converting-enzyme, ARB = angiotensin receptor blocker.

DISCUSSION

The results of the HOWOLD-BP study offer a comprehensive insight into the clinical characteristics of older hypertensive patients in Korea, focusing on demographic, laboratory, clinical, lifestyle, frailty, functional (physical, cognitive) aspects, as well as adverse events related to antihypertensive medication. In this study, 60.4% (n = 1,260) of participants had controlled blood pressure, which means systolic BP of less than 140 mmHg and diastolic BP of less than 90 mmHg. Although the participants of this study did not represent the general older population because they were recruited at national university hospitals and visited for hypertension, the control rate of this study was relatively higher than the general adult population according to the 2023 fact sheet released by the Korean Society of Hypertension, which reported a 47.4% control rate among hypertensive patients in Korea.[5] However, older hypertensive patients often contend with other chronic diseases, including dyslipidemia (66.5%), diabetes (28.9%), a history of coronary revascularization (19.7%), myocardial infarction (7.9%), and stroke (6.0%).

Prevalence of obesity (body mass index ≥ 25 kg/m^2) in the HOWOLD-BP study was 53.6%, which aligns closely with the results of the study conducted in China (54.2% among 65–74 and 47.4% among patients aged ≥ 75 years).[20] Unhealthy lifestyles choices, such as smoking and heavy drinking, were relatively rare (current smoker: 6.5%, alcohol consumption more than twice per week: 14.0%). Nevertheless, only about half of the patients engaged in regular physical activity (52.5%). Given that lifestyle modifications, particularly weight loss for obese patients, are well-tolerated and effective in reducing cardiovascular risk, it is crucial to emphasize lifestyle changes, including weight management and exercise, for older patients with hypertension in Korea.[21,22]

https://doi.org/10.3346/jkms.2024.39.e84

The study reveals a significant association between frailty status and factors, such as older age, female gender, higher pulse pressure, lower hemoglobin, and a higher prevalence of comorbidities like diabetes and stroke, and a history of hospitalization. Predictively, older pre-frail to frail hypertensive patients displayed a higher likelihood of dependence on IADL, weaker grip strength, slower walking speed, lower quality of life, and diminished cognitive function compared to the robust population. The composite event (syncope, acute kidney injury, electrolyte imbalance, falls, hypotension), which is considered a possible adverse event during hypertension treatment in frail elderly, indeed occurred more in the pre-frail to frail group (7.5%) compared to the robust group (3.9%, $P < 0.001$). Therefore, it is essential to comprehensively evaluate older hypertensive patients and to monitor disease-related or drug-related adverse events more frequently during regular check-ups for pre-frail to frail older patients with hypertension. The result of the gender difference in frailty status among older hypertensive patients is consistent with previous research on the general population that females had higher frailty status than males at all ages, and male mortality rates exceeded female mortality rates.[23] The findings from this study have contributed to a better understanding of the implication of frailty on hypertension management in older adults.

While the study offers several valuable insights, it has some inevitable limitations. First, the study's cross-sectional nature limits the ability to infer causality between frailty and clinical characteristics. For example, pre-frail to frail older patients engaged in regular physical exercise less frequently, but there were fewer cases of being a current smoker or drinking more than twice a week. It is difficult to determine whether the lifestyle pattern is a cause or a result of frailty. Second, beta-blockers were chosen as the preferred third medication over diuretics for the pre-frail to frail patients, but it is unclear whether this is due to the comorbidity pattern or whether frailty status influences the choice of medication and the number of medications. Even though heart failure with decreased ejection fraction was excluded, the prevalence of atrial fibrillation was more frequent in the prefrail to frail group than in the robust group (8.2% [n = 68] vs. 4.6% [n = 47], $P = 0.001$, missing 9.5% [n = 215]) according to the initially collected electrocardiogram. Future research should employ longitudinal designs to explore the causal relationships and the long-term impacts of different treatment approaches to explore causal relationships and the long-term impacts of different treatment approaches on frail, older hypertensive patients. Additionally, further studies should investigate the underlying mechanisms linking frailty, hypertension, and adverse health outcomes, which could inform the development of targeted interventions to effectively manage hypertension in older adults with varying frailty statuses.

In conclusion, the HOWOLD-BP study verifies the characteristics of older hypertensive patients in Korea and identifies the intricate relationship between frailty and clinical characteristics among older hypertensive patients. These findings underscore the importance of considering frailty status in managing hypertension in older adults, advocating for personalized treatment approaches and lifestyle modifications. When determining the optimal BP target (< 130 mmHg vs. < 140 mmHg of SBP), which is the research goal of the HOWOLD-BP study, considering frailty is essential. Future research aimed at unraveling the complexities of hypertension management in the aging population will be needed, ultimately contributing to improved management and monitoring strategies, clinical outcomes, and quality of life for older hypertensive patients.

https://doi.org/10.3346/jkms.2024.39.e84

REFERENCES

1. Kontis V, Bennett JE, Mathers CD, Li G, Foreman K, Ezzati M. Future life expectancy in 35 industrialised countries: projections with a Bayesian model ensemble. *Lancet* 2017;389(10076):1323-35. PUBMED | CROSSREF
2. Baek JY, Lee E, Jung HW, Jang IY. Geriatrics fact sheet in Korea 2021. *Ann Geriatr Med Res* 2021;25(2):65-71. PUBMED | CROSSREF
3. Feigin VL, Roth GA, Naghavi M, Parmar P, Krishnamurthi R, Chugh S, et al. Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol* 2016;15(9):913-24. PUBMED | CROSSREF
4. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet* 2006;367(9524):1747-57. PUBMED | CROSSREF
5. Kim HC, Lee H, Lee HH, Lee G, Kim E, Song M, et al. Korea hypertension fact sheet 2022: analysis of nationwide population-based data with a special focus on hypertension in the elderly. *Clin Hypertens* 2023;29(1):22. PUBMED | CROSSREF
6. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M146-56. PUBMED | CROSSREF
7. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005;173(5):489-95. PUBMED | CROSSREF
8. Fedarko NS. The biology of aging and frailty. *Clin Geriatr Med* 2011;27(1):27-37. PUBMED | CROSSREF
9. Williamson JD, Supiano MA, Applegate WB, Berlowitz DR, Campbell RC, Chertow GM, et al. Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults aged ≥75 years: a randomized clinical trial. *JAMA* 2016;315(24):2673-82. PUBMED | CROSSREF
10. Zhang W, Zhang S, Deng Y, Wu S, Ren J, Sun G, et al. Trial of intensive blood-pressure control in older patients with hypertension. *N Engl J Med* 2021;385(14):1268-79. PUBMED | CROSSREF
11. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2018;138(17):e484-594. PUBMED
12. Lee HY, Shin J, Kim GH, Park S, Ihm SH, Kim HC, et al. 2018 Korean Society of Hypertension Guidelines for the management of hypertension: part II-diagnosis and treatment of hypertension. *Clin Hypertens* 2019;25(1):20. PUBMED | CROSSREF
13. Mancia G, Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A, et al. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). *J Hypertens* 2023;41(12):1874-2071. PUBMED | CROSSREF
14. Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. *Md State Med J* 1965;14:61-5. PUBMED
15. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969;9(3):179-86. PUBMED | CROSSREF
16. Jung HW, Yoo HJ, Park SY, Kim SW, Choi JY, Yoon SJ, et al. The Korean version of the FRAIL scale: clinical feasibility and validity of assessing the frailty status of Korean elderly. *Korean J Intern Med* 2016;31(3):594-600. PUBMED | CROSSREF
17. Lee JY, Cho SJ, Na DL, Kim SK, Youn JH, Kwon M, et al. Brief screening for mild cognitive impairment in elderly outpatient clinic: validation of the Korean version of the Montreal Cognitive Assessment. *J Geriatr Psychiatry Neurol* 2008;21(2):104-10. PUBMED | CROSSREF
18. Kim MH, Cho YS, Uhm WS, Kim S, Bae SC. Cross-cultural adaptation and validation of the Korean version of the EQ-5D in patients with rheumatic diseases. *Qual Life Res* 2005;14(5):1401-6. PUBMED | CROSSREF
19. Lee DH, Lee JH, Kim SY, Lee HY, Choi JY, Hong Y, et al. Optimal blood pressure target in the elderly: rationale and design of the HOW to Optimize eLDerly systolic Blood Pressure (HOWOLD-BP) trial. *Korean J Intern Med* 2022;37(5):1070-81. PUBMED | CROSSREF
20. Zhang Y, Zhang WQ, Tang WW, Zhang WY, Liu JX, Xu RH, et al. The prevalence of obesity-related hypertension among middle-aged and older adults in China. *Front Public Health* 2022;10:865870. PUBMED | CROSSREF
21. Whelton PK, Appel LJ, Espeland MA, Applegate WB, Ettinger WH Jr, Kostis JB, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). *JAMA* 1998;279(11):839-46. PUBMED | CROSSREF

22. Moore LL, Visioni AJ, Qureshi MM, Bradlee ML, Ellison RC, D'Agostino R. Weight loss in overweight adults and the long-term risk of hypertension: the Framingham study. *Arch Intern Med* 2005;165(11):1298-303. PUBMED | CROSSREF

23. Gordon EH, Peel NM, Samanta M, Theou O, Howlett SE, Hubbard RE. Sex differences in frailty: a systematic review and meta-analysis. *Exp Gerontol* 2017;89:30-40. PUBMED | CROSSREF