Lipids in Health and Disease

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Predictive value of remnant cholesterol for left ventricular hypertrophy and prognosis in hypertensive patients with heart failure: a prospective study

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Abstract

Background and Aim Remnant cholesterol (RC) is substantially related to negative outcomes in cardiac patients. Patients with coexisting hypertension and heart failure (HF) often develop left ventricular hypertrophy (LVH) and have poor prognoses. This study investigated baseline RC levels and LV remodelling and patients' prognoses.

Methods and results Six hundred thirty consecutive individuals with hypertension and HF participated in this prospective trial from October 2018 to August 2020. Based on left ventricular mass index (LVMI), 560 those eligible were separated into LVH and non-LVH groups. Multiple linear regression and receiver operating characteristic (ROC) curves examined the RC and LV relationship. A Cox regression analysis was conducted to examine the predictive value of RC for clinical outcomes. The LVH group presented significantly elevated values of RC, triglyceride, and cholesterol and decreased high-density lipoprotein cholesterol (HDLC). The optimal cutoff value for RC to predict LV remodelling was 0.49. The subjects were observed for a median of 58 months, and 104 participants met the primary endpoint. The risk models involving the two Cox models were adjusted to incorporate confounding factors, which revealed that those with elevated baseline levels of RC were more susceptible to cardiovascular mortality, as shown by an increased hazard ratio. (HR: 1.91, 95% CI: 1.62–2.26 vs. HR: 1.75, 95% CI: 1.43–2.16, $P < 0.001$).

Conclusions RC is linked to LV remodelling in patients with hypertensive HF, with LVH having greater RC values. Moreover, patients with hypertensive HF who had a higher RC suffered from an increased risk of cardiovascular mortality.

Trial registration NCT 03727828, 21 Oct 2018.

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Keywords Remnant cholesterol (RC), Hypertension, Heart failure (HF), Left ventricular hypertrophy (LVH), Prognosis

Introduction

Left ventricular hypertrophy (LVH) is a disorder that occurs when the left ventricle (LV) of the heart becomes enlarged as a result of prolonged exposure to high blood pressure. This condition can eventually result in heart failure (HF) [1, 2]. Thus, it is of the utmost importance to swiftly identify the risk variables that produce adverse variations in the LV and then immediately make the appropriate adjustments to these risk factors. However, diagnosing ventricular remodelling with echocardiography is costly, making it crucial to identify biomarkers for LVH.

Abnormal blood lipid profiles are significant cardiovascular risk factors [3]. Risks of cardiovascular events are enhanced in correlation with greater none high-density lipoprotein cholesterol (HDLC) and lower HDLC levels [4–6]. RC is the kind of cholesterol neither HDLC nor low-density lipoproteins (LDLC) carry, which includes the cholesterol linked to very low-density lipoproteins (VLDLs) and intermediate-density lipoproteins (IDLs) while fasting and the remnants of chylomicrons while not fasting [7]. Research has shown that RC may raise the potential hazards of complications for HF [8]. In addition, current studies have suggested that elevated RC levels may contribute to LV remodelling [9, 10]. However, these studies included few hypertensive patients and lacked comprehensive prognostic data and subgroup analyses. The potential of RC as a biomarker for predicting cardiac remodelling and dysfunction in hypertensive patients with HF remains uncertain.

Therefore, the objective of the current investigation was to recruit patients with HF concomitant with hypertension, conduct an extensive long-term follow-up, elucidate the relationship between initial RC values and LV remodelling, and explore patient prognosis.

Materials and methods

Research methodology and participants

The study was conducted as a prospective cohort study. From October 2018 to August 2020, all the eligible patients were admitted to the cardiac department of the Shanghai Tenth People's Hospital. Admissions for HF with hypertension were considered if the patient was 18 or older. Two cardiologists confirmed each patient's diagnosis following the guidelines' recommended diagnostic criteria [11]. All patients underwent echocardiography during hospitalization, and LVH was assessed. The criteria for LVH diagnosis were an LV mass index (LVMI) >115 g/m^2 in males and ≥ 95 g/m^2 in females. Anyone with secondary hypertension, acute myocardial infarction, hypertrophic cardiomyopathy, LV assist device (LVAD) implantation, incomplete follow-up, and a lack of cholesterol level data or echocardiographic data were excluded. There were 630 patients enrolled, as shown in Fig. 1. Due to insufficient blood samples or echocardiography data, 55 participants were subsequently removed from the research. Additionally, 15 patients were lost to follow-up. Participants who fulfilled the inclusion criteria made up the cohort for this study, which totaled 560 individuals. In accordance with the participants' previous LVMI values, the participants were separated into two groups: those who were given LVH and those who were not given LVH. After each patient was enrolled, written informed consent was obtained.

Echocardiographic and clinical factors

The blood samples were taken twelve hours after admission. In particular, patients had their blood obtained from the vein in the front of the elbow after an 8-hour fast, and on the morning of the first day after admission, they had vacuum tubes taken for measurements. The Clinical Laboratory of the Shanghai Tenth People's Hospital conducted hematological analyses for all patients. The time interval between the blood test and the diagnosis based on the NYHA functional classification (NYHA) was, at most, 12 h. Clinical, analytical, and echocardiographic data were gathered by reviewing hospital charts.

Measurement of RC

Prospective analyses were performed using RC as the independent variable.

RC = Total cholesterol - LDL-C -HDL-C.

Outcomes and follow-up

Patients received outpatient or phone calls every eight weeks after discharge. The follow-up frequency was subsequently adjusted every six months. The primary endpoint considered was cardiovascular death. Data on outcomes for discharged patients were collected during routine follow-up visits.

Data analysis

The means ± SDs were used to display continuous data. If variables were normally distributed, t-tests were employed to compare them. Compare frequencies (n) or ratios (n/N) of categorical data using the chi-square test. Receivers operating characteristic (ROC) curves and the Z test were used to evaluate RC's ability to predict LVH in enrolled patients. The connection between RC and patients' cardiac ultrasonography parameters was examined using multiple linear regression. Using univariate and multivariate Cox regression, we calculated hazard

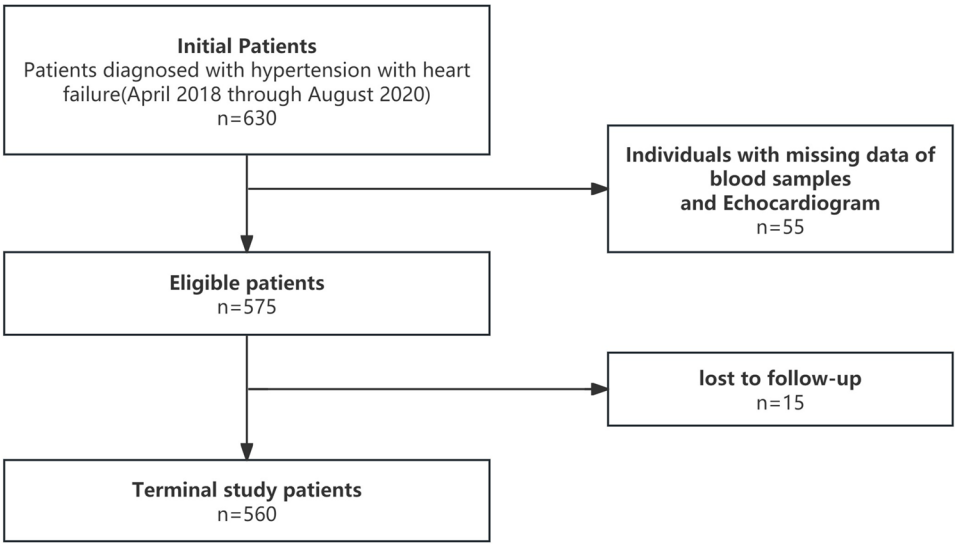

Fig. 1 Flow diagram of the screening and enrolment of study participants

ratios (HR) and 95% confidence intervals (CIs) to evaluate the correlations between baseline RC levels and time to cardiovascular mortality. Furthermore, the risk of RC occurring at the endpoint event was described using a restricted cubic spline (RCS). The log-rank test was performed on K–M survival curves to determine the prognosis of patients with different concentrations of RC.

By previous research and guidelines [11, 12], different models were constructed by adjusting for various covariates for analysis. A subgroup analysis of key variables (age, sex, BMI, diabetes status, smoking status, and whether patients developed LVH) also evaluated the effects and potential interaction effects stratified by prespecified risk factors. P-values below 0.05 indicated significance. The statistical analysis used either SPSS 20.0 or the R programming language (version 4.1.2).

Results

Participant characteristics

The 560 participants were split evenly between the 320 LVH group and the 240 non-LVH group (Table 1). In the present investigation, 66% were males. The patients' average age was 71.8±10.1 years in the LVH group and 70.7±11.6 years in the non-LVH group. Moreover, 79% of patients enrolled in the study resided in urban areas, whereas 21% lived in rural areas. Notably, 91% of the patients in the LVH group were urban residents. The rates of occurrence of CHD, CKD, and diabetes mellitus were 28%, 11.7%, and 35.7%, respectively. The LVH group demonstrated better NYHA functional class and NT-proBNP levels than the non-LVH group. However, no significant BMI, HR, or SBP changes were detected. RC baseline was 0.64±0.57 mmol/L. with higher levels observed in the LVH group for RC, TC, TG, and TyG, which were 0.82±0.68 mmol/L, 3.85±1.09 mmol/L, 1.67±1.10 mmol/L and 8.86±0.65, respectively, while HDL-C was lower at 0.40±0.50 mmol/L. In terms of echocardiographic parameters, the LVH group had a lower LVEF of 44.75±14.05, and other indices, including LVDD, LVDS, LVPWD, IVS, and LAS, which were substantially higher in the LVH group. The LVMI was 134.85±27.67 g/m2 in the LVH group and 91.94±12.51 g/m2 in the non-LVH group. Furthermore, neither of the two groups exhibited any significant differences in the utilization of antihypertensive medications (ACEI/ARB/CCB), lipid-lowering (statins), antiplatelet (aspirin), antiarrhythmics (β-blockers/ivabradine) or antidiabetic (metformin/sulfonylureas) drugs.

Baseline RC is linked to the LV function

Considering the possible correlation that exists in the initial RC and the function of the LV, this study initially assessed the accuracy of the baseline RC in predicting the occurrence of LVH via ROC curve analysis. Additional Fig. 1 shows that the AUC was 0.810, with a 95% CI ranging from 0.778 to 0.844. For the purpose of diagnosing LVH, the ideal cutoff value for RC was 0.49, which had a sensitivity of 71.56% and a specificity of 76.67%. The correlations between the baseline RCs and echocardiographic parameters were subsequently evaluated via multivariate linear regressions (Table 2). Model 1, which included baseline RC, sex, age, BMI, smoking status, and drinking status as covariates, Unveiled a robust positive linear connection between the initial RC and LVDD, IVS, LVPWD, and LVMI ($P<0.001$). Furthermore, in Model 2, TyG, GLU, and LDLC were incorporated as covariates in addition to those in Model 1. The investigation showed a favourable association between the initial RC, LVDD,

Table 1 Baseline clinical characteristics by LVH grouping

Variable	Total	No LVH	LVH	*P*
Number	**560**	**240**	**320**	
Age, years	71.2 ± 10.9	71.8 ± 10.1	70.7 ± 11.6	0.218
Male				
Man	371 (66)	165 (69)	206 (64)	0.142
Woman	189 (34)	75 (31)	114 (36)	
Blood pressure, mmHg				
SBP	140.18 ± 23.07	138.75 ± 23.45	141.25 ± 22.77	0.310
DBP	78.12 ± 15.32	75.87 ± 14.07	79.76 ± 13.00	0.006
Living Region				*P* < 0.001
Rural	117(21)	88(37)	29(9)	
Urban	445(79)	152(63)	280(91)	
HR, bpm	84.93 ± 17.73	80.30 ± 18.98	84.73 ± 17.05	0.789
BMI, kg/m2	24.35 ± 3.74	24.39 ± 3.96	24.32 ± 3.56	0.881
Risk factors				
Drinking, n(%)	24 (4.3)	8 (3.3)	16(5.0)	0.355
Smoking, n(%)	100 (17.8)	36 (15)	64(19)	0.178
CHD, n(%)	68(28)	68(28)	95 (30)	0.727
CKD, n(%)	63(11.2)	22(9.2)	41(13)	0.177
Diabetes mellitus, n(%)	200 (35.7)	82 (34)	118 (37)	0.508
NYHA functional class, n(%)				*P* < 0.001
II	302(54)	177(74)	125(39)	
III	195(35)	53(22)	142(44)	
IV	63(11)	10(4)	53(17)	
Hemoglobin, g/dl	127.35 ± 19.57	128.14 ± 19.49	126.75 ± 19.64	0.41
Creatinine, mg/dl	103.62 ± 62.98	99.33 ± 55.33	106.84 ± 69.26	0.163
Blood urea nitrogen, mg/dl	8.08 ± 4.54	7.86 ± 4.86	8.24 ± 4.29.77	0.338
NT-proBNP, pg/ml	1557.50 (680.62, 4060.25)	1529.50 (532.50, 3163.75)	2005.00 (809.90, 5108.00)	*P* < 0.001
LDLC, mmol/L	1.62 ± 0.97	1.56 ± 0.91	1.67 ± 1.00	0.173
TC, mmol/L	3.73 ± 1.07	3.57 ± 1.02	3.85 ± 1.09	0.002
TG, mmol/L	1.43 ± 0.95	1.10 ± 0.50	1.67 ± 1.10	*P* < 0.001
RC, mmol/L	0.64 ± 0.57	0.39 ± 0.21	0.82 ± 0.68	*P* < 0.001
HDLC, mmol/L	0.49 ± 0.52	0.61 ± 0.53	0.40 ± 0.50	*P* < 0.001
TyG	8.69 ± 0.65	8.46 ± 0.58	8.86 ± 0.65	*P* < 0.001
HBA1C, %	5.85 ± 1.56	5.86 ± 1.57	5.84 ± 1.56	0.877
Glu, mmol/L	6.47 ± 2.86	6.29 ± 2.82	6.60 ± 2.88	0.205
Echocardiogram				
LVEF, %	46.86 ± 13.75	49.66 ± 12.85	44.75 ± 14.05	*P* < 0.001
LVDD, mm	51.05 ± 7.69	46.61 ± 5.13	54.38 ± 7.61	*P* < 0.001
LVDS, mm	36.80 ± 11.12	33.75 ± 10.02	39.08 ± 11.76	*P* < 0.001
LVPWD, mm	10.26 ± 1.22	9.81 ± 0.96	10.60 ± 1.29	*P* < 0.001
IVS, mm	10.52 ± 1.49	10.00 ± 1.03	10.91 ± 1.66	*P* < 0.001
LAS, mm	41.61 ± 6.94	40.41 ± 1.60	42.51 ± 7.06	*P* < 0.001
LVMI, g/m2	116.46 ± 30.91	91.94 ± 12.51	134.85 ± 27.67	*P* < 0.001
Medications				
Aspirin, n(%)	425 (76)	182 (76)	243 (76)	0.977
Statins, n(%)	435 (77)	182 (77)	253(79)	0.364
ACE inhibitors/ARB, n(%)	150 (61)	150 (63)	190 (60)	0.770
CCB, n(%)	144 (26)	58 (24)	86 (27)	0.468
Ivabradine, n(%)	24(4)	11(2)	13(2)	0.288
Blocker, n(%)	351 (63)	148 (62)	203 (63)	0.668

Table 1 (continued)

Variable	Total	No LVH	LVH	*P*
Number	**560**	**240**	**320**	
Metformin, n(%)	159(28)	60(25)	99(31)	0.131
Sulfonylureas, n(%)	125(22)	57(24)	68(21)	0.539

Patients were separated into two groups according to their previous LVMI values: the LVH group and the non-LVH group

SBP systolic blood pressure; *DBP* diastolic blood pressure; *HR* heart rate; *BMI* body mass index; *CHD* coronary heart disease; *CKD* chronic kidney disease; *TC* total cholesterol; *TG* triglyceride; *RC* remnant cholesterol; *HDL-C* high-density lipoprotein cholesterol; *LDL* low-density lipoprotein cholesterol; *Glu* fasting blood glucose; *LVDD* left ventricular end-diastolic dimension; *LVDS* left ventricular end-systolic dimension; *LVEF* left ventricular ejection fraction; *IVS* interventricular septum; *LAS* left atrial dimension; *LVPWD* left ventricular posterior wall diameter; *LVMI* left ventricular mass index; *ACEI* angiotensin-converting enzyme inhibitor; *ARB* angiotensin II receptor blocker; *CCB* acronym calcium channel blockers

The data are expressed as the means ± SDs or numbers (%), medians (quartile l, quartile 3), or n (%)

Table 2 Multivariate linear regressions between RCs and echocardiograms

	Model 1		Model 2	
Variant	**β (95% CI)**	***P***	**β (95% CI)**	***P***
LVEF, %	0.51 (-2.46, 1.42)	0.600	-5.65(-9.49, 1.82)	0.442
LVDD, mm	2.70 (1.69, 3.72)	< 0.001	4.77 (2.76, 6.78)	< 0.001
LVDS, mm	-0.31 (-1.83, 1.22)	0.690	2.89 (-0.15, 5.93)	0.062
IVS, mm	0.48 (0.27, 0.67)	< 0.001	0.244(-0.174, 0.662)	0.252
LVPWD, mm	0.62 (0.45, 0.78)	< 0.001	0.589(0.26, 0.91)	< 0.001
LAS, mm	-0.34 (-1.35, 0.67)	0.504	0.887 (-1.07, 2.85)	0.374
E/e'	-1.41 (-3.61, 0.34)	0.113	-0.093 (-0.28, 0.09)	0.334
LVMI, g/m2	19.00 (14.91, 23.10)	< 0.001	27.44 (19.31, 35.56)	< 0.001

Model 1: adjusted for sex, age, BMI, smoking status, alcohol consumption status, and statin use

Model 2: further adjusted for LDLC, Glu, TyG

LVDD Left ventricular end-diastolic dimension; *LVDS* Left ventricular end-systolic dimension; *LVEF* Left ventricular ejection fraction; *IVS* Interventricular septum; *LAS* left atrial dimension; *LVPWD* left ventricular posterior wall diameter; *LVMI* left ventricular mass index

LVPWD, and LVMI. No significant correlation was found between RC and IVS. These data reveal a strong link between baseline RC levels and LV function in patients.

RC and cardiovascular mortality in hypertensive HF patients

After the average follow-up of 58 months, 104 individuals (18.57%) developed cardiovascular mortality. RC cutoff values for LVH prediction split patients into two groups. Twenty patients (7.63%) were in the RC < 0.49 mmol/L group, while 84 (28.19%) were in the RC > 0.49 mmol/L group. Cardiovascular mortality was higher in those with RCs > 0.49 mmol/L compared to those with RCs < 0.49 mmol/L, as seen by the K–M curves (log-rank $p < 0.001$). (Fig. 2). A positive connection was seen between baseline RC levels and the risk of cardiovascular death, as indicated by an unadjusted Cox analysis (HR: 1.86, 1.59–2.17). Model 1, adjusted for age, sex, BMI, smoking status, fasting blood glucose, blood pressure, alcohol consumption status, diabetes status and NT-proBNP, revealed an increased risk (HR: 1.91, 1.62–2.26). Model 2, which was further adjusted for TyG, antihypertensive drugs (ACEI/ARB/CCB), lipid-lowering drugs (statins), antiplatelet drugs (aspirin), antiarrhythmics (β-blockers/ivabradine) and antidiabetic drugs (metformin/sulfonylureas) in Model 1, still demonstrated a higher potential for occurrences (HR: 1.75, 1.43–2.16) (Additional Table 1). A rise in the baseline levels of RC was found to be related to a greater risk of mortality from cardiovascular causes. Figure 3 illustrates RCS plots of baseline RC levels in the unadjusted model, Models 1 and 2, with HRs for cardiovascular death.

Cardiovascular mortality and RC in subgroups

To guarantee the accuracy of the Cox analysis findings, we performed stratified analyses to account for potential confounding factors. These subgroups were defined by covariates known to play significant roles in the adverse prognosis of patients with hypertension combined with HF, including age, sex, BMI, diabetes mellitus status, NYHA functional classification, and the occurrence of LVH (Fig. 4). Except for the stratifying covariates, any of these evaluations have been adjusted to account for sex, drinking status, age, smoking status, BMI, fasting blood glucose, cholesterol, blood pressure, NT-proBNP, TyG, antihypertensive drugs (ACEI/ARB/CCB), lipid-lowering drugs (statins), antiplatelet drugs (aspirin), antiarrhythmics (β-blockers/ivabradine), and antidiabetic drugs (metformin/sulfonylureas). The results indicated that although there were varying risks of cardiovascular death among the different subgroups, the interaction tests revealed no heterogeneity ($P > 0.05$). Therefore, this study suggested that, regardless of the subset, the risk of cardiovascular death increases with increasing levels of RC.

Discussion

This study aimed to determine whether there was a connection between RC at baseline and LV remodelling in hypertensive patients with HF. These data also examined the baseline RC's cardiovascular mortality prediction. First, baseline RC levels were related to LV remodelling, which mainly predicts LVH in hypertensive HF patients.

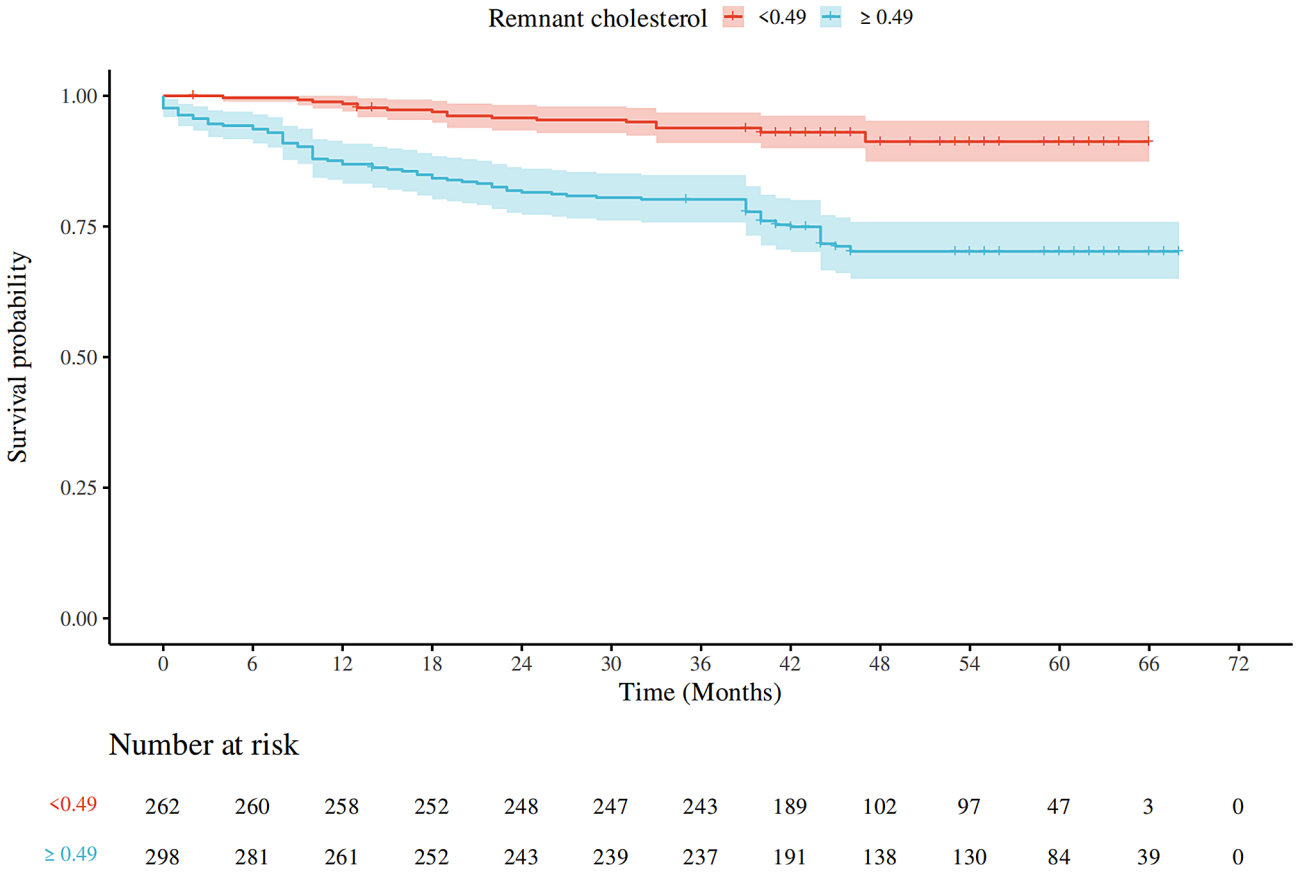

Fig. 2 Kaplan–Meier analysis of the ability of the RC cutoff to predict cardiovascular death in patients with LVH. The cutoff of RC to predict LVH was 0.49 mmol/L. Log-rank $p < 0.001$

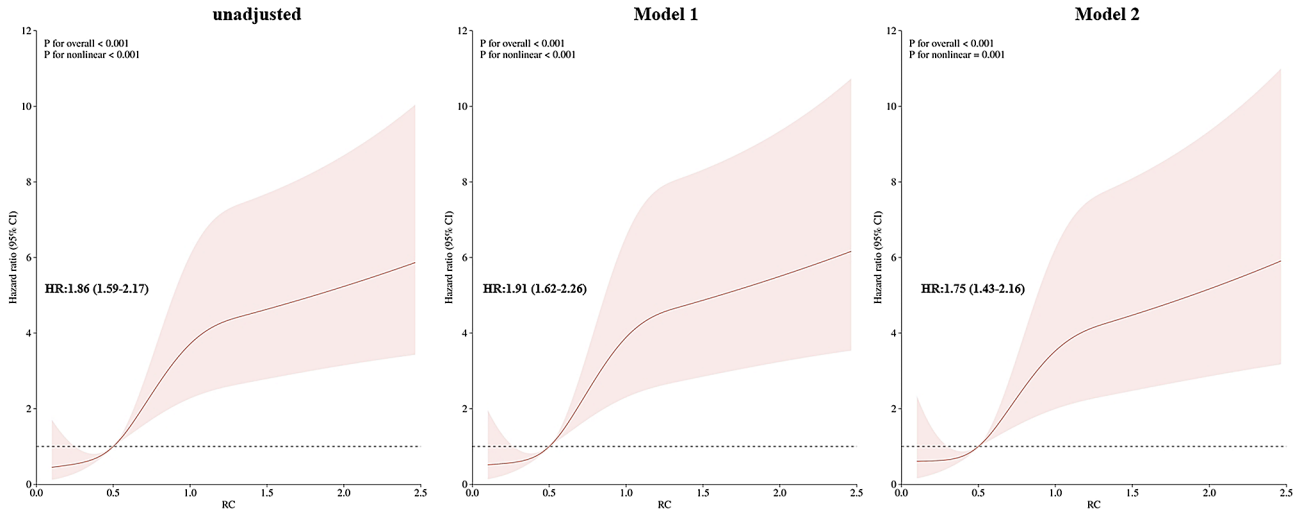

Fig. 3 Adjusted risk of cardiovascular death according to the remnant cholesterol level. The restricted cubic spline (RCS) in the unadjusted model, Model 1 and Model 2, was used to explore the association between remnant cholesterol and the risk of cardiovascular death. Unadjusted model; Model 1: adjusted for sex, age, BMI, smoking status, drinking status, diabetes mellitus status, Glu, SBP, and NT-proBNP; Model 2: further adjusted for TyG, antihypertensive drugs (ACEI/ARB/CCB), lipid-lowering drugs (statins), antiplatelet drugs (aspirin), antiarrhythmics (β-blockers/ivabradine) and antidiabetic drugs (metformin/sulfonylureas)

Variables	n (%)	HRC	LRC	HR (95%CI)	*p*	Interaction
		No. of events/ No. of total				
All patients	560 (100.00)	84/298	20/262	0.36 (0.19 ~ 0.69)	0.002	
LVH						0.728
No	240 (42.86)	11/64	9/176	0.10 (0.02 ~ 0.60)	0.012	
Yes	320 (57.14)	73/234	11/86	0.35 (0.13 ~ 0.90)	0.029	
Age						0.914
<65	145 (25.89)	21/91	4/54	0.71 (0.14 ~ 3.67)	0.686	
>65	415 (74.11)	63/207	16/208	0.33 (0.15 ~ 0.70)	0.004	
Sex						0.543
Female	189 (33.75)	28/100	5/89	0.67 (0.11 ~ 4.11)	0.669	
Male	371 (66.25)	56/198	15/173	0.45 (0.20 ~ 0.98)	0.046	
BMI						0.575
<25	347 (61.96)	56/172	13/175	0.30 (0.13 ~ 0.72)	0.007	
>25	213 (38.04)	28/126	7/87	0.48 (0.14 ~ 1.71)	0.258	
Smoking						0.863
Current	98 (17.50)	17/73	4/25	0.38 (0.06 ~ 2.42)	0.304	
Former	462 (82.50)	67/225	16/237	0.38 (0.16 ~ 0.90)	0.028	
Diabetes						0.125
No	360 (64.29)	48/189	8/171	0.29 (0.10 ~ 0.80)	0.016	
Yes	200 (35.71)	36/109	12/91	0.57 (0.17 ~ 1.87)	0.354	
NYHA						0.075
II	304 (54.48)	33/136	11/168	0.30 (0.11 ~ 0.83)	0.020	
III	169 (30.29)	26/107	3/62	0.03 (0.01 ~ 0.47)	0.013	
IV	85 (15.23)	25/55	6/30	0.64 (0.10 ~ 4.00)	0.632	

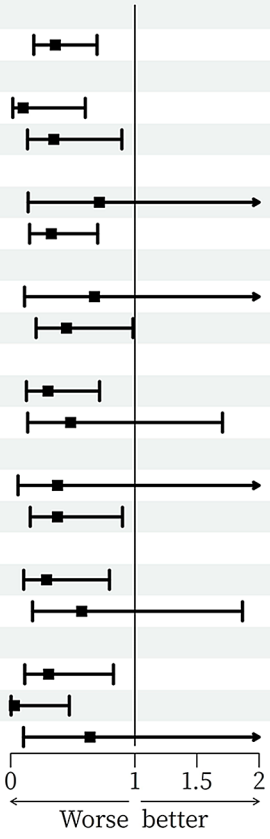

Fig. 4 Subgroup analyses were conducted to determine the predictive significance of remnant cholesterol for cardiovascular death. The dots and lines represent the hazard ratio estimates for cardiovascular death per unit increase in remnant cholesterol, along with their accompanying 95% confidence intervals. The multivariate Cox regression model was adjusted for sex, age, BMI, smoking status, drinking status, SBP, TC, Glu, NT-proBNP, TyG, antihypertensive drugs (ACEI/ARB/CCB), lipid-lowering drugs (statins), antiplatelet drugs (aspirin), antiarrhythmics (β-blockers/ivabradine) and antidiabetic drugs (metformin/sulfonylureas). However, the stratified variable was not included in the adjustment

Moreover, the results of the investigation showed a correlation between a higher risk of cardiovascular death and greater levels of RC. This connection was consistent across all stratified analyses, which suggests that RC possessed a high predictive value regardless of the covariates considered.

Previous studies have demonstrated the association between conventional lipids and the LV structure [10, 13, 14]. Additionally, in patients with diabetes mellitus, RC has been shown to exacerbate LV diastolic dysfunction [15]. These results provide more evidence that RC has an impact on the remodelling of the LV by causing negative alterations in its structure and function. According to recent research, the development of LVH in hypertensive individuals is significantly influenced by the triglyceride-glucose (TyG) index, which signifies insulin resistance [16, 17]. Increased TyG levels correlate with a greater risk of LVH, independent of blood pressure and BMI. To determine whether RC is an independent predictor of LVH, we included TyG also as a covariate in our analysis. Multivariate linear regression identified a correlation between RC levels at baseline and LV remodelling among hypertensive heart failure patients. Notably, individuals with LV hypertrophy, who tend to exhibit higher RC levels, demonstrate a solid association. RC calculations have been utilized in large-scale studies and have yielded reliable results. In ischaemic heart disease, RC can accumulate in the arterial intima, forming atherosclerotic plaques after being engulfed by immune cells and smooth muscle cells [18, 19]. This accumulation increases the risk of atherosclerosis progression and exacerbates LV remodelling. Increased arterial stiffness is indicated by an elevated RC [20], which may cause the left ventricle afterload to rise, resulting in compensatory remodelling of the left ventricle [21]. Research has also suggested that RC may contribute to cardiac inflammation [22]. The combination of these factors links RC to LV remodelling in patients.

It has been proven in prior studies that high levels of RC have a detrimental effect on the outcomes of cardiovascular disease [23–26]. A follow-up study involving 106,937 individuals in Copenhagen over 15 years showed that patients with higher RCs had a fivefold increase in peripheral arterial disease [27]. A large clinical study in

China focusing on RC and CAD combined with diabetes mellitus demonstrated that higher RC have been related to a poorer prognosis [28]. Importantly, HF and other cardiovascular problems may be more likely to occur if there are adverse alterations to the LV [29, 30]. A higher risk of unfavourable outcomes corresponds to a baseline RC greater than 0.49, which was found to be connected with an increased likelihood of developing LVH in this study.

Interestingly, a recent study shows a correlation between low admission RC levels and more excellent mortality rates in HF patients. This finding implies that higher RC levels could sustain the contractile activity of cardiomyocytes under HF settings by providing them with more energy [31]. This finding contradicts the results of most current studies, indicating the need for further larger-scale clinical research to validate these findings.

In the subgroup stratification analysis, we focused on age, BMI, smoking status, NYHA functional classification, diabetes status, and LVH status. It has been demonstrated that sulfonylureas, particularly gliclazide, can considerably reduce LVMI in type II diabetic patients [32]. Furthermore, increased LVMI and reduced diastolic function are likely to compromise glucose tolerance [33], given the large number of diabetics in our population. To ensure the study's reliability, daily medication use in diabetic patients and TyG, a biomarker of insulin resistance, were included as confounding variables. Independent of these confounding factors, the results demonstrated a robust association between RC levels and cardiovascular risk, crediting prior research and indicating that RC possesses substantial predictive power [34, 35]. In conclusion, our research findings reveal unique clinical evidence that supports the implementation of cholesterol control measures in patients with hypertension and HF.

Study strengths and limitations

This study has substantial clinical importance, given the large cohort of patients with hypertension and HF recruited and followed over an extended period. This study's results prove that RC screening should be done more frequently and earlier to better identify patients with LV remodelling and start treatment to improve prognosis. Additionally, our study provides novel and robust clinical evidence supporting lipid management strategies in patients with hypertension combined with HF, even after multivariable-adjusted analyses were conducted, thus demonstrating the importance of maintaining RC levels below 0.49 mmol/L. However, this study has several limitations worth noting. First, since we collected clinical baseline data from participants, there may have been changes during the follow-up period. Therefore, we may consider conducting continuous RC measurements for these patients in the future to ensure the reliability and accuracy of our data. In contrast to previous studies conducted in hypertensive populations [35], our hypertensive patient population lacked baseline data on the type of diet, physical activity, and type of job of the patients, so it was impossible to exclude the effects of these confounding variables.

Conclusions

According to the findings of this research, RC levels were found to be associated with LV remodelling in patients who had both hypertension and HF, with LVH having greater RC values. Consequently, RC could serve as a predictor for the diagnosis of LVH. Furthermore, elevated baseline RC was found to correlate with rising risk of cardiovascular death.

Abbreviations

RC	Remnant cholesterol
HF	Heart failure
LVH	Left ventricular hypertrophy
SBP	Systolic blood pressure, DBP, Diastolic blood pressure, HR, Heart rate
BMI	Body mass index
CHD	Coronary heart disease
CKD	Chronic kidney disease
CCB	Acronym calcium channel blockers
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
Glu	Fasting blood glucose LVDD: Left ventricular end-diastolic dimension
LVDS	Left ventricular end-systolic dimension
LVEF	Left ventricular ejection fraction
IVS	Interventricular septum
LAS	Left atrial dimension
LVPWD	Left ventricular posterior wall diameter
LVMI	Left ventricular mass index
ACEI	Angiotensin-converting enzyme inhibitor
ARB	Angiotensin II receptor blocker
NYHA	New York Heart Association (NYHA) functional classification
RCS	Restricted cubic spline
ROC	Receiver operating characteristic curves

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-024-02282-y.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Acknowledgements

We express gratitude to the professors who support us to write this article in the Department of Cardiology of Shanghai Tenth People's Hospital.

Author contributions

Conception and study design: WL, DJ. Administrative support: WL, YX. Provision of study materials or patients: JS, YZ, TW, ZZ. Collection and assembly of data: ZW, ZZ. Data analysis and interpretation: ZW, ZZ. Manuscript writing: ZW, WL. Final approval of manuscript: ZW, JS, YZ, TW, ZZ, WL, YX.

Funding

This study was supported by the Science and Technology Commission of Shanghai Municipality (Grant No. 22Y11910000).

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study has been registered in clinicaltrals.gov (NCT 03727828), approved by the local ethics committee of Shanghai Tenth People's Hospital.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Received: 17 April 2024 / Accepted: 31 August 2024
Published online: 12 September 2024

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