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Age-stratified association between isolated diastolic hypertension and carotid intima-media thickness: results from the Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC) Study

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Background: The clinical significance of isolated diastolic hypertension (IDH), particularly in relation to subclinical vascular changes, remains unclear and may vary across age groups. This study evaluated the age-stratified association between IDH and carotid intima-media thickness (IMT).

Methods: This cross-sectional study included 6,759 Korean adults aged 30–64 years from the Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC) cohort. Participants with a history of cardiovascular disease or use of antihypertensive medication were excluded. Blood pressure was classified according to the 2017 American College of Cardiology/American Heart Association guidelines into four categories: no hypertension, IDH, isolated systolic hypertension, and systolic diastolic hypertension. Carotid IMT was measured by B-mode ultrasonography, and vascular thickening was defined as IMT ≥0.857 mm (75th percentile). Multivariable logistic regression analyses were performed with age stratification.

Results: Among participants younger than 50 years, IDH was significantly associated with carotid IMT thickening after adjustment for age, sex, body mass index, educational attainment, physical activity, smoking, diabetes, total cholesterol, high-density lipoprotein cholesterol, lipid-lowering drug use, C-reactive protein, and study site (odds ratio [OR], 1.57; 95% confidence interval [CI], 1.10–2.26). No significant association was observed in participants aged 50 years or older (OR, 0.89; 95% CI, 0.72–1.09). Both isolated systolic hypertension and systolic diastolic hypertension were associated with carotid IMT thickening in all age groups.

Conclusions: IDH was associated with subclinical vascular changes in younger adults but not in older adults. These findings highlight the age-specific nature of the association of IDH with cardiovascular risk.

Keywords: Isolated diastolic hypertension; Carotid intima-media thickness; Atherosclerosis; Cardiovascular diseases

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INTRODUCTION

Elevated blood pressure (BP) is a well-established risk factor for cardiovascular disease (CVD) [1]. Although elevated systolic BP (SBP) has been consistently associated with adverse CVD outcomes, the prognostic relevance of diastolic BP (DBP) has been deemed less clear, especially when elevated in isolation. The 2017 American College of Cardiology/American Heart Association (ACC/AHA) hypertension guideline lowered the diagnostic threshold for hypertension to SBP ≥130 mmHg or DBP ≥80 mmHg, substantially increasing the prevalence of isolated diastolic hypertension (IDH), particularly among younger adults [2].

IDH, defined as elevation of DBP without elevation of SBP (e.g., DBP ≥80 mmHg with SBP <130 mmHg), occurs more frequently in early adulthood. However, its prognostic significance has been sometimes questioned [3–5]. While some large cohort studies have reported that IDH increases the risk of CVD, others have found no significant association [6,7]. This inconsistency may reflect the limitations of event-based analyses, in which events are rare at younger ages where IDH is most common. Furthermore, individuals with IDH eventually progress to isolated systolic hypertension (ISH) or systolic diastolic hypertension (SDH), making it difficult to isolate the effects of IDH [8]. In this regard, subclinical vascular markers may provide a more accurate assessment of the early vascular burden of IDH before overt disease develops [9].

The hemodynamic mechanisms of IDH vary by age. In younger individuals, IDH often reflects increased peripheral vascular resistance and heightened sympathetic activity, which may contribute to early vascular remodeling [8,10–12]. In older adults, arterial stiffening leads to elevated SBP and widened pulse pressure, reducing the prognostic value of DBP [10]. These age-dependent differences in mechanisms signal the need for an age-stratified reappraisal of the clinical implications of IDH.

Carotid intima-media thickness (IMT) is a sensitive marker for atherosclerotic cardiovascular risk in younger individuals, in whom IDH is clinically relevant. As a validated indicator of early subclinical atherosclerosis, carotid IMT independently predicts cardiovascular events while minimizing reverse causation bias [13]. Nevertheless, the association between IDH and carotid IMT remains uncertain, particularly across different age groups. This cross-sectional study aimed to investigate the age-stratified associations between IDH and carotid IMT in a middle-aged Korean population.

METHODS

Ethics statement

The study's protocol was approved by the institutional review boards of Severance Hospital, Yonsei University College of Medicine (No. 4-2013-0661) and Ajou University Hospital, Ajou University School of Medicine (No. AJIRB-BMR-SUR-13-272). Written informed consent was obtained from all participants. This study was conducted in compliance with the principles of the Declaration of Helsinki.

Study population

This study used baseline data from the Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC) cohort, which recruited community-dwelling, middle-aged adults aged 30–64 years between 2013 and 2018. The cohort was designed to identify novel risk factors and develop prevention strategies for cardiovascular and metabolic diseases. Data were collected at two study sites in Korea (Yonsei University College of Medicine, Seoul; Ajou University College of Medicine, Suwon).

Participants were eligible if they had lived at their current residence for at least 8 months, had no plans to relocate within the following 2 years, and could provide informed consent. Exclusion criteria were a history of major CVD (myocardial infarction, heart failure, or stroke), a cancer diagnosis or treatment within the preceding two years, participation in clinical trials, and pregnancy at enrollment. Additional details of the CMERC study design and methodology have been described previously [14,15].

Of the 8,097 initial participants (2,808 men and 5,289 women), we excluded 18 participants with missing BP or carotid IMT data, one participant with missing blood chemistry information, and 1,320 participants who were taking antihypertensive medications. These exclusions ensured accurate BP classification and minimized confounding due to treatment effects. The final study population included 6,759 participants aged 30–64 years (Fig. 1).

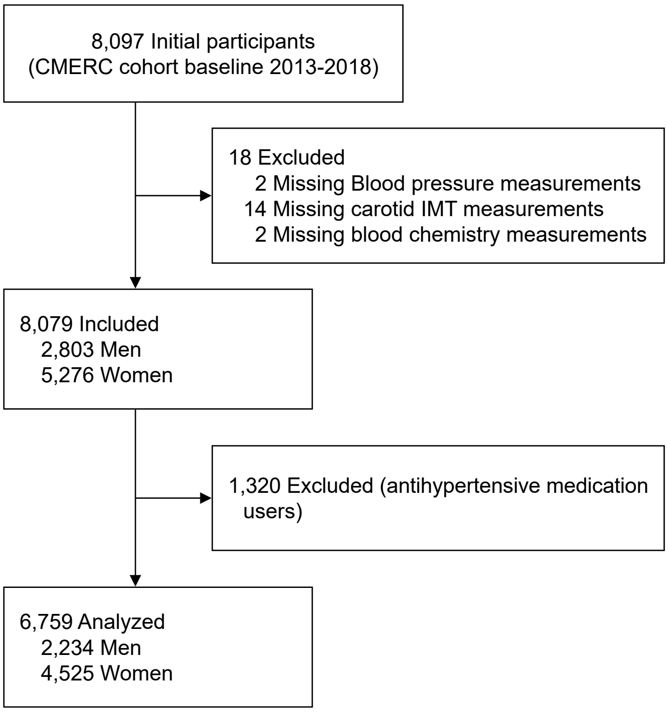

Fig. 1. Flowchart of the study population. CMERC, Cardiovascular and Metabolic Diseases Etiology Research Center; IMT, intima-media thickness.

BP measurements and classification of hypertension subtypes

BP was measured at both study sites following a standardized protocol using an automated oscillometric device (HEM-7080, Omron Health). Participants were asked to rest in a seated position for at least 5 minutes before measurement and to remain relaxed throughout the procedure. Trained research staff obtained three BP readings at 2-minute intervals, and the mean of the second and third measurements was used for analysis. Hypertension subtypes were defined according to the 2017 ACC/AHA guidelines: IDH as SBP <130 mmHg with DBP ≥80 mmHg; ISH as SBP ≥130 mmHg with DBP <80 mmHg; and SDH as SBP ≥130 mmHg with DBP ≥80 mmHg [2]. Based on these classifications, participants were assigned to one of four mutually exclusive categories: no hypertension (including both normal and elevated BP), IDH, ISH, or SDH.

Assessment of carotid IMT

Carotid ultrasonography was performed at Yonsei University College of Medicine using Accuvix XG (Samsung Medison) and at Ajou University College of Medicine using Logiq S8 (GE Healthcare). Trained sonographers conducted all examinations using a standardized protocol [15]. Quality control procedures were applied across sites to ensure consistency in participant positioning and measurement locations. Carotid IMT was assessed using high-resolution B-mode ultrasonography. Interreader and intrareader reliability analyses demonstrated acceptable reproducibility and good agreement among sonographers [14,16].

Carotid IMT was measured in a 1-cm segment of the distal common carotid artery proximal to the carotid bulb, with measurements taken at the R-wave on the electrocardiogram. Both mean and maximum carotid IMT values were obtained using dedicated image analysis software; however, the maximum IMT values from both the left and right carotid arteries were used for the primary analysis. IMT thickening was defined as a maximum carotid IMT greater than or equal to the 75th percentile of the study population, consistent with the American Society of Echocardiography criteria, which consider values above this threshold indicative of increased CVD risk. In this study, the 75th percentile cutoff for maximum IMT was 0.857 mm [17]. Age-adjusted carotid IMT values were further estimated using regression models with age as a covariate.

Covariates

At baseline, trained interviewers collected data on demographic characteristics, socioeconomic status, medical and medication history, and lifestyle factors using a structured questionnaire based on a standardized protocol. Educational attainment was classified as low for participants who had completed high school or less, and as high for those who had attended college or achieved higher education. Physical activity was assessed using the Korean short-form version of the International Physical Activity Questionnaire, which evaluated activity levels over the past 7 days and categorized participants into low, moderate, or high activity groups [18]. Smoking status was classified as never, past, or current. Body weight was measured to the nearest 0.1 kg using a digital scale (DB-150, CAS), and standing height was measured to the nearest 0.1 cm using a stadiometer (DS-102, Jenix). Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Fasting blood samples were obtained after at least eight hours of overnight fasting. Serum lipid profiles, including total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C), were measured using enzymatic methods. High-sensitivity C-reactive protein levels were assessed using a turbidimetric method on the ADVIA 1800 AutoAnalyzer (Siemens Medical Solutions). Diabetes and the use of lipid-lowering medications at baseline were self-reported and recorded as binary variables (yes or no).

Statistical analysis

Participant characteristics were summarized as mean and standard deviation for continuous variables and as frequency and percentage for categorical variables. For skewed continuous variables, median and interquartile range were reported. Baseline characteristics and carotid IMT values were compared across hypertension subtypes to evaluate group differences descriptively without formal hypothesis testing for statistical significance (Table 1).

Associations between hypertension subtypes and carotid IMT thickening were estimated using multivariable logistic regression models, with results expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Models were adjusted for age, sex, educational attainment, physical activity, smoking, BMI, TC, HDL-C, high-sensitivity C-reactive protein, diabetes, lipid-lowering drug use, and study site. Age was categorized as <50 years and ≥50 years and further stratified in 10-year intervals, consistent with prior studies on age-related BP changes and the distribution of our study population (median age, 50 years) [7,19]. Age-stratified analyses were then performed to examine potential age-related associations between hypertension subtypes and carotid IMT thickening. Effect modification by age was tested using an interaction term in the regression models.

We performed additional sensitivity analyses to test the robustness of the results. First, participants taking antihypertensive medications (n=1,324) were included, and results were compared with those obtained after excluding these individuals. Second, associations between hypertension subtypes and carotid IMT were evaluated using mean IMT values, calculated as the average of left and right carotid artery measurements. Third, the main analyses were repeated using alternative IMT cutoffs, including the 80th and 90th percentiles, as well as age- and sex-specific thresholds [20,21].

All analyses were conducted using SAS ver. 9.4 (SAS Institute Inc) or R ver. 4.0.3 (R Foundation for Statistical Computing). A P-value of <0.05 was considered statistically significant.

RESULTS

Participants' characteristics

The final analytical sample included 6,759 participants (mean age, 50.5±8.9 years; 66.9% women) who were not receiving antihypertensive treatment. Of these, 961 (14.2%), 192 (2.8%), and 1,151 participants (17.0%) were classified as having IDH, ISH, and SDH, respectively. Participants with IDH were younger (49.9±8.5 years) than those with ISH (55.7±8.4 years) or SDH (51.9±8.3 years), and they had lower fasting glucose, TC, and BMI levels. HDL-C levels, however, were comparable across groups. Carotid IMT was lower in the IDH group (0.783±0.136 mm) compared with the ISH group (0.882±0.187 mm) and SDH group (0.839±0.155 mm). Similarly, the prevalence of increased IMT (≥0.857 mm) was lower in participants with IDH (24.6%) than in those with ISH (46.9%) and SDH (39.4%) (Table 1).

A total of 4,093 participants (60.6%) were aged ≥50 years. Compared with those <50 years, older participants had higher SBP and DBP, while BMI and HDL-C levels were similar between groups. Participants <50 years had significantly lower IMT (0.694±0.120 mm) compared with those ≥50 years (0.802±0.192 mm), and the prevalence of increased IMT was also lower in the younger group (10.0% vs. 34.8%) (Table S1).

The prevalence of IDH exceeded that of SDH in participants aged 30–39 years (13.6% vs. 12.3%) and 40–49 years (15.3% vs. 13.8%). In contrast, SDH was more common than IDH in participants aged 50–59 years (15.0% vs. 11.3%) and 60–64 years (14.2% vs. 8.4%). A similar distribution was observed among participants with untreated hypertension. Notably, although IDH was predominantly observed in younger adults, many transitioned to SDH or ISH phenotypes over time as SBP increased with aging (Fig. 2) [7].

Association between BP subtypes and carotid IMT

The association between hypertension subtypes and in-

Table 1. Characteristics of participants according to hypertension subtypes (n=6,759)

Characteristic	No hypertension (n=4,455)	IDH (n=961)	ISH (n=192)	SDH (n=1,151)
Age (yr)	50.0±9.0	49.9±8.5	55.7±8.4	51.9±8.3
Sex				
Male	1,074 (24.1)	483 (50.3)	58 (30.2)	619 (53.8)
Female	3,381 (75.9)	478 (49.7)	134 (69.8)	532 (46.2)
Educational attainment				
Low	2,434 (54.6)	515 (53.5)	140 (72.9)	698 (60.6)
High	2,021 (45.4)	446 (46.5)	52 (27.1)	453 (39.4)
Moderate to vigorous physical activity				
Low	2,320 (52.1)	465 (48.4)	97 (50.5)	574 (49.9)
Middle	590 (13.2)	143 (14.9)	27 (14.1)	152 (13.2)
High	1,545 (34.7)	353 (36.7)	68 (35.4)	425 (36.9)
Smoking status				
Never	3,419 (76.7)	556 (57.9)	143 (74.5)	632 (54.9)
Former	547 (12.3)	217 (22.6)	27 (14.1)	307 (26.7)
Current	489 (11.0)	188 (19.6)	22 (11.5)	212 (18.4)
Body mass index (kg/m^2)	23.3±2.8	24.6±3.1	24.7±3.2	25.2±3.1
Systolic blood pressure (mmHg)	110.1±8.9	122.7±4.6	135.4±6.0	141.1±10.5
Diastolic blood pressure (mmHg)	69.9±5.8	83.8±3.4	75.4±3.8	90.3±7.6
Fasting glucose (mg/dL)	91.9±16.9	95.4±20.4	101.0±24.0	99.2±24.1
Total cholesterol (mg/dL)	195±34.2	199.2±34.0	204±37.3	203.7±33.9
HDL-C (mg/dL)	57.8±14.1	54.2±14.1	54.9±14.0	53.9±14.0
hs-CRP (mg/L)	0.5 (0.3–1.0)	0.6 (0.4–1.4)	0.6 (0.4–1.1)	0.7 (0.4–1.4)
Diabetes				
No	4,291 (96.3)	924 (96.1)	169 (88.0)	1,099 (95.5)
Yes	164 (3.7)	37 (3.9)	23 (12.0)	52 (4.5)
Use of lipid-lowering drugs				
No	4,146 (93.1)	889 (92.5)	178 (92.7)	1,075 (93.4)
Yes	309 (6.9)	72 (7.5)	14 (7.3)	76 (6.6)
Carotid IMT (mm)	0.765±0.139	0.783±0.136	0.882±0.187	0.839±0.155
Age-adjusted carotid IMT (mm)	0.768±0.002	0.787±0.004	0.844±0.009	0.829±0.004
IMT thickening (≥0.857 mm)[a]	913 (20.5)	236 (24.6)	90 (46.9)	453 (39.4)

Values are presented as mean±standard deviation, number (%), or median (interquartile range). Percentages may not total 100 due to rounding.
HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; IDH, isolated diastolic hypertension; IMT, intima-media thickness; ISH, isolated systolic hypertension; SDH, systolic diastolic hypertension.
[a]The 75th percentile cutoff.

creased carotid IMT varied significantly by age. In the multivariable-adjusted model, IDH was significantly associated with increased carotid IMT among participants <50 years (OR, 1.57; 95% CI, 1.10–2.26), whereas no significant association was observed among those ≥50 years (OR, 0.89; 95% CI, 0.72–1.09). There was a heterogeneity between age <50 versus ≥50 years in the association of IDH with increased carotid IMT (P for interaction=0.003) (Table 2).

Further analyses stratified by 10-year age intervals revealed consistent age-dependent patterns. In the multivariable-adjusted model, IDH was associated with higher carotid IMT in both the 30–39 and 40–49 age groups; however, the association reached statistical significance only in the 40–49 age group (OR, 1.52; 95% CI, 1.00–2.29). In contrast, IDH was inversely associated with carotid IMT in the 50–59 and 60–64 age groups, although these associations were not statistically significant. ISH demonstrated the strongest association with increased carotid IMT across most age

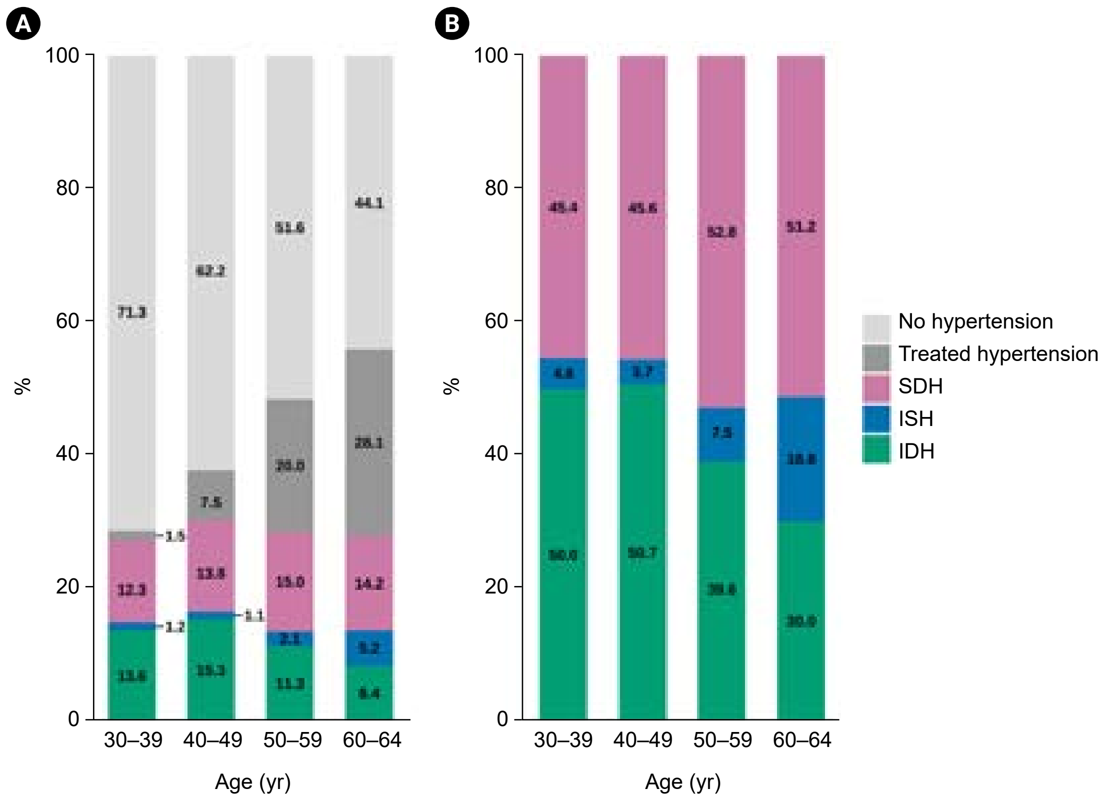

Fig. 2. Age-specific proportions of hypertension subtypes by age stratum. (A) Overall participants. (B) Untreated hypertension. Data are presented as the percentage of participants exposed to each hypertension subtype within age groups (30–39, 40–49, 50–59, and 60–64 years). Hypertension subtypes were defined as follows: no hypertension, systolic blood pressure (SBP) <130 mmHg and diastolic blood pressure (DBP) <80 mmHg without antihypertensive treatment; treated hypertension, use of antihypertensive medication regardless of blood pressure level; isolated diastolic hypertension (IDH), SBP <130 mmHg and DBP ≥80 mmHg; isolated systolic hypertension (ISH), SBP ≥130 mmHg and DBP <80 mmHg; and systolic diastolic hypertension (SDH), SBP ≥130 mmHg and DBP ≥80 mmHg.

groups, except for the 40–49 and 60–64 groups (Table S2).

Sensitivity analyses

Multiple sensitivity analyses were performed to confirm the robustness of the findings. First, when participants taking antihypertensive medications (n=1,324) were included, the positive association between IDH and increased carotid IMT among those <50 years remained statistically significant (Table S3). Second, when mean IMT values (calculated as the average of left and right carotid measurements) were used instead of maximum values, a similar association was observed in younger adults, although statistical significance was lost after multivariable adjustment (Table S4). Third, analyses using alternative IMT cutoffs showed that the 80th percentile (0.882 mm) produced results consistent with the main findings, whereas the 90th percentile (0.972 mm) attenuated the association in participants <50 years (Table S5). Finally, sex- and age-specific analyses demonstrated similar trends, with IDH associated with higher carotid IMT in both men and women <50 years, although these associations were not statistically significant. In contrast, among participants ≥50 years, the direction of association varied by sex (Table S6).

DISCUSSION

In this population-based cohort of Korean adults aged 30–64 years, IDH was associated with increased carotid IMT among individuals <50 years, but not among those ≥50 years. This age-dependent association remained consistent across multiple sensitivity analyses, reinforcing the conclu-

Table 2. Age-stratified analyses of the association between hypertension subtype and carotid IMT (≥0.857 mm vs. <0.857 mm)

Age group	IMT thickening (≥0.857 mm)[a]	Crude model		Age-adjusted model		Multivariable-adjusted model[b),c)]	
		OR	95% CI	OR	95% CI	OR	95% CI
Total (n=6,759)							
No hypertension (n=4,455)	913 (20.5)	1.00	Reference	1.00	Reference	1.00	Reference
IDH (n=961)	236 (24.6)	1.26	1.07–1.49	1.34	1.13–1.59	1.03	0.86–1.24
ISH (n=192)	90 (46.9)	3.42	2.56–4.59	2.21	1.62–3.02	1.89	1.37–2.60
SDH (n=1,151)	453 (39.4)	2.52	2.19–2.89	2.36	2.04–2.74	1.77	1.51–2.07
<50 yr (n=2,666)							
No hypertension (n=1,851)	121 (6.5)	1.00	Reference	1.00	Reference	1.00	Reference
IDH (n=411)	62 (15.1)	2.54	1.83–3.52	2.41	1.73–3.36	1.57	1.10–2.26
ISH (n=33)	6 (18.2)	3.18	1.29–7.84	3.72	1.47–9.41	2.35	0.87–6.30
SDH (n=371)	78 (21.0)	3.81	2.79–5.19	3.56	2.60–4.89	2.10	1.48–2.98
≥50 yr (n=4,093)							
No hypertension (n=2,604)	792 (30.4)	1.00	Reference	1.00	Reference	1.00	Reference
IDH (n=550)	174 (31.6)	1.06	0.87–1.29	1.10	0.90–1.35	0.89	0.72–1.09
ISH (n=159)	84 (52.8)	2.56	1.86–3.54	2.06	1.48–2.86	1.91	1.35–2.68
SDH (n=780)	375 (48.1)	2.12	1.80–2.49	2.12	1.79–2.50	1.70	1.43–2.03

The OR was calculated from multivariable logistic regression models in age stratification, using the maximum of both right and left IMT maximum measurements.
CI, confidence interval; IDH, isolated diastolic hypertension; IMT, intima-media thickness; ISH, isolated systolic hypertension; OR, odds ratio; SDH, systolic diastolic hypertension.
[a)]The 75th percentile cutoff. [b)]Adjusted for age, sex, educational attainment, physical activity, smoking status, body mass index, total cholesterol, high-density lipoprotein cholesterol, high-sensitivity C-reactive protein, diabetes, lipid-lowering drug use, and study site. [c)]P for interaction between each hypertension subtype and age group in the multivariable-adjusted model: IDH, 0.003; ISH, 0.720; SDH, 0.153.

sion that the cardiovascular implications of IDH vary substantially by age. Our findings suggest that IDH is associated with higher subclinical atherosclerotic burden in younger adults, where IDH is more prevalent and potentially carries greater long-term cardiovascular significance.

Previous studies have reported inconsistent results regarding the association between IDH and cardiovascular outcomes. Analyses from the National Health and Nutrition Examination Survey, UK Biobank, and the Atherosclerosis Risk in Communities (ARIC) reported no strong associations between IDH and cardiovascular outcomes [3,5]. However, most of these prior investigations lacked sufficient sample sizes for adequate statistical power and included heterogeneous populations composed of many older adults and individuals on antihypertensive therapy. Such heterogeneity may have obscured age-specific effects in younger populations where IDH is more common. With UK Biobank, inconsistent findings emerged depending on analytical methods [5,10]. In contrast, the IDACO (International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcomes) study, which used 24-hour ambulatory BP monitoring, demonstrated that CVD risk associated with IDH was particularly pronounced among younger adults, underscoring that age-specific vulnerability may be more critical than the method of BP measurement [4].

Evidence from large-scale population studies with sufficient statistical power supports the association of IDH with CVD. A Korean nationwide health screening database of more than 6.4 million young adults aged 20–39 years demonstrated a clear increase in CVD risk associated with IDH at both stage 1 and 2 thresholds of the 2017 ACC/AHA guidelines [8]. Similarly, a Japanese study using a health claims database from the Japan Medical Data Center found that both stage 1 and 2 IDH were independently associated with cardiovascular risk regardless of age or sex, even after comprehensive covariate adjustment [6]. The prospective Kailuan study, which included 87,346 antihypertensive-naïve participants aged 18–98 years, also confirmed the association between IDH and increased CVD events [22]. Another important aspect of these studies is the inclusion of only participants untreated at baseline, as the phenotypes of IDH, ISH, and SDH are only relevant to diagnostic or treatment-initiating thresholds but not treatment goals or on-treatment BP. Together, these studies employing rigorous BP measurement protocols strengthen the clinical evidence for IDH, particularly its diagnostic and prognostic relevance in younger adults.

The inconsistency across studies also stems from the limitations of event-based analyses, particularly as events are rare among younger adults, for whom IDH is clinically most relevant. Furthermore, progression of IDH to other hypertension phenotypes may obscure its distinct risk profile [8]. Given its age-dependent prevalence and hemodynamic mechanisms, subclinical vascular assessment is useful for studying the vascular burden of IDH before phenotypic transition occurs, particularly in younger adults. Age-related hemodynamic differences further support the rationale for age-stratified evaluations using subclinical markers to better define the clinical significance of IDH and identify individuals at elevated risk for future cardiovascular complications [23–25].

Several studies have demonstrated associations between IDH and subclinical markers of atherosclerosis. A large Chinese multiethnic study of 14,618 adults [26] and a Korean study of 4,666 untreated individuals [27] reported that IDH was associated with increased carotid IMT and coronary plaque presence. By contrast, the Multi-Ethnic Study of Atherosclerosis found no significant association between IDH and coronary artery calcification (CAC) [28,29]. This discrepancy likely reflects the low sensitivity of CAC as a marker of early vascular burden in younger adults, who most likely have zero CAC scores. These limitations are further accentuated in populations with low overall atherosclerotic risk, like in high-income East Asian populations. Consequently, carotid IMT and coronary plaque may provide more sensitive measures for identifying IDH-related subclinical atherosclerosis, particularly in younger adults, for whom early detection is most clinically relevant.

Our results are consistent with prior analyses demonstrating age-specific associations between IDH and subclinical atherosclerosis [26,27,30]. Age-stratified findings show that IDH is associated with subclinical atherosclerosis in younger adults, but the association is weaker or absent in older individuals, likely due to arterial stiffening, BP measurement error, or misclassification of IDH [30]. Many individuals with IDH eventually develop systolic hypertension, and the condition is more common in younger populations, who also experience fewer cardiovascular events overall [7,11,31]. Elevated DBP reflects increased peripheral vascular resistance and vascular stress [19]. With aging, however, SBP tends to rise while DBP falls, reducing the prognostic value of DBP in older adults [6,32–34]. As many individuals with IDH progress to SDH over time, their CVD risk increases [35]. These observations highlight the clinical relevance of identifying and managing IDH in younger adults. Although absolute cardiovascular risk remains relatively low in this group, early intervention may help reduce the long-term burden of CVD, underscoring the importance of targeted prevention [36].

Strengths and limitations

This study has several strengths. The inclusion of a healthy population without clinical CVD allowed for accurate evaluation of IDH, which has often been regarded as conferring modest cardiovascular risk. Standardized protocols and rigorous quality control in the CMERC cohort minimized measurement bias and ensured reliable carotid IMT assessment across sites. Additionally, extensive adjustment for multiple confounders enhanced the robustness of our findings. As relatively few studies have investigated age-specific associations between IDH and carotid IMT in Asian populations, this study provides new insights into an important but understudied group. Nonetheless, several limitations should be noted. First, BP was measured during a single office visit rather than by 24-hour ambulatory BP monitoring, which may have led to misclassification of hypertension subtypes, particularly among younger adults more prone to white-coat or masked hypertension [4]. Second, despite comprehensive covariate adjustment, residual confounding cannot be excluded. Certain medications, such as hormone therapy and corticosteroids among older women, were not fully accounted for [37]. Other potentially important factors, including inflammatory biomarkers, dietary sodium intake, and psychosocial stress, were not incorporated into this analysis [38,39]. Finally, the cross-sectional design precludes causal inference regarding the relationship between

IDH and carotid IMT.

Conclusions

These findings underscore the clinical importance of IDH in younger adults and support a proactive approach to its identification and management. Early detection and intervention may help prevent long-term vascular damage and reduce future CVD risk. Further research is warranted to improve age-specific risk stratification and to develop preventive strategies for younger adults with IDH.

ARTICLE INFORMATION

Author contributions

Conceptualization: HL, HCK; Data curation: HC, SJJ, JSS, HL, HCK; Formal analysis: MC, JH, HC; Funding acquisition: HL, HCK; Investigation: JH; Methodology: HL, HCK; Validation: MC, HC, HL; Writing–original draft: MC, JH; Writing–review & editing: all authors. All authors read and approved the final manuscript.

Conflicts of interest

Hokyou Lee reported receiving grants from the National Research Foundation of Korea during the conduct of the study and grants from the Korea Medical Institute outside the submitted work. The authors have no other conflicts of interest to declare.

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Additional information

This study includes materials from Jiyen Han's master's thesis, submitted to Yonsei University in June 2022.

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Supplementary materials

Table S1. Characteristics of participants according to age group (n=6,759)
Table S2. Age-stratified analyses of the association between hypertension subtype and carotid IMT by 10-year age stratification
Table S3. Age-stratified analyses of the association between hypertension subtype and carotid IMT including treated participants
Table S4. Age-stratified analyses of the association between hypertension subtype and carotid IMT applying a different measurement (mean) of IMT
Table S5. Age-stratified analyses of the association between hypertension subtype and carotid IMT using different cut-offs of IMT
Table S6. Sex- and age- specific analyses of the association between hypertension subtype and carotid IMT
Supplementary materials are available from https://doi.org/10.36011/cpp.2025.7.e18.

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