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ORIGINAL ARTICLE

Combined superposition effect of hypertension and dyslipidemia on left ventricular hypertrophy

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Abstract

Background: Hypertension and dyslipidemia are considered reversible risk factors for cardiovascular disease. The purpose of this study was to explore the impact of traditional and nontraditional blood lipid profiles on the risk of left ventricular hypertrophy (LVH) and to explore the superposition effect of dyslipidemia combined with hypertension.

Methods: Data on 9134 participants (53.5 ± 10.3 years old) from the Northeast China Rural Cardiovascular Health Study (NCRCHS) were statistically analyzed. The blood lipid profile was measured by total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total glyceride (TG), and calculated nontraditional blood lipid indices including non-HDL-C, atherosclerosis index (AI), TC/HDL-C, and residual cholesterol (RC).

Results: After the adjustment of age and gender, the odds ratios (ORs) of LVH in patients with hypertension, high LDL-C, high non-HDL-C, high AI, and high TC/HDL-C were 3.97 (3.31–4.76), 1.27 (1.02–1.59), 1.21 (1.04–1.39), 1.33 (1.15–1.53), and 1.42 (1.22–1.65), respectively. After full adjustment of potential confounding factors, high AI and TC/HDL-C were associated with LVH rather than traditional blood lipid indices. The combination of hypertension and nontraditional dyslipidemia (defined by high AI and TC/HDL-C) was associated with the highest risk of LVH, especially in participants under 45 years of age. The risk was more significant in men, 5.09-fold and 6.24-fold, respectively, compared with 3.66-fold and 4.01-fold in women.

Conclusions: People with dyslipidemia defined by nontraditional blood lipid indices (high AI and high TC/HDL-C) and hypertension were more likely to develop LVH.

KEYWORDS
atherosclerosis, dyslipidemia, hypertension, left ventricular hypertrophy

1 | INTRODUCTION

Left ventricular hypertrophy (LVH) is not only a risk factor for cardiovascular disease[1,2] but also a major independent risk factor for stroke,[3] cognitive impairment,[4] and all-cause death.[5] The left ventricle is the main target of hypertensive organ injury. Cumulative evidence has shown that an increase in blood pressure promotes the occurrence and development of LVH.[6] Analyses have shown that 36%–41% of patients with hypertension have LVH.[7] For every 19 mmHg increment in systolic blood pressure, the incidence of LVH

increased by 49%.[8] Controlling blood pressure by changing lifestyle and using antihypertensive drugs cannot eliminate LVH, because hemodynamic variables such as hypertension usually contribute no more than 25% to LVH.[3] There are still some nonhemodynamic determinants, including age, obesity, hormones, genetic factors, hyperinsulinemia,[9] and chronic kidney disease,[10] that affect LVH. Dyslipidemia is one of the most important risk factors of cardiovascular disease, as well as other chronic degenerative diseases with long-term natural history such as hypertension. Blood pressure and blood lipids have complex lifestyles and genetic relationships with each other.

At present, there is no consensus on the correlation between dyslipidemia and left ventricular mass (LVM). Research in the child population has shown total triglycerides (TG) and hypertriglyceridemia are associated with left ventricular mass (LVM).[11] Adult studies have reported a direct correlation between total cholesterol (TC) and LVM, but only in men.[12] However, some studies have demonstrated high-density lipoprotein cholesterol (HDL-C) is negatively correlated with LVM in patients with untreated hypertension, but TC or low-density lipoprotein cholesterol (LDL-C) is not correlated with LVM.[13] Similarly, Giuseppe et al. have reported that HDL-C has a protective effect on LVH.[13] However, some studies failed to find a significant correlation between LVH and any other laboratory parameters such as blood lipids.[14,15] At present, there is only evidence supporting that an increased TG/HDL-C ratio (representing the level of insulin resistance) in people with obesity is related to the development of eccentric LVH.[16] Recent studies have found LVH to be more common in women than in men (43% versus 32%), suggesting that there may be gender differences in the incidence of LVH.[17] Therefore, it is necessary to explore the impacts of traditional and nontraditional dyslipidemia on LVH among the Chinese general population.

The inconsistent results obtained in previous studies may also be attributed to ethnic, regional, age, and gender differences. Considering the possible potential relationship between hypertension, dyslipidemia, and LVH, based on the Northeast China Rural Cardiovascular Health Study (NCRCHS), this study aimed to explore the correlation between LVH and traditional and nontraditional dyslipidemia in people from rural Northeast China. Moreover, we discussed the relative risk of LVH according to the coexistence of dyslipidemia and hypertension.

2 | METHODS

2.1 | Study design and participants

As a representative sample of the Chinese population in Liaoning Province, NCRCHS was a continuous, observational, and multistage rural community study to systematically assess the risk of cardiovascular-related diseases in the middle-aged and elderly. NCRCHS began in 2012–2013 and conducted a cross-sectional epidemiological survey. The research design and detailed scheme of NCRCHS had been described in detail elsewhere.[18] In the first stage, 3 counties (Dawa County, Zhangwu County, and Liaoyang County) were selected from the eastern, southern, and northern regions of Liaoning Province. In the second stage, one town (a total of 3 towns) was randomly selected from each county. In the third stage, 8–10 rural villages (26 rural villages in total) were randomly selected from each town. Participants with pregnancy, malignancies, and mental disorders were excluded from this study. In total, 11 956 permanent residents (35 years or older) in each village were invited to participate in this study. The response rate was 89.4%. Of these, 10 700 participants agreed and qualified to participate in our follow-up study, and baseline information on each subject was collected. Participants with incomplete physical examination, incomplete cardiac ultrasound data, and moderate or severe valvular heart disease (n = 1566) were excluded for our analysis. A total of 9134 participants based in rural communities were included for analysis in this study. This study protocol was approved by the ethics committee of China Medical University (Shenyang, China AF-SDP-7-1, 0-01), and all subjects obtained written informed consent.

2.2 | Sample size evaluation

This study used a multistage random sampling method. We used the following methods for reference to calculate the sample size required for analysis:

$$n = z^2_{1-a/2} \times p\,(1-p)/d^2$$

$z_{1-a/2} = 1.96 \approx 2$ at 5% type I error. p, representing the prevalence of LVH, was approximately 10%, and d, representing the absolute error or precision, was 10% of p in this cross-sectional study. As a result, n was 3600. The final sample size of our study for analysis was sufficient.

2.3 | Anthropometric measurements and biological parameter collection

Anthropometric and lifestyle factors (including age, gender, current smoking, current drinking, education level, regular exercise, and history of hypertension) were measured and recorded by trained researchers using standard technology. The quality assurance of data collection was controlled by the Central Steering Committee. All investigators were trained. The detailed methods and definition of lifestyle have been described previously.[18] Body mass index (BMI) followed the following formula: BMI = weight (kg)/square of body height (m^2). For the measurement of blood pressure, we used the standard scheme recommended by guidelines, which required avoiding stimulating drinks after resting for at least 5 minutes in a relaxed, seated state. We used an electronic sphygmomanometer (HEM-907; Omron, Tokyo, Japan) to measure clinical blood pressure 3 times every 2 minutes in a quiet room. The average of 3 blood pressure measurements was used as clinical blood pressure for analysis. Hypertension was

defined as blood pressure greater than or equal to 140/90 mmHg or self-reported history of antihypertensive medication.[19] After fasting for at least 12 hours, fasting blood samples of each participant were collected by experienced nurses at a relatively fixed time in the morning. Analyzed and collected blood biochemical information included fasting blood glucose (FBG), serum creatinine (Cr), serum uric acid (UA), TG, TC, LDL-C, HDL-C, and calculated estimated glomerular filtration rate (eGFR) using the formula of chronic kidney disease epidemiology Cooperation (CKD-EPI).[20] According to the American Society of Echocardiography (ASE) recommendation, the mean value of 5 consecutive cardiac cycles was used to calculate the M-mode echocardiography data.[21] Transthoracic echocardiographic examination was performed using a commercially available Doppler echocardiograph (Vivid, GE Healthcare, USA) with a 3.0 MHz transducer, including M-mode, 2-dimensional, spectral, and color Doppler. The echo did not have a clinical indication but was done at specific study visits. Echocardiographic analyses and readings were conducted by 3 doctors specialized in echocardiography, and there was a high degree of intra-observer and inter-observer reproducibility for interpretation of the echoes. The parasternal long-axis view was measured to record interventricular septal thickness dimension (IVSTd), left ventricular (LV) end-diastolic internal dimension (LVIDd), LV end-systolic internal dimension (LVIDs), and posterior wall thickness (PWTd). The left ventricular mass (LVM) was also calculated according to the American Society of Echocardiography (ASE) formula[22]: $LVM = 0.8 \times \{1.04 \times [(IVSd + LVIDd + PWTd)^3 - LVIDd^3] + 0.6\,g$ (the specific inner diameters are presented in Table 1). The LV end-diastolic volume (LVEDV) and LV end-systolic volume (LVESV) were estimated by Teichholz equations: $LVEDV\ (ml) = LVIDd^3 \times 7.0/(2.4 + LVIDd)$, $LVESV\ (ml) = LVIDs^3 \times 7.0/(2.4 + LVIDs)$. When there were abnormalities in cardiac structure and function, we used the biplane Simpson's rule for volume calculations from both the apical 4-chamber and 2-chamber views. LV ejection fraction (LVEF) was calculated as $[(LVEDV - LVESV)/LVEDV] \times 100\%$.

2.4 | Definitions

BMI ≥ 28 kg/m^2 was defined as obesity according to Chinese standards.[23] The traditional 4 indicators of dyslipidemia were defined as follows according to NCEPATPIII[24]: TC > 6.21 mmol/L, TG > 2.26 mmol/L, LDL-C > 4.16 mmol/L, and HDL-C > 1.03 mmol/L. On the basis of this, the nontraditional blood lipid comprehensive indices were calculated as follows: non-HDL-C = TC−(HDL-C),[25] TC/HDL-C = TC/(HDL-C),[26] atherosclerosis index (AI) = (TC−(HDL-C))/(HDL-C).[27] The residual cholesterol (RC) was calculated as follows: RC = TC−(HDL-C)−(LDL-C).[28] Among the 4 blood lipids comprehensive indices obtained by calculation, TC/HDL-C was grouped according to 3.5, and the other nontraditional blood lipids were divided into 2 groups according to the median. Sex-specific and indexation of LVM was used to diagnose echo-LVH according to criteria as follows: left ventricular mass index (LVMI) greater than 115 g/m^2 and greater than 95 g/m^2 for males and females when LVM was indexed to the body surface area.[22]

2.5 | Statistical analysis

Continuous variables were shown as mean ± standard deviation. The means of multiple samples were compared by one-way analysis of variance (ANOVA), the differences between groups were tested by multiple-comparison least significant difference (LSD) test, and the *p*-value was corrected by the Bonferroni method. The continuous variable of skew distribution was described by median and interquartile spacing. If the variance was uneven or the data distribution was not normal, Kruskal-Wallis *H* test and Mann-Whitney *U* test were also used to analyze the differences between groups. Categorical variables were expressed in absolute numbers and percentages in parentheses. Chi-square analysis or Fisher's exact test was used for statistical analysis. Multivariate logistic regression analysis was used and adjusted for race, age, current smoking or drinking, diabetes mellitus, marriage, education, income level, eGFR, exercise, snoring, and UA to estimate the independent effects of each blood lipid index and hypertension on LVH, and presented with odds ratios (ORs) and 95% confidence intervals (CIs). Subgroup analyses were performed after classifying the participants according to age, gender, and the presence of hypertension with or without dyslipidemia (blood lipids with statistical significance in model 2). SPSS version 23.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

3 | RESULTS

3.1 | Characteristics of the study population

Among the subjects included in our analysis, 915 had LVH (10.02%). The demographic characteristics of 9134 eligible participants are presented in Table 1. In total, 45.30% of the subjects were men, with an average age of 53.51 ± 10.37 years. Among the people with hypertension, 47.9% of them (2237/4665) were men. Age, current drinking, marriage, education, family history of diabetes, family history of hypertension, exercise, snoring, income level, diabetes mellitus, blood lipid profiles, UA, blood pressure, BMI, obesity rate, IVSTd, LVIDd, and PWTd were different among the 4 subgroups according to the presence or absence of hypertension and dyslipidemia. There was no significant difference in race, current smoking, sleep duration, eGFR, and LVEF among the 4 groups. The group with hypertension and dyslipidemia had the largest LVM and higher levels of TC, TG, LDL-C, non-HDL-C, AI, TC/HDL-C, and RC.

3.2 | Partial correlation analysis of blood pressure, lipid indices, and left ventricular mass index

The partial correlation coefficients between blood pressure, lipid indices and LVMI are presented in Table 2. Race, age, current smoking or drinking, diabetes, marriage, education, income level, eGFR, exercise, snoring, and UA were adjusted for partial correlation analysis. Among LVMI and other indices, SBP had the greatest correlation

TABLE 1 Baseline characteristics of the study population according to the existence of hypertension and dyslipidemia

		Hypertension (−)		Hypertension (+)		
	Total	Dyslipidemia (−)	Dyslipidemia (+)	Dyslipidemia (−)	Dyslipidemia (+)	
Variables	*n* = 9134	*n* = 3288	*n* = 1181	*n* = 2912	*n* = 1753	*p*-value
Age (years) (%)	53.51 ± 10.37	49.55 ± 9.38	51.31 ± 9.71[a]	56.67 ± 10.32[ab]	57.18 ± 9.61[ab]	<0.01
35–45	2355 (25.78)	1301 (39.57)	373 (31.58)	458 (15.73)	223 (12.72)	
46–55	2923 (32.00)	1145 (34.82)	420 (35.56)	858 (29.46)	500 (28.52)	
56–65	2669 (29.22)	644 (19.59)	286 (24.22)	1028 (35.30)	711 (40.56)	
>65	1187 (13.00)	198 (6.02)	102 (8.64)	568 (19.51)	319 (18.20)	
Gender, male (%)	4138 (45.30)	1372 (41.73)	529 (44.79)	1389 (47.70)[a]	848 (48.37)[a]	
Race						0.263
Other	513 (5.62)	179 (5.44)	63 (5.33)	183 (6.28)	88 (5.02)	
Han	8621 (94.38)	3109 (94.56)	1118 (94.67)	2729 (93.72)	1665 (94.98)	
Current smoking (%)						0.054
No	5884 (64.42)	2156 (65.57)	723 (61.22)[a]	1865 (64.05)	1140 (65.03)	
Yes	3250 (35.58)	1132 (34.43)	458 (38.78)[a]	1047 (35.95)	613 (34.97)	
Current drinking (%)						<0.01
No	7075 (77.46)	2619 (79.65)	934 (79.09)[a]	2167 (74.42)[b]	1355 (77.30)	
Yes	2059 (22.54)	669 (20.35)	247 (20.91)[a]	745 (25.58)[b]	398 (22.70)	
Marriage (%)						<0.01
No	8318 (91.07)	3094 (94.10)	1095 (92.72)	2588 (88.87)[ab]	1541 (87.91)[ab]	
Yes	816 (8.93)	194 (5.90)	86 (7.28)	324 (11.13)[ab]	212 (12.09)[ab]	
Education (%)						<0.01
Illiteracy (%)	822 (9.00)	199 (6.05)	97 (8.21)	298 (10.23)[a]	228 (13.01)[ab]	
Middle school or below	7495 (82.06)	2765 (84.09)	972 (82.30)	2372 (81.46)[a]	1386 (79.06)[ab]	
High school or above	817 (8.94)	324 (9.85)	112 (9.48)	242 (8.31)[a]	139 (7.93)[ab]	
Family diabetes (%)						<0.01
No	7918 (86.69)	2902 (88.26)	1000 (84.67)[a]	2559 (87.88)[b]	1457 (83.11)[ac]	
Yes	1216 (13.31)	386 (11.74)	181 (15.33)[a]	353 (12.12)[b]	296 (16.89)[ac]	
Family hypertension (%)						<0.01
No	7028 (76.94)	2633 (80.08)	960 (81.29)	2159 (74.14)[ab]	1276 (72.79)[ab]	
Yes	2106 (23.06)	655 (19.92)	221 (18.71)	753 (25.86)[ab]	477 (27.21)[ab]	
Exercise (%)						<0.01
No	7253 (79.41)	2755 (83.79)	939 (79.51)[a]	2305 (79.16)[a]	1254 (71.53)[abc]	
Yes	1881 (20.59)	533 (16.21)	242 (20.49)[a]	607 (20.84)[a]	499 (28.47)[abc]	
Snoring (%)						<0.01
No	5599 (61.30)	2267 (68.95)	750 (63.51)[a]	1704 (58.52)[ab]	878 (50.09)[abc]	
Yes	3535 (38.70)	1021 (31.05)	431 (36.49)[a]	1208 (41.48)[ab]	875 (49.91)[abc]	
Sleep duration (hours)	7.27 ± 1.67	7.29 ± 1.58	7.26 ± 1.69	7.25 ± 1.70	7.29 ± 1.78	0.736
Income level (CYN) (%)						<0.01
≤5000	1080 (11.82)	309 (9.40)	93 (7.87)	452 (15.52)[ab]	226 (12.89)[abc]	
5000–20000	5050 (55.29)	1771 (53.86)	615 (52.07)	1685 (57.86)[ab]	979 (55.85)[abc]	
≥20000	3004 (32.89)	1,208 (36.74)	473 (40.05)	775 (26.61)[ab]	548 (31.26)[abc]	
Diabetes (%)						<0.01
No	8230 (90.10)	3169 (96.38)	1089 (92.21)[a]	2585 (88.77)[ab]	1387 (79.12)[abc]	
Yes	904 (9.90)	119 (3.62)	92 (7.79)[a]	327 (11.23)[ab]	366 (20.88)[abc]	
FBG (mmol/L)	5.88 ± 1.59	5.54 ± 1.12	5.82 ± 1.42[a]	5.94 ± 1.59[ab]	6.46 ± 2.18[abc]	<0.01

TABLE 1 (Continued)

Variables	Total	Hypertension (−)		Hypertension (+)		p-value
		Dyslipidemia (−)	Dyslipidemia (+)	Dyslipidemia (−)	Dyslipidemia (+)	
	n = 9134	n = 3288	n = 1181	n = 2912	n = 1753	
TC (mmol/L)	5.24 ± 1.09	4.83 ± 0.72	5.64 ± 1.43[a]	5.03 ± 0.69[ab]	6.08 ± 1.36[abc]	<0.01
TG (mmol/L)	1.60 ± 1.44	1.12 ± 0.52	2.14 ± 1.99[a]	1.30 ± 0.60[ab]	2.64 ± 2.27[abc]	<0.01
LDL-C (mmol/L)	2.95 ± 0.84	2.61 ± 0.57	3.23 ± 1.00[a]	2.83 ± 0.58[ab]	3.57 ± 1.05[abc]	<0.01
HDL-C (mmol/L)	1.42 ± 0.39	1.47 ± 0.32	1.25 ± 0.42[a]	1.51 ± 0.38[ab]	1.30 ± 0.44[abc]	<0.01
Non-HDL-C (mmol/L)	3.82 ± 1.07	3.36 ± 0.73	4.39 ± 1.20	3.52 ± 0.73	4.78 ± 1.18	<0.001
AI	2.89 ± 1.12	2.40 ± 0.76	3.72 ± 1.09	2.49 ± 0.82	3.92 ± 1.15	<0.001
TC/HDL	3.89 ± 1.12	3.40 ± 0.76	4.72 ± 1.09	3.49 ± 0.82	4.92 ± 1.15	<0.001
RC (mmol/L)	0.87 ± 0.57	0.74 ± 0.41	1.16 ± 0.65	0.69 ± 0.42	1.21 ± 0.76	<0.001
UA (mg/dl)	4.83 ± 1.39	4.54 ± 1.25	4.99 ± 1.44[a]	4.80 ± 1.35[ab]	5.33 ± 1.52[abc]	<0.01
Mean SBP (mmHg)	141.89 ± 23.36	123.80 ± 9.74	124.88 ± 9.72[a]	158.41 ± 19.20[ab]	159.83 ± 20.15[abc]	<0.01
Mean DBP (mmHg)	82.06 ± 11.68	74.60 ± 7.35	76.20 ± 7.22[a]	88.07 ± 10.81[ab]	90.02 ± 11.39[abc]	<0.01
BMI (kg/m^2)	24.81 ± 3.66	23.60 ± 3.38	25.12 ± 3.67[a]	25.08 ± 3.53[a]	26.46 ± 3.61[abc]	<0.01
Obesity (%)						<0.01
No	7504 (82.15)	3000 (91.24)	945 (80.02)[a]	2,344 (80.49)[a]	1,215 (69.31)[abc]	
Yes	1630 (17.85)	288 (8.76)	236 (19.98)[a]	568 (19.51)[a]	538 (30.69)[abc]	
eGFR (ml/min × 1.73 m^2)	93.74 ± 15.36	93.84 ± 15.28	93.95 ± 14.66	93.31 ± 15.36	94.11 ± 15.98	0.302
IVSTd (cm)	0.87 ± 0.12	0.84 ± 0.10	0.86 ± 0.11[a]	0.89 ± 0.12[ab]	0.92 ± 0.13[abc]	<0.01
LVIDd (cm)	4.70 ± 0.41	4.68 ± 0.40	4.72 ± 0.39[a]	4.71 ± 0.41[a]	4.68 ± 0.46[bc]	0.001
PWTd (cm)	0.85 ± 0.10	0.82 ± 0.09	0.84 ± 0.09[a]	0.87 ± 0.10[ab]	0.88 ± 0.11[abc]	<0.01
LVEF (%)	62.82 ± 3.74	62.78 ± 3.76	62.87 ± 3.73	62.82 ± 3.67	62.87 ± 3.84	0.822
LVMI (g/m^2)	81.63 ± 18.57	75.94 ± 14.53	76.99 ± 15.32	86.43 ± 20.36[ab]	87.43 ± 20.18[ab]	<0.01
LVH (LVMI_BSA) (%)						<0.01
No	8219 (89.98)	3169 (96.38)	1141 (96.61)	2460 (84.48)[ab]	1449 (82.66)[ab]	
Yes	915 (10.02)	119 (3.62)	40 (3.39)	452 (15.52)[ab]	304 (17.34)[ab]	

Note: Dyslipidemia means that any one of the 4 traditional blood lipids indexes is abnormal.

[a]Means versus hypertension (−) and dyslipidemia (−) $p < 0.05$;

[b]Means versus hypertension (−) and dyslipidemia (+) $p < 0.05$;

[c]Means versus hypertension (+) and dyslipidemia (−) $p < 0.05$.

TABLE 2 Partial correlation coefficients between blood pressure, lipid indices, and LVMI

	LVMI	SBP	DBP	TC	TG	LDL-C	HDL-C	Non-HDL-C	AI	RC	TC/HDL-C
LVMI	1										
SBP	0.265	1									
DBP	0.217	0.722	1								
TC	0.004*	0.102	0.136	1							
TG	0.011*	0.095	0.13	0.32	1						
LDL-C	0.014*	0.144	0.133	0.843	0.101	1					
HDL-C	−0.057	0.065	−0.006	0.261	−0.255	0.078	1				
Non-HDL-C	0.017*	0.081	0.143	0.935	0.423	0.84	−0.098	1			
AI	0.043	0.033	0.118	0.481	0.511	0.511	−0.658	0.737	1		
RC	0.052	0.062	0.068	0.484	0.63	0.079	−0.294	0.606	0.605	1	
TC/HDL-C	0.043	0.033	0.118	0.481	0.511	0.511	−0.658	0.737	1	0.605	1

* means $p > 0.05$ (no statistical significance).

with LVMI, with a coefficient of 0.265. Among the 4 traditional blood lipids, only HDL-C had a weak negative correlation with LVMI, while AI, RC, and TC/HDL-C as the nontraditional blood lipids had weak positive correlation with LVMI. Among blood pressure and blood lipid indices, the correlation coefficient between LDL-C and SBP was the largest ($r = 0.144$).

3.3 | Risk factors for left ventricular hypertrophy

Table 3 presents the results of logistic regression analysis, which explored the independent risk factors of LVH. Hypertension and dyslipidemia measured by high LDL-C, high non-HDL-C, high AI, and high TC/HDL-C were important risk factors for LVH. After the adjustment of age and sex (Model 1), the OR of LVH in subjects with hypertension was 3.97 (3.31–4.76), while ORs were 1.27 (1.02–1.59), 1.21 (1.04–1.39), 1.33 (1.15–1.53), and 1.42 (1.22–1.65), respectively, in those with dyslipidemia measured by high LDL-C, high non-HDL-C, high AI, and high TC/HDL-C. After further adjustment for confounding factors (Model 2), including race, age, smoking, drinking, diabetes, marriage, education, income level, eGFR, exercise, snoring, and UA, these correlations changed. Only dyslipidemia measured by high AI and high TC/HDL-C had statistical significance, which were 1.23 (1.06–1.43) and 1.33 (1.14–1.56) respectively. Similarly, in Model 2, the subgroups grouped by male or female were further analyzed. The effects of high AI and high TC/HDL-C on LVH in men were slightly greater than those in women; OR was 1.24 (1.01–1.57) for men compared with 1.21 (1.02–1.46) for women and 1.34 (1.04–1.71) for men compared with 1.30 (1.06–1.60) for women, respectively. Therefore, we observed gender differences in the effects of high-percentile AI and TC/HDL-C on LVH.

TABLE 3 Multivariate logistic regression of the association of left ventricular hypertrophy with dyslipidemia and hypertension

		Model 1 (total)		Model 2 (total)		Model 2 (female)		Model 2 (male)	
	Statistics	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Hypertension	*n* (%)								
No	4469 (48.93%)	1		1		1		1	
Yes	4665 (51.07%)	3.97 (3.31, 4.76)	<0.01	3.82 (3.17–4.59)	<0.01	3.37 (2.69–4.22)	<0.01	4.85 (3.48–6.75)	<0.01
High TC									
No	7605 (83.26%)	1		1		1		1	
Yes	1529 (16.74%)	1.11 (0.93–1.32)	0.23	1.07 (0.90–1.28)	0.44	1.10 (0.89–1.36)	0.37	0.96 (0.69–1.34)	0.83
High TG									
No	8508 (93.15%)	1		1		1		1	
Yes	626 (6.85%)	1.29 (0.99–1.67)	0.05	1.10 (0.84–1.44)	0.47	1.18 (0.85–1.65)	0.33	0.92 (0.57–1.48)	0.72
High LDL-C									
No	8395 (91.91%)	1		1		1		1	
Yes	739 (8.09%)	1.27 (1.02–1.59)	0.03	1.22 (0.97–1.52)	0.08	1.23 (0.95–1.60)	0.12	1.14 (0.74–1.77)	0.55
Low HDL-C									
No	7892 (86.40%)	1		1		1		1	
Yes	1242 (13.60%)	1.19 (0.98–1.46)	0.08	1.11 (0.90–1.36)	0.32	1.04 (0.78–1.39)	0.77	1.19 (0.88–1.61)	0.26
Dichotomous non-HDL-C									
Low	4564 (49.97%)	1		1		1		1	
High	4570 (50.03%)	1.21 (1.04–1.39)	0.01	1.14 (0.98–1.32)	0.08	1.12 (0.92–1.36)	0.27	1.15 (0.91–1.45)	.24
Dichotomous AI									
Low	4565 (49.98%)	1		1		1		1	
High	4569 (50.02%)	1.33 (1.15–1.53)	<0.01	1.23 (1.06–1.43)	<0.01	1.21 (1.02–1.46)	0.04	1.24 (1.01–1.57)	0.04
Categorical TC/HDL									
<3.5	3680 (40.29%)	1		1		1		1	
≥3.5	5454 (59.71%)	1.42 (1.22–1.65)	<0.01	1.33 (1.14–1.56)	<0.01	1.30 (1.06–1.60)	0.01	1.34 (1.04–1.71)	0.02
Dichotomous RC									
Low	4563 (49.96%)	1		1		1		1	
High	4571 (50.04%)	1.14 (0.99–1.31)	0.07	1.09 (0.95–1.27)	0.22	0.93 (0.77–1.12)	0.46	1.43 (1.12–1.81)	<0.01

Note: Model 1 adjusted factors: age, gender. Model 2 adjusted factors: race, age, gender, smoking, drinking, diabetes marriage, education, income level, eGFR, exercise, snoring, and uric acid.

3.4 | Prevalence of left ventricular hypertrophy with different coexistence of hypertension and dyslipidemia

Figure 1A,B shows the prevalence of LVH grouped by gender with and without hypertension and dyslipidemia defined by high TC/HDL-C or high AI. Among the 4 groups, the prevalence of LVH was the highest in people with both dyslipidemia and hypertension. Figure 2A,B shows the prevalence of LVH in different age groups with and without hypertension and dyslipidemia defined by high TC/HDL-C or high AI. Among all groups, the prevalence of LVH in people with both dyslipidemia and hypertension was the highest in all age groups, and the prevalence of LVH also increased with age.

3.5 | Subgroup analysis according to coexistence of hypertension and dyslipidemia

Table 4 presents the ORs and 95% CI of LVH in different combinations of hypertension and dyslipidemia according to age and gender. Individuals without these 2 conditions were considered the reference. Race, age, current smoking or drinking, diabetes mellitus, marriage, education, income level, eGFR, exercise, snoring, and UA were adjusted for analysis. In the whole population, the risk of LVH in individuals with both hypertension and high AI was nearly 4.27 times higher than in individuals without both conditions. The risk of individuals with hypertension alone was also higher than that of the reference, while the risk of LVH was not higher in the high AI group than that in the reference group ($p > 0.05$). The risk of LVH increased 7.75-fold (95% CI 3.88–15.47) in participants with hypertension and high AI in the relatively youngest group (35–45 years old), but gradually decreased to 2.74-fold (95% CI 1.52–4.95) in the highest age group (age > 65 years old) with aging. It should be noted that both men and women with hypertension and high AI had an increased risk of LVH, but the risk for men (OR 5.09) was greater than that for women (OR 3.66). Similarly, men with hypertension and high TC/HDL-C had a significantly increased risk of LVH, which was 6.24 times higher than that of men without these 2 conditions; the coexistence of hypertension and high TC/HDL-C in relatively young groups was associated with the highest risk of LVH. The risk was as high as 10.64-fold, 5.60-fold, 3.52-fold, and 2.82-fold in the age groups 35–44 years old, 45–54 years old, 55–64 years old, and over 65 years old, respectively.

Figure 3A,B shows the risk of LVH in different age subgroups according to blood pressure and dyslipidemia. The coexistence of dyslipidemia defined by high AI or high TC/HDL-C and hypertension had a greater impact on LVH in relatively young groups. Figure 4 shows the ORs of LVH with hypertension and dyslipidemia, including high AI or high TC/HDL-C stratified by gender. For men, individuals with both hypertension and high AI had the greatest risk of LVH. For women, individuals with both hypertension and high TC/HDL-C had the greatest risk of LVH. The results also showed that, among the different combinations of blood lipids and hypertension, the risk of LVH was the highest in patients with both conditions, regardless of gender and age.

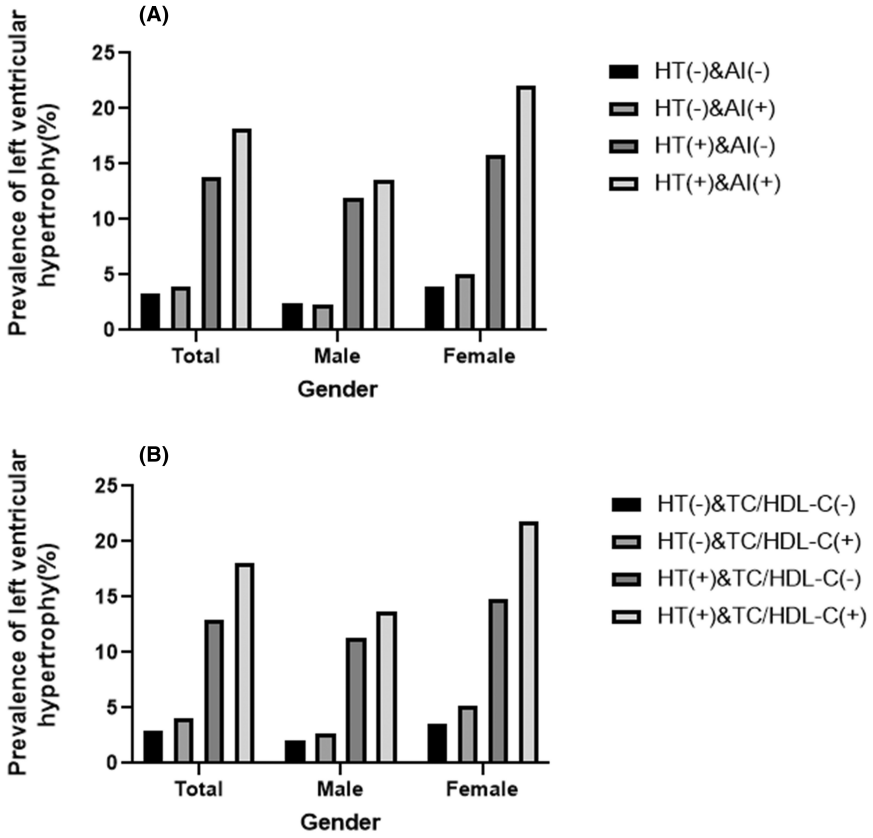

FIGURE 1 Prevalence of left ventricular hypertrophy according to the coexistence of hypertension and dyslipidemia (grouped by gender). (A) Coexistence of HT and AI. (B) Coexistence of HT and TC/HDL-C. AI, atherosclerosis index; HT, hypertension; TC/HDL-C, ratio of total cholesterol to high-density lipoprotein cholesterol; (–) represents no or low percentile or low range; (+) represents yes or high percentile or high range.

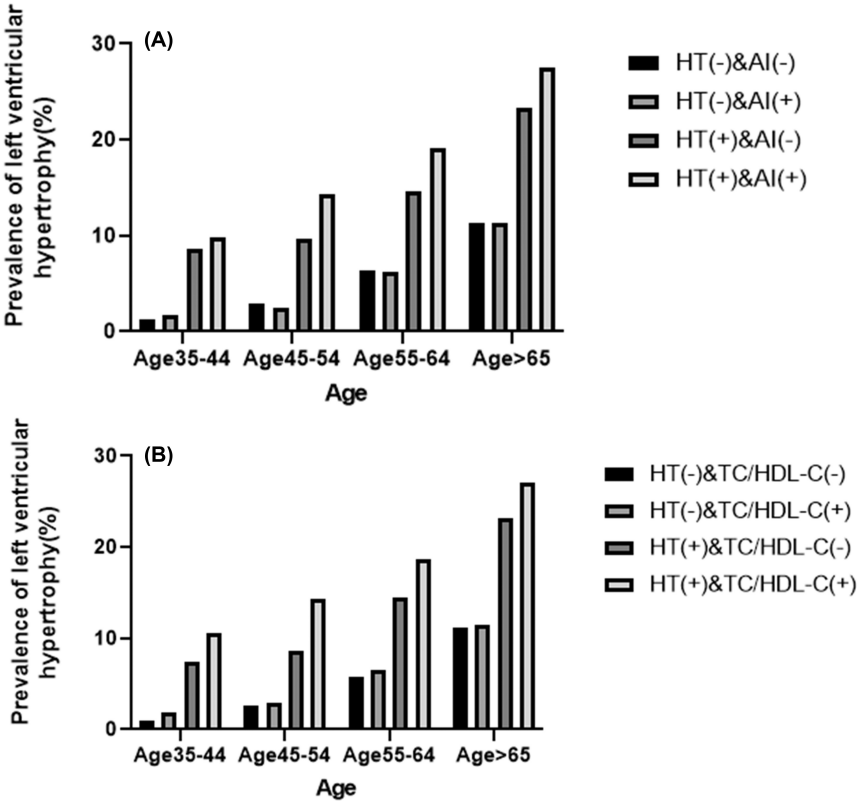

FIGURE 2 Prevalence of left ventricular hypertrophy according to the coexistence of hypertension and dyslipidemia (grouped by age). (A) Coexistence of HT and AI. (B) Coexistence of HT and TC/HDL-C. AI, atherosclerosis index; HT, hypertension; TC/HDL-C, ratio of total cholesterol to high-density lipoprotein cholesterol; (−) represents no or low percentile or low range; (+) represents yes or high percentile or high range.

TABLE 4 Odds ratios for left ventricular hypertrophy according to coexistence of hypertension and dyslipidemia

	HT (−) and AI (−)	HT (−) and AI (+)	HT (+) and AI (−)	HT (+) and AI (+)
Statistics (%)	**2469 (27)**	**2000 (21.9)**	**2096 (22.9)**	**2569 (28.1)**
OR(95%CI)				
Total	1 (reference)	1.00 (0.72–1.38)	3.45 (2.66–4.49)*	4.27 (3.30–5.53)*
Gender, female	1 (reference)	0.97 (0.66–1.42)	2.88 (2.07–4.00)*	3.66 (2.66–5.04)*
Gender, male	1 (reference)	0.90 (0.49–1.65)	4.18 (2.69–6.50)*	5.09 (3.28–7.88)*
Age 35–44 years	1 (reference)	1.38 (0.61–3.13)	7.39 (3.77–14.46)*	7.75 (3.88–15.47)*
Age 45–54 years	1 (reference)	0.77 (0.42–1.44)	3.65 (2.24–5.93)*	4.80 (3.00–7.69)*
Age 55–64 years	1 (reference)	0.85 (0.50–1.46)	2.44 (1.57–3.78)*	3.25 (2.13–4.96)*
Age over 65 years	1 (reference)	0.93 (0.45–1.92)	2.43 (1.34–4.41)*	2.74 (1.52–4.95)*
Statistics (%)	**HT (−) and TC/HDL-C (−)**	**HT (−) and TC/HDL-C (+)**	**HT (+) and TC/HDL-C (−)**	**HT (+) and TC/HDL-C (+)**
	1994 (21.8)	**2475 (27.1)**	**1686 (18.4)**	**2979 (32.6)**
OR (95% CI)				
Total	1 (reference)	1.23 (0.88–1.71)	3.73 (2.75–5.05)*	4.86 (3.64–6.49)*
Gender, female	1 (reference)	1.13 (0.76–1.69)	3.00 (2.06–4.38)*	4.01 (2.82–5.70)*
Gender, male	1 (reference)	1.30 (0.71–2.40)	4.84 (2.85–8.25)*	6.24 (3.73–10.45)*
Age 35–44 years	1 (reference)	1.78 (0.77–4.12)	7.39 (3.34–16.39)*	10.64 (4.97–22.77)*
Age 45–54 years	1 (reference)	1.03 (0.55–1.93)	3.73 (2.09–6.65)*	5.60 (3.28–9.57)*
Age 55–64 years	1 (reference)	1.05 (0.59–1.84)	2.69 (1.61–4.48)*	3.52 (2.17–5.70)*
Age over 65 years	1 (reference)	1.00 (0.47–2.12)	2.51 (1.29–4.88)*	2.82 (1.48–5.36)*

Note: (−) represents no or low percentile or low range; (+) represents yes or high percentile or high range.

Abbreviations: AI, atherosclerosis index; CI, confidence interval; HT, hypertension; OR, odds ratio; TC/HDL-C, ratio of total cholesterol to high-density lipoprotein cholesterol.

*means $p < 0.05$.

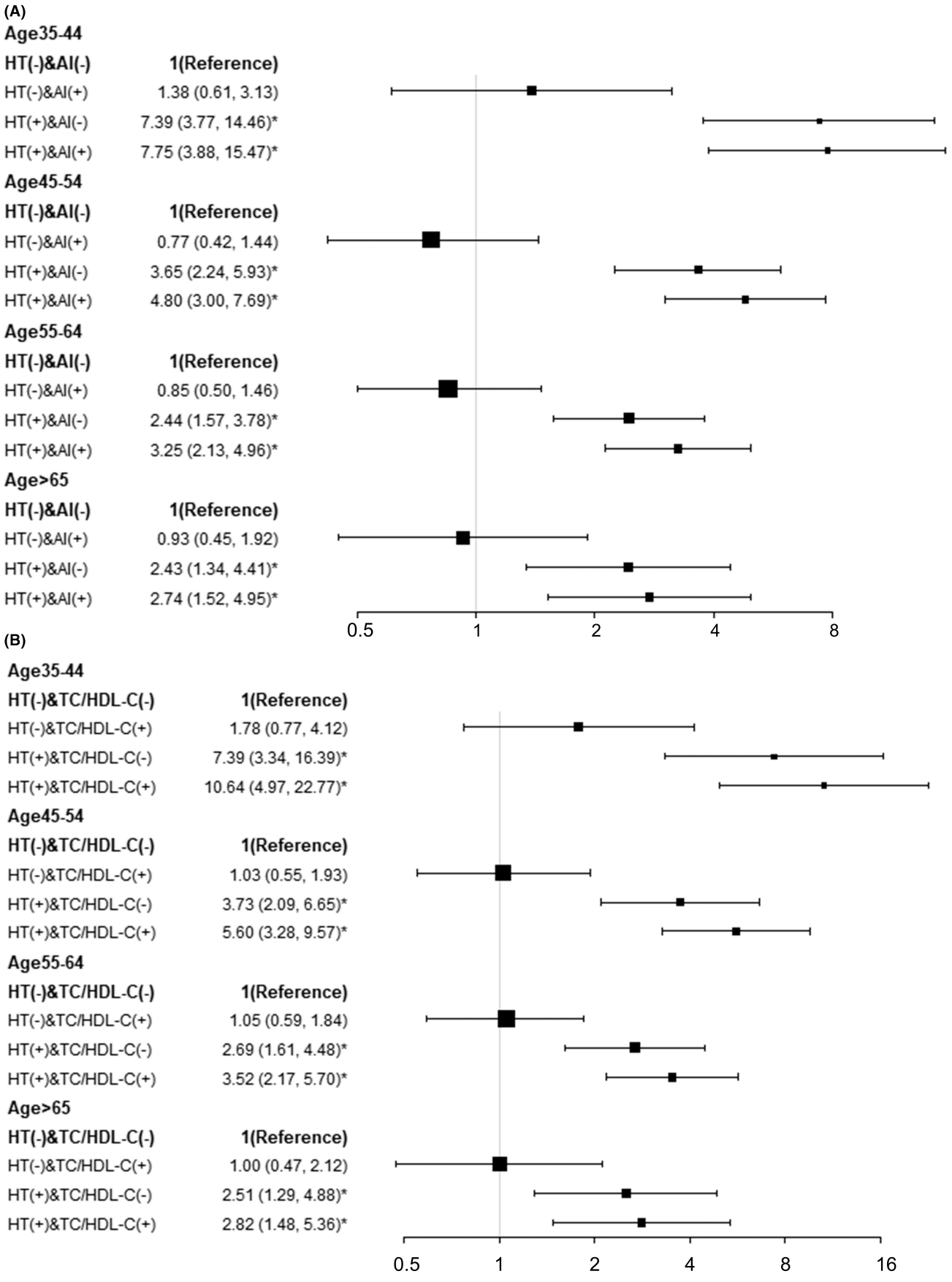

FIGURE 3 Forest plots showing ORs of left ventricular hypertrophy (grouped by age). (A) Coexistence of HT and AI. (B) Coexistence of HT and TC/HDL-C. AI, atherosclerosis index; CI, confidence interval; HT, hypertension; OR, odds ratio; TC/HDL-C, ratio of total cholesterol to high-density lipoprotein cholesterol. (–) represents no or low percentile or low range; (+) represents yes or high percentile or high range.

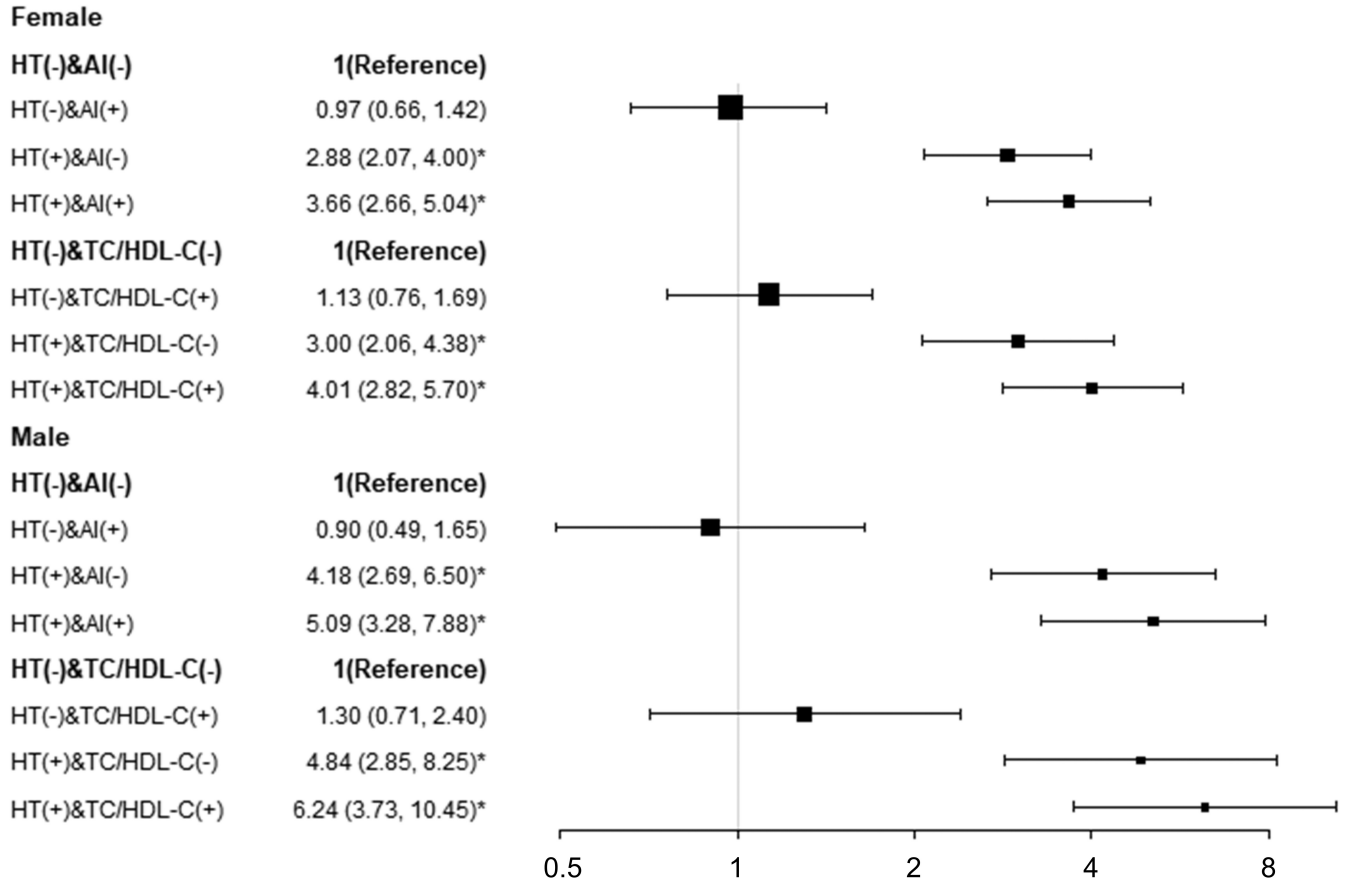

FIGURE 4 Forest plots showing odds ratios of left ventricular hypertrophy (grouped by gender). AI, atherosclerosis index; CI, confidence interval; HT, hypertension; OR, odds ratio; TC/HDL-C, ratio of total cholesterol to high-density lipoprotein cholesterol. (–) represents no or low percentile or low range; (+) represents yes or high percentile or high range.

4 | DISCUSSION

Our results showed that hypertension and dyslipidemia (high AI or high TC/HDL-C) were independently and positively correlated with the increased risk of LVH in the middle-aged and elderly population. Most importantly, these risk factors had significant combined effects. Combination of hypertension and high AI or high TC/HDL-C was associated with the highest risk of LVH, especially in men, which were 5.09 and 6.24 times higher than those without these 2 conditions, while in women, they were 3.66 and 4.01 times higher, respectively. The results showed that hypertension had a greater impact on the risk of LVH than dyslipidemia. LVH is usually a response to chronic stress or volume load. The 2 most common conditions associated with left ventricular pressure or volume load status are systemic hypertension and valvular disease. Although moderate or severe valvular disease was an exclusion criterion of this study, 48% of the study population had hypertension. Consistent with this, our study also confirmed that hypertension was a strong risk factor for LVH in patients without dyslipidemia.

Our study found that the prevalence of LVH in women was higher than in men, similar to previous studies.[29,30] At the same time, the 4 blood lipid contents including, TC, TG, HDL-C, and LDL-C, were not observed to be related to LVH after multifactor adjustment, which was consistent with some previous findings in the literature.[14,15] However, it was in contrast to the research conclusions from a population with hypertension,[13] which found no protective effect of HDL-C on LVH. We believe that the difference may be related to the adjusted metabolic factors and the basic differences of the study population since other relevant metabolic factors were relatively fully adjusted in our general community-based population study. The nontraditional comprehensive blood lipid indexes obtained by simple calculation have attracted increasing attention in recent years. Our study confirmed that high AI and high TC/HDL-C were associated with increased LVH risk. Although the specific mechanism needs to be further explored, many epidemiological studies have shown that nontraditional blood lipid indices can better predict the risk of cardiovascular disease,[25,26,31] better reflect the degree of oxidative stress[27] and abnormal degree of blood lipid metabolism,[32] and predict the left ventricular configuration.[33] At present, abnormal lipid metabolism leading to left ventricular hypertrophy was explained by the accumulation of lipids in or around myocytes. A study on the human heart showed that fat deposition in the left ventricle constituted a direct risk of myocardial hypertrophy[34]; abnormal lipid metabolism can be manifested by strong systemic or local inflammation and mitochondrial oxidative stress[35] and/or increased production of reactive oxygen species in NADPH oxidase complex, resulting in oxidative modification of LDL, thereby amplifying the

inflammatory potential[36]; abnormal lipid metabolism was usually accompanied by insulin resistance in the animal model of high-fat feeding[37] and promoted LVH[38]; neurohumoral effects[39] included the effects of the sympathetic nervous system,[9] renal angiotensin aldosterone system (RAAS), and other hormones. In addition, other signaling pathways caused by dyslipidemia also played important roles in the development of myocardial hypertrophy. Studies have shown that VLDL can promote the excessive production of aldosterone through the PLC/IP3/PKC signaling pathway, which can induce left ventricular hypertrophy or remodeling, independent of the hemodynamic effect of blood pressure.[40] Therefore, it may be reasonable that AI and TC/HDL-C have potential predictive value for LVH.

The combined effects of hypertension and lipid metabolism on LVM were more significant in men than in women. It was inferred that one of the reasons was that there may be gender differences in lipid metabolism itself. Compared with men, women had higher HDL-C and lower TC/HDL-C.[41] Healthy lipid profile was related to the retention of maximum blood flow in the myocardium.[42] Second, estrogen had a regulatory effect on RAAS, indirectly inhibiting the development of LVH.[43] In conclusion, the gender difference of the combined effect of blood pressure and blood lipid on LVH may be reasonable, but it may also be due to the influence of other unknown factors.

The advantage of this study was that we used multistage random cluster sampling to select a large sample of rural community population, which increased the applicability of our research results to the rural areas of Liaoning Province. In addition, we also explored the impact of nontraditional blood lipid comprehensive indices on LVH and analyzed them in combination with hypertension to accurately evaluate their prediction of LVH risk in different age and gender groups. The limitations of this study mainly came from the cross-sectional design. The causal relationship between risk factors still needs to be further verified by longitudinal follow-up studies. In addition, because our research area included only Northeast China, owing to its special geographical and climatic environment and eating habits, the extrapolation of our research results may be limited. Furthermore, given that the analysis was based on the general population rather than on patients seeking diagnosis and treatment in a hospital, it was not clinically possible to accurately determine if the hypertension was secondary hypertension (though it was relatively less likely) and adopt a gold standard technique for diagnosis. Despite its limitations, the results of this study provided a basis for the development of a strategy to prevent target organ damage in hypertension.

4.1 | Conclusions

The combined effects of hypertension and increased nontraditional blood lipid comprehensive indexes (high-percentile AI or high TC/HDL-C) were synergistically related to LVH, and their effects were more significant in men. Hypertension was also a strong risk factor for LVH in patients without dyslipidemia. Better control of blood pressure may have long-term health benefits, whether or not accompanied by any type of dyslipidemia. In addition, the combined effects of blood lipid and blood pressure decreased with aging, suggesting that the younger the group, the more blood lipids and blood pressure should be monitored.

AUTHOR CONTRIBUTIONS

Xueyao Zhang provided the concept of research, literature retrieval, data search and interpretation, and drafting of the article. Guangxiao Li and Chuning Shi performed data search and data analysis. Dongyuan Zhang provided critical revision of important knowledge content. Yingxian Sun contributed to study conception and design. All authors read and approved the final version of the manuscript.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest regarding the present study. Dongyuan Zhang is an assistant editor of AMEM and a co-author of this article.To minimize bias,they were excluded from all editorial decision making related to the acceptance of this article for publication.

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