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Predictive Value of Remnant Cholesterol for Left Ventricular Hypertrophy and Prognosis in Hypertensive Patients with Heart

Abstract

Background: 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 remodeling and patients' prognoses.

Method: 630 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. The subjects were observed for a median of 58 months, and 104 participants met the primary endpoint. Multiple linear regression and receiver operating characteristic (ROC) curves examined the RC and LV remodelling relationship. A Cox regression analysis was conducted to examine the predictive value of RC for clinical outcomes.

Result: There were 560 people in total, split evenly between the 320 LVH patients and the 240 non-LVH patients. The LVH group presented significantly elevated values of RC, TC, and TG and decreased of HDLC. The optimal cut-off value for RC was 0.49. The risk models involving the two Cox models were adjusted to incorporate confounding factors. The study revealed that those with elevated baseline levels of RC were more susceptible to cardiovascular mortality, as shown by an elevated hazard ratio. (HR: 1.91, 95% CI: 1.62-2.26 vs. HR: 1.94, 95% CI: 1.64-2.32, $p < 0.001$).

Conclusion: 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.

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

to 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 non-HDL-C and lower HDL-C levels(4-6). RC is the kind of cholesterol neither high-density lipoproteins nor low-density lipoproteins carry. This 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, recent research has 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.

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) $>115 \text{ g/m}^2$ in males and $\geq 95 \text{ g/m}^2$ 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 Figure 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 hours. 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 $\pm$ 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 ratios (HRs) 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 utilisation of antihypertensive medications

(ACEI/ARB/CCB), lipid-lowering (statins), antiplatelet (aspirin), antiarrhythmics (β -blockers/ivabradine) or antidiabetic (metformin/sulfonylureas) drugs.

Table 1

Baseline RC is linked to the LV function.

Considering the possible correlation that exists in the initial RC and 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 Figure 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 cut-off 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 favorable association between the initial RC, LVDD, 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 cut-off 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 $p < 0.001$). (Figure 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 (Figure 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 remodeling, which mainly predicts LVH in hypertensive HF patients. Moreover, The results of the investigation showed a correlation between a higher risk of cardiovascular death and greater levels of RC. The 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 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 causes 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 study 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 and impaired glucose tolerance(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 unfavorable outcomes corresponds to a baseline RC greater than 0.49, which was found to be connection 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. Furthermore, increased LVMI and reduced diastolic function are likely to compromise glucose tolerance. Given the high 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 (32, 33). 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 earlier 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. Some studies have conducted continuous measurements of RC(10). 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(34), 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.

Conclusion

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.

References

1. Yildiz M, Oktay AA, Stewart MH, Milani RV, Ventura HO, Lavie CJ. Left ventricular hypertrophy and hypertension. *Prog Cardiovasc Dis.* 2020;63(1):10-21.
2. Lavie CJ, Patel DA, Milani RV, Ventura HO, Shah S, Gilliland Y. Impact of echocardiographic left ventricular geometry on clinical prognosis. *Prog Cardiovasc Dis.* 2014;57(1):3-9.
3. Kopin L, Lowenstein C. Dyslipidemia. *Ann Intern Med.* 2017;167(11):Itc81-ite96.
4. Aung N, Sanghvi MM, Piechnik SK, Neubauer S, Munroe PB, Petersen SE. The Effect of Blood Lipids on the Left Ventricle: A Mendelian Randomization Study. *J Am Coll Cardiol.* 2020;76(21):2477-88.
5. Horwich TB, Hernandez AF, Dai D, Yancy CW, Fonarow GC. Cholesterol levels and in-hospital mortality in patients with acute decompensated heart failure. *Am Heart J.* 2008;156(6):1170-6.
6. Mehra MR, Uber PA, Lavie CJ, Milani RV, Park MH, Ventura HO. High-density lipoprotein cholesterol levels and prognosis in advanced heart failure. *J Heart Lung Transplant.* 2009;28(9):876-80.
7. Tada H, Nohara A, Inazu A, Mabuchi H, Kawashiri MA. Remnant lipoproteins and atherosclerotic cardiovascular disease. *Clin Chim Acta.* 2019;490:1-5.
8. Liu H, Zhang J, Li Z, Liu J, Lian S, Le J. Association between remnant cholesterol and heart failure: A prospective cohort study. *Front Cardiovasc Med.* 2022;9:938647.
9. Jørgensen PG, Jensen MT, Biering-Sørensen T, Mogelvang R, Galatius S, Fritz-Hansen T, et al. Cholesterol remnants and triglycerides are associated with decreased myocardial function in patients with type 2 diabetes. *Cardiovasc Diabetol.* 2016;15(1):137.
10. Xu X, Wang Z, Huang R, Guo Y, Xiong Z, Zhuang X, et al. Remnant Cholesterol in Young Adulthood Is Associated With Left Ventricular Remodelling and Dysfunction in Middle Age: The CARDIA Study. *Circ Cardiovasc Imaging.* 2023;16(11):e015589.
11. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for managing arterial hypertension. *Eur Heart J.* 2018;39(33):3021-104.
12. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021;42(36):3599-726.
13. Rietzschel ER, Langlois M, De Buyzere ML, Segers P, De Bacquer D, Bekaert S, et al. Oxidized low-density lipoprotein cholesterol is associated with decreases in cardiac function independent of vascular alterations. *Hypertension.* 2008;52(3):535-41.
14. Gao S, Zhao D, Wang M, Zhao F, Han X, Qi Y, et al. Association Between Circulating Oxidized LDL and Atherosclerotic Cardiovascular Disease: A Meta-analysis of Observational Studies. *Can J Cardiol.* 2017;33(12):1624-32.
15. Wang R, Gerstein HC, Van Spall HGC, Lip GYH, Olier I, Ortega-Martorell S, et al. Relationship between remnant cholesterol and risk of heart failure in participants with diabetes mellitus. *Eur Heart J Qual Care Clin Outcomes.* 2023;9(5):537-45.
16. Su G, Cao H, Xu S, Lu Y, Shuai X, Sun Y, et al. Left atrial enlargement in the early stage of hypertensive heart disease: a common but ignored condition. *J Clin Hypertens (Greenwich).* 2014;16(3):192-7.
17. Zhai Y, Fu H, Li Y, Li S, Zhang W, Yue J, et al. Relationship between four insulin resistance surrogates and left ventricular hypertrophy among hypertensive adults: a case-control

study. *Endocr Connect*. 2024;13(4).

18. Borén J, Williams KJ. The central role of arterial retention of cholesterol-rich apolipoprotein-B-containing lipoproteins in the pathogenesis of atherosclerosis: a triumph of simplicity. *Curr Opin Lipidol*. 2016;27(5):473-83.

19. Varbo A, Nordestgaard BG. Directly measured vs. calculated remnant cholesterol identifies additional overlooked individuals in the general population at higher risk of myocardial infarction. *Eur Heart J*. 2021;42(47):4833-43.

20. Liu J, Fan F, Liu B, Li K, Jiang Y, Jia J, et al. Association between remnant cholesterol and arterial stiffness in a Chinese community-based population: A cross-sectional study. *Front Cardiovasc Med*. 2022;9:993097.

21. Ohya Y, Ambale-Venkatesh B, Noda C, Chugh AR, Teixido-Tura G, Kim JY, et al. Association of Aortic Stiffness With Left Ventricular Remodelling and Reduced Left Ventricular Function Measured by Magnetic Resonance Imaging: The Multi-Ethnic Study of Atherosclerosis. *Circ Cardiovasc Imaging*. 2016;9(7).

22. Murphy SP, Kakkar R, McCarthy CP, Januzzi JL, Jr. Inflammation in Heart Failure: JACC State-of-the-Art Review. *J Am Coll Cardiol*. 2020;75(11):1324-40.

23. Langsted A, Madsen CM, Nordestgaard BG. Contribution of remnant cholesterol to cardiovascular risk. *J Intern Med*. 2020;288(1):116-27.

24. Deng J, Tang R, Chen J, Zhou Q, Zhan X, Long H, et al. Remnant cholesterol as a risk factor for all-cause and cardiovascular mortality in incident peritoneal dialysis patients. *Nutr Metab Cardiovasc Dis*. 2023;33(5):1049-56.

25. Chen Y, Li G, Guo X, Ouyang N, Li Z, Ye N, et al. The Effects of Calculated Remnant-Like Particle Cholesterol on Incident Cardiovascular Disease: Insights from a General Chinese Population. *J Clin Med*. 2021;10(15).

26. Castañer O, Pintó X, Subirana I, Amor AJ, Ros E, Hernáez Á, et al. Remnant Cholesterol, Not LDL Cholesterol, Is Associated With Incident Cardiovascular Disease. *J Am Coll Cardiol*. 2020;76(23):2712-24.

27. Wadström BN, Wulff AB, Pedersen KM, Jensen GB, Nordestgaard BG. Elevated remnant cholesterol increases the risk of peripheral artery disease, myocardial infarction, and ischaemic stroke: a cohort-based study. *Eur Heart J*. 2022;43(34):3258-69.

28. Hu X, Liu Q, Guo X, Wang W, Yu B, Liang B, et al. The role of remnant cholesterol beyond low-density lipoprotein cholesterol in diabetes mellitus. *Cardiovasc Diabetol*. 2022;21(1):117.

29. Choi EY, Rosen BD, Fernandes VR, Yan RT, Yoneyama K, Donekal S, et al. Prognostic value of myocardial circumferential strain for incident heart failure and cardiovascular events in asymptomatic individuals: the Multi-Ethnic Study of Atherosclerosis. *Eur Heart J*. 2013;34(30):2354-61.

30. de Hartog-Keyzer JM, Pop VJ, Rodwell L, Nijveldt R, Messaoudi SE. Prediction of cardiovascular events in older patients with hypertension in primary care: a cohort study. *Br J Gen Pract*. 2024;74(741):e219-e26.

31. Zhao L, Zhao X, Tian P, Liang L, Huang B, Huang L, et al. Predictive value of remnant cholesterol level for all-cause mortality in heart failure patients. *Front Cardiovasc Med*. 2023;10:1063562.

32. Cao YX, Zhang HW, Jin JL, Liu HH, Zhang Y, Gao Y, et al. The longitudinal association

of remnant cholesterol with cardiovascular outcomes in patients with diabetes and pre-diabetes. *Cardiovasc Diabetol*. 2020;19(1):104.

33. Wadström BN, Pedersen KM, Wulff AB, Nordestgaard BG. Elevated remnant cholesterol and atherosclerotic cardiovascular disease in diabetes: a population-based prospective cohort study. *Diabetologia*. 2023;66(12):2238-49.

34. Joseph G, Marott JL, Biering-Sørensen T, Johansen MN, Saeveid HA, Nielsen G, et al. Level of Physical Activity, Left Ventricular Mass, Hypertension, and Prognosis. *Hypertension*. 2020;75(3):693-701.

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