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Cross-Sectional Associations of Lipid Concentrations to Left Ventricular Structural Attributes

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Abstract

Although previous investigations reported on the associations of lipid concentrations with left ventricular remodeling in specific sub-populations, few data exist on these associations in a community-based sample of individuals without cardiovascular disease. We examined 3554 Framingham Heart Study participants (mean age 47 years; 53% women) without pre-existing clinical cardiovascular disease, and did not observe any meaningful associations of high-density lipoprotein cholesterol or non-high density lipoprotein cholesterol with echocardiographic indices of left ventricular structure. In conclusion, our data do not support an independent association between lipid concentrations and left ventricular structure.

Keywords

left ventricle; remodeling; lipids; epidemiology

Introduction

Dyslipidemia is a key risk factor for coronary heart disease (CHD) and cardiovascular death.[1] Several lines of experimental and clinical observations also associate abnormal lipid concentrations with systolic and diastolic left ventricular (LV) function,[2,3] peripheral vascular resistance,[4] aortic stiffness[5] and LV remodeling after myocardial infarction (MI).[6] These observations raise the possibility of dyslipidemia-induced LV remodeling. Such an association, however, has not been systematically investigated in people without prevalent CHD. We therefore evaluated the cross-sectional associations of blood lipid concentrations to echocardiographic indices of LV structure. We hypothesized that increasing concentrations of non-high density lipoprotein cholesterol (non-HDL-C) are associated with increasing LV mass

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(LVM), LV end-diastolic dimension (LVDD), LV end-systolic dimension (LVSD) and LV wall thickness (LVWT). We also posited that HDL-C concentrations have opposite associations (relative to non-HDL-C) to these echocardiographic measures.

Methods

The details of the Framingham Heart Study original[7] and offspring[8] cohorts have been published previously. Attendees at examination cycle 16 (1979–1982; n = 2351) of the original cohort and at examination cycle 2 (1979–1983; n = 3863) of the offspring cohort were eligible for the present investigation. We excluded participants with the following conditions at these examinations: MI (n = 111), heart failure (n = 69), valvular heart disease (n = 152), estimated glomerular filtration rate < 60ml/min/1.73m^2 (n = 609), current use of antihypertensive (n = 936) or lipid-modifying therapy (n = 34), and missing covariate or echocardiographic data (n = 749). A total of 3558 participants (1666 men; 1888 women) formed the sample for this investigation. All participants provided written informed consent and the study protocol was approved by the Institutional Review Board of Boston University Medical Center.

Plasma samples for lipid measurement were collected in 0.1% EDTA and lipid concentrations were measured on freshly drawn plasma before freezing. Total cholesterol was measured by the Abell and Kendall method. HDL-C was measured after heparin-manganese chloride precipitation. HDL-C was subtracted from total cholesterol to calculate non-HDL-C.

We measured LVDD, LVSD, and the end-diastolic thicknesses of the interventricular septum (IVS) and LV posterior wall (LVPW) from two-dimensionally-guided M-mode echocardiograms (which were performed at the examination where lipids and covariates were assessed) according to American Society of Echocardiography recommendations.[9] LVM[10] and LVWT were calculated as: LVM (gm) = $0.8\{1.04[(\text{LVDD+IVS+LVPW})^3 - (\text{LVDD})^3]\} + 0.6$; LVWT= IVS+LVPW.

We related non-HDL-C and HDL-C concentrations separately to each echocardiographic measure individually in sex-specific multivariable-adjusted general linear models that included the following covariates: age, body mass index, systolic blood pressure, diabetes and current smoking. A two-sided p-value < 0.05 denoted statistical significance.

Results

The clinical, lipid and echocardiographic characteristics of the study sample are presented in Table 1. In women, we observed a small inverse relationship of non-HDL-C concentrations to LVDD and LVSD (Table 2.B); non-HDL-C was not associated with any other echocardiographic variables. In men, we observed a small inverse relationship of non-HDL-C concentrations to LVM, LVWT and LVDD, but not to LVSD (Table 2.B). We observed no statistically significant associations between HDL-C and any of the LV measures in men or women (Table 2.A).

Discussion

Experimental evidence suggests that dyslipidemia has deleterious effects on systolic and diastolic LV function and on LV remodeling in response to injury.[2,6] Investigators also have reported that dyslipidemia is related to altered LV geometry.[4] In our present study, we did not find any demonstrable associations of non-HDL-C and HDL-C to LV structure. The statistically significant associations between non-HDL-C and some of the echocardiographic measures are of small magnitude and in a direction opposite to our a priori hypothesis, and may reflect chance findings.

Previous investigations addressing the associations of lipid concentrations with indices of LV structure were case series[3,11,12] or small case-control studies,[4] or based on samples confined to those with treated[11] or untreated[12] hypertension or people with coronary artery disease[3] whereas our investigation evaluated a community-based sample after excluding participants with conditions commonly associated with LV remodeling. Thus prior reports may have overestimated the relationship between lipids and LV remodeling, and our null results are probably reflective of a lack of true association.

Our investigation used observational data. Therefore, we cannot exclude residual confounding, or that lipids are an intermediate mechanism between other factors (diabetes, etc) and changes in LV structure. Our sample consisted of middle-aged to elderly white adults of European descent; the generalizability to younger individuals or other ethnicities is uncertain. Lipid concentrations are highly variable and a single measurement may not be adequate to clearly evaluate their contribution to LV remodeling. M-mode echocardiography has limitations, particularly for the assessment of three-dimensional changes in LV structure; newer, higher precision imaging modalities like cardiovascular magnetic resonance imaging may help further clarify the associations between lipid concentrations and LV structure. Our study is cross-sectional and cannot evaluate if lipid concentrations are related to longitudinal changes in LV measures.

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Table 1

Characteristics of Participants by Sex

Variable	Men (N = 1666)	Women (N =1888)
Age (years)	47 (13)	47 (14)
Body mass index (kg/m^2)	26.3 (3.5)	24.5 (4.4)
Systolic blood pressure (mm Hg)	126 (16)	120 (18)
Diabetes Mellitus	4%	2%
Smokers	35%	36%
High Density Lipoprotein Cholesterol (mg/dl)	42 (36–50)	53 (45–63)
Non-High Density Lipoprotein Cholesterol (mg/dl)	159 (133–185)	146 (121–76)
Echocardiographic Traits		
Left Ventricular Mass (gm)	186 (42)	128 (29)
Left Ventricular Wall Thickness (cm)	1.9 (0.3)	1.7 (0.2)
Left Ventricular End-Diastolic Dimension (cm)	5.1 (0.4)	4.6 (0.4)
Left Ventricular End-Systolic Dimension (cm)	3.3 (0.4)	2.9 (0.3)

Cells present mean (standard deviation) for age, body mass index, systolic blood pressure and echocardiographic traits, percentages for diabetes and smoking, and median (interquartile range; Q1 – Q3) for high density lipoprotein cholesterol and non- high density lipoprotein cholesterol.

Table 2

Multivariable Analyses Relating Lipid Concentrations to Echocardiographic Measures

Variable	Men (N = 1666)		Women (N =1888)	
	β (SE)	p-value	β (SE)	p-value
A. Relations of High Density Lipoprotein Cholesterol to Echocardiographic Traits				
Left Ventricular Mass (gm)	1.25 (1.00)	0.21	−0.22 (0.60)	0.72
Left Ventricular Wall Thickness (cm)	0.001 (0.01)	0.81	−0.01 (0.01)	0.052
Left Ventricular End-Diastolic Dimension (cm)	0.01 (0.01)	0.16	0.01 (0.01)	0.11
Left Ventricular End-Systolic Dimension (cm)	0.01 (0.01)	0.38	0.01 (0.01)	0.33
B. Relations of Non-High Density Lipoprotein Cholesterol to Echocardiographic Traits				
Left Ventricular Mass (gm)	−3.76 (1.01)	0.0002	−0.03 (0.02)	0.08
Left Ventricular Wall Thickness (cm)	−0.01 (0.01)	0.02	0.00 (0.00)	0.83
Left Ventricular End-Diastolic Dimension (cm)	−0.03 (0.01)	0.005	−0.0006 (0.0002)	0.003
Left Ventricular End-Systolic Dimension (cm)	−0.02 (0.01)	0.08	−0.0004 (0.0002)	0.02

β (SE) = beta-coefficient estimate (standard error)