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# Pericardial, But Not Hepatic, Fat by CT Is Associated With CV Outcomes and Structure

## The Multi-Ethnic Study of Atherosclerosis

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## ABSTRACT

**OBJECTIVES** The study sought to determine the associations between local (pericardial) fat and incident cardiovascular disease (CVD) events and cardiac remodeling independent of markers of overall adiposity.

**BACKGROUND** The impact of pericardial fat—a local fat depot encasing the heart—on myocardial function and long-term CV prognosis independent of systemic consequences of adiposity or hepatic fat is an area of active debate.

**METHODS** We studied 4,234 participants enrolled in the MESA (Multi-Ethnic Study of Atherosclerosis) study with concomitant cardiac magnetic resonance imaging and computed tomography (CT) measurements for pericardial fat volume and hepatic attenuation (a measure of liver fat). Poisson and Cox regression were used to estimate the annualized risk of incident hard atherosclerotic CVD (ASCVD), all-cause death, heart failure, all-cause CVD, hard coronary heart disease, and stroke as a function of pericardial and hepatic fat. Generalized additive models were used to assess the association between cardiac magnetic resonance indices of left ventricular (LV) structure and function and pericardial fat. Models were adjusted for relevant clinical, demographic, and cardiometabolic covariates.

**RESULTS** MESA study participants with higher pericardial and hepatic fat were more likely to be older, were more frequently men, and had a higher prevalence of cardiometabolic risk factors (including dysglycemia, dyslipidemia, hypertension), as well as adiposity-associated inflammation. Over a median 12.2-year follow-up (interquartile range: 11.6 to 12.8 years), pericardial fat was associated with a higher rate of incident hard ASCVD (standardized hazard ratio: 1.22; 95% confidence interval: 1.10 to 1.35; $p = 0.0001$). Hepatic fat by CT was not significantly associated with hard ASCVD (standardized hazard ratio: 0.96; 95% confidence interval: 0.86 to 1.08; $p = 0.52$). Higher pericardial fat was associated with greater indexed LV mass (37.8 g/m$^{2.7}$ vs. 33.9 g/m$^{2.7}$, highest quartile vs. lowest quartile; $p < 0.01$), LV mass-to-volume ratio (1.2 vs. 1.1, highest quartile vs. lowest quartile; $p < 0.01$). In adjusted models, a higher pericardial fat volume was associated with greater LV mass ($p < 0.0001$) and concentricity ($p < 0.0001$).

**CONCLUSIONS** Pericardial fat is associated with poorer CVD prognosis and LV remodeling, independent of insulin resistance, inflammation, and CT measures of hepatic fat. (J Am Coll Cardiol Img 2017;■:■–■)
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**ABBREVIATIONS AND ACRONYMS**

**ASCVD** = atherosclerotic cardiovascular disease

**BMI** = body mass index

**CHD** = coronary heart disease

**CI** = confidence interval

**CMR** = cardiac magnetic resonance

**CT** = computed tomography

**CVD** = cardiovascular disease

**GAM** = generalized additive model

**HOMA-IR** = homeostatic model assessment for insulin resistance

**IDI** = integrated discrimination index

**LV** = left ventricular

**LVEF** = left ventricular ejection fraction

Obesity is associated with subclinical abnormalities in cardiovascular (CV) structure and function that predispose to heart failure (HF) (1–5). The adverse CV effects of obesity are postulated to originate in part from proinflammatory adipose tissue depots that exert toxic effects on the heart either locally (e.g., pericardial fat) or remotely via inflammation or insulin resistance. Although several recent investigations have suggested that visceral and hepatic fat may play a primary role in CV disease (CVD) risk and myocardial remodeling (6,7), an emerging body of evidence supports the idea that pathologic expansion of pericardial fat—generally felt to be a cache of metabolic fuel for the heart—may function as a visceral-like fat depot, promoting atrial fibrillation, coronary artery calcification, and vascular disease (7–9). Indeed, a case-control study conducted early during the MESA (Multi-Ethnic Study of Atherosclerosis) study demonstrated that pericardial fat, but not body mass index (BMI) or waist circumference (markers of overall and regional adiposity), was associated with coronary heart disease (CHD) (10). Given a potential metabolic and proinflammatory role for pericardial fat, evaluating its impact on CV risk and structure is warranted.

To address this important issue, we investigated the association between pericardial fat and CVD outcomes after accounting for systemic markers of adiposity (insulin resistance and inflammation) and measures of hepatic fat in the MESA study. We further sought to understand the relationship between pericardial fat and CV structure using comprehensive cardiac magnetic resonance (CMR) assessment of left ventricular (LV) structure and function. We hypothesized that greater pericardial fat would be associated with poorer CVD outcomes and prevalent abnormalities in LV structure and function by CMR.

## METHODS

**STUDY POPULATION.** The overall design of the MESA study has been described previously (11). Briefly, the MESA study is a longitudinal cohort study consisting of 6,814 men and women 45 to 84 years of age, free of clinical CV disease at study enrollment. Participants were enrolled from July 2000 through August 2002 in Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; New York, New York; and St. Paul, Minnesota (12). At the baseline visit (exam 1), standardized questionnaires were used to collect information on demographics, income and education, medical history, medication use, smoking status, alcohol use, and physical activity. Physical activity was calculated based on duration and intensity of total intentional exercise (metabolic equivalent minutes/week). Resting blood pressure, fasting blood glucose and insulin, BMI, and dysglycemia status were also assessed at exam 1, as described (13). The homeostatic model assessment was used to quantify insulin resistance (homeostatic model assessment for insulin resistance [HOMA-IR]; fasting insulin × fasting glucose/405) (13). C-reactive protein was measured as described (14).

From the initial MESA cohort studied at exam 1, we excluded patients with missing liver attenuation (or liver attenuation values >200 Hounsfield units, n = 201), missing pericardial fat volume (n = 25), those not included in CMR assessment of LV structure and function (n = 1,804), cirrhosis (n = 9), significant alcohol use (>7 drinks per week in women and >14 drinks per week in men; n = 232), and self-reported cancer (n = 345) or kidney disease (n = 99), yielding

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