Association of Epicardial Fat With Cardiovascular Risk Factors and Incident Myocardial Infarction in the General Population

The Heinz Nixdorf Recall Study

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Objectives
This study sought to determine whether epicardial fat volume predicts coronary events in the general population.

Background
Epicardial adipose tissue (EAT) is suggested to promote plaque development in the coronary artery tree.

Methods
We quantified EAT volume in participants from the prospective population-based Heinz Nixdorf Recall cohort study free of cardiovascular disease. Incident coronary events were assessed during a follow-up period of 8.0 ± 1.5 years. Multivariable association of EAT with cardiovascular risk factors, coronary artery calcification (CAC), and coronary events was assessed using regression analysis.

Results
From the overall 4,093 participants (age 59.4 years, 47% male), 130 subjects developed a fatal or nonfatal coronary event. Incidence of coronary events increased by quartile of EAT (0.9% vs. 4.7% for 1st and 4th quartile, respectively, p < 0.001). Doubling of EAT was associated with a 1.5-fold risk of coronary events when adjusting for cardiovascular risk factors (hazard ratio [HR] [95% confidence interval (CI)]: 1.54 [1.09 to 2.19]), which remained unaltered after further adjustment for CAC score (HR [95% CI]: 1.50 [1.07 to 2.11]). For discrimination of subjects with events from those without, we observed a trend for improvement of Harrell’s C and explained variance by EAT over traditional cardiovascular risk factors, which, however, did not reach statistical significance (0.720 to 0.730 for risk factors alone and with EAT added, respectively, p = 0.10, R² from 2.73% to 2.92%, time-dependent integrated discrimination improvement = 0.196%).

Conclusions
Epicardial fat is associated with fatal and nonfatal coronary events in the general population independent of traditional cardiovascular risk factors and complements information from cardiac computed tomography above the CAC score. (J Am Coll Cardiol 2013;61:1388–95) © 2013 by the American College of Cardiology Foundation

Epicardial adipose tissue (EAT) is a visceral adipose tissue surrounding the heart and the coronary arteries. Because of its endocrine and paracrine activity, secreting pro-inflammatory and anti-inflammatory cytokines and chemokines, it has been suggested to influence coronary atherosclerosis development (1–5). EAT is associated with cardiovascular risk factors (6,7), coronary atherosclerosis (8–10), and prevalent coronary artery disease (11–13). In addition, a case-control study, drawn from the MESA (Multi-Ethnic Study of Atherosclerosis), suggested a role of increased EAT volume for coronary event manifestation (14). However, to date, large-population–based longitudinal data on the prognostic value of EAT fat for prediction of hard coronary events are lacking.

Cardiac computed tomography (CT) imaging of the heart is the gold standard for EAT quantification with non-contrast enhanced cardiac CT enabling risk assessment through coronary artery calcification (CAC) quantification.

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(15–17). However, because EAT is associated with coronary atherosclerosis, implications of EAT on risk assessment above CAC remains unknown.

Therefore, the aim of the present study was to determine the association of epicardial fat volume with incident fatal and nonfatal coronary events in the population-based cohort of the Heinz Nixdorf Recall study. Furthermore, we aimed to investigate whether or not a potential prognostic value of EAT is independent of CAC.

Methods

Study cohort. The Heinz Nixdorf Recall study is a population-based prospective cohort study, designed to assess the predictive value of novel markers for risk stratification in addition to traditional cardiovascular risk factors. The participants (age 45 to 75 years) were randomly selected from mandatory lists of residence from the 3 adjacent cities of Bochum, Essen, and Mülheim, and enrolled between 2000 and 2003. Details for recruitment and study design have been previously published (15,18). Overall response rate was 56%. For this analysis, we excluded subjects with known coronary artery disease, history of myocardial infarction, or history of open heart surgery (including bypass and valve surgery) at baseline. All participants provided written informed consent, and the study was approved by the institutional ethics committee.

Cardiovascular risk factor assessment. Traditional cardiovascular risk factors were measured at baseline, with details being previously published (19). Waist circumference was measured at the leanest circumference between the costal arch and the iliac crest. Standardized enzymatic methods were used to determine serum total cholesterol level, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol. Diabetes was defined as a history of diabetes, being on medical treatment for diabetes, or having blood glucose levels as previously published (20). Smoking history was classified in current and former smokers, as well as in patients with no history of smoking, assessed by computer-assisted interview (21).

Cardiac CT. As part of the study, subjects underwent cardiac CT for quantification of artery CAC. Electron beam CT scans were performed utilizing a C-100 or C-150 scanner (GE Imatron, South San Francisco, California) without the use of contrast media. Imaging was prospectively triggered at 80% of the RR interval, and contiguous 3-mm-thick slices from the right pulmonary artery to the diaphragm were obtained at an image acquisition time of 100 ms. CAC was defined as a focus of at least 4 contiguous pixels with a CT density >130 Hounsfield units (HU) and quantified using the Agatston method (22).

Epicardial fat volume quantification. Epicardial fat volume was assessed using a dedicated workstation. The pericardium was manually traced from the right pulmonary artery to the diaphragm to determine a region of interest. Within the region of interest, fat was defined as pixels within a window of −195 to −45 HU and a window center of −120 HU. Overall, only pixels with Hounsfield units equivalent to fat within the pericardial sac were counted as epicardial adipose tissue. Reproducibility was excellent (intraclass correlation coefficient = 0.988, p < 0.0001, for interobserver and intraclass correlation coefficient = 0.996, p < 0.0001, for intraobserver variability). Details of EAT quantification have been previously described in detail (8). In addition to overall epicardial fat volume, we determined the pericoronary fat area of each of the 3 coronary vessels in a subgroup of participants that received initial revascularization of a single coronary artery for acute treatment of the coronary event. Therefore, the area of the epicardial fat around the coronary artery in the middle of the proximal segment was quantified by manual delineation after 3-dimensional reconstruction of an image perpendicular to the coronary vessel.

Follow-up and endpoint definition. Primary endpoints were defined as incident coronary events that met predefined study criteria as previously described (18). In brief, questionnaires on the current state of health including questions about current medications, hospital admissions, and outpatient diagnosis of cardiovascular disease were annually sent to the participants. In parallel, all death certificates were regularly screened. Incident cardiovascular morbidity and fatal events were validated by review of hospital records and records of the attending physicians, and classified by an external endpoint committee, blinded to the risk factor status and the CAC score. Myocardial infarction was defined based on symptoms, electrocardiographic signs, and enzymes (levels of creatine kinase, as well as troponin T or I), and necropsy as: 1) nonfatal acute myocardial infarction; and 2) coronary death.

Statistical analysis. Continuous variables are reported as mean ± SD or median (interquartile range). Discrete variables are given in frequency and percent. Distribution of cardiovascular risk factors was assessed per quartiles of EAT. Differences between quartiles of EAT were assessed using trend test (tests for non-zero Spearman correlation). Linear regression analysis was used to investigate the multivariable-adjusted association of EAT with cardiovascular risk factors, including age, sex, waist circumference, systolic blood pressure, hypertensive medication, diabetes, and smoking. Log2(EAT) was used to adjust for right skewness of EAT volume, and regression coefficients were retransformed to demonstrate multiplicative effect sizes on EAT volume related to covariates. Likewise, the association of EAT with CAC was assessed using linear regression
analysis, adjusting for cardiovascular risk factors. Due to the distributional properties of log(CAC + 1), we cross-checked the association of EAT and CAC using tertiles of CAC. In this model, CAC increases the coefficient of determination with a negative regression coefficient, which hints towards CAC being a negative suppressor in the model (23). Partial correlation further demonstrates this effect. Mean epicardial fat volume in subjects with and without events was compared using t test, and a smoothed kernel estimate was used to depict differences in distribution between both groups. Association of EAT with coronary events during follow-up was assessed using Cox regressions with adjustment sets as follows: 1) unadjusted; 2) age and sex adjusted; 3) additional adjustment for traditional risk factors including waist circumference, systolic blood pressure, hypertensive medication, LDL-cholesterol, HDL-cholesterol, lipid-lowering medication, diabetes, smoking; and 4) model 3 + CAC score (as log(CAC + 1) or as tertiles of CAC). Hazard ratios (HRs) were calculated per each doubling of EAT (log2(EAT)). Due to the high correlation of waist circumference, systolic blood pressure, hypertensive medication, diabetes, smoking; and 4) model 3 + CAC score (as log(CAC + 1) or as tertiles of CAC). Hazard ratios (HRs) were calculated per each doubling of EAT (log2(EAT)). Due to the high correlation of waist circumference and body mass index in our cohort (r = 0.81, p < 0.0001), ancillary adjustment of body mass index in multivariable models was not possible. For sex- and CAC-specific analyses, unadjusted models were used due to the limited amount of events in each subgroup.

Pericoronary fat area was normally distributed. A t test was used to evaluate a potential difference in pericoronary fat area in vessels with the culprit lesion compared with those without.

To investigate a predictive value of EAT (log2(EAT)), Harrell’s C and time-dependent integrated discrimination improvement (IDI(t)) were used (24). All analyses were performed using SAS software (version 9.2, SAS Institute, Cary, North Carolina) except comparison of Harrell’s C, which was evaluated using Stata/IC version 11.2 (StataCorp LP, College Station, Texas). A p value of <0.05 indicated statistical significance.

## Results

In this analysis, 4,093 subjects (mean age 59.4 years, 47.1% men) were included with detailed study characteristics depicted in Table 1. From the initial cohort of 4,814 subjects (response rate 56%), 327 subjects were excluded due to coronary heart disease at baseline, and 9 of the remaining individuals had prior valve surgery. A CT scan was not available for EAT quantification in an additional 313 subjects, and 1 or more covariables were missing in 72 of the remaining individuals.

Overall, EAT volume showed a wide range with a median (quartile 1; quartile 3) volume of 85.9 ml (61.4; 120.9; range 12.99 to 390.0 ml). Prevalence of traditional cardiovascular risk factors increased with quartiles of EAT (all p < 0.05) (Table 1). This trend remained in multivariable analysis, with EAT being significantly associated with all investigated risk factors except for systolic blood pressure and lipid-lowering medication (Table 2). Similar results were observed when stratifying by sex (detailed data not shown).

In univariate analysis, the median CAC score increased with quartiles of EAT (1.0 for the 1st quartile, 58.8 for the 4th quartile, p < 0.001). However, there was a trend towards lower EAT in subjects with increased CAC score after adjusting for traditional cardiovascular risk factors, with a multiplicative effect size below unity (0.99 [95% confidence interval (CI): 0.99 to 1.00], p = 0.02), yet

### Table 1 Baseline Characteristics of the Entire Cohort and Stratified by Quartiles of Epicardial Fat

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (N = 4,093)</th>
<th>1st Quartile (n = 1,023)</th>
<th>2nd Quartile (n = 1,022)</th>
<th>3rd Quartile (n = 1,024)</th>
<th>4th Quartile (n = 1,024)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>59.4 ± 7.8</td>
<td>56.8 ± 7.5</td>
<td>59.0 ± 7.4</td>
<td>60.0 ± 7.8</td>
<td>61.7 ± 7.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Men</td>
<td>1,928 (47.1)</td>
<td>218 (21.3)</td>
<td>391 (38.3)</td>
<td>559 (54.6)</td>
<td>760 (74.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>93.7 ± 13.3</td>
<td>82.8 ± 10.0</td>
<td>90.1 ± 9.8</td>
<td>96.8 ± 9.6</td>
<td>105.2 ± 11.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>132.9 ± 20.7</td>
<td>125.3 ± 20.2</td>
<td>130.6 ± 19.7</td>
<td>136.2 ± 20.2</td>
<td>139.5 ± 20.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>81.5 ± 10.8</td>
<td>78.0 ± 10.3</td>
<td>80.8 ± 10.0</td>
<td>82.8 ± 10.8</td>
<td>84.4 ± 11.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antihypertensive medication</td>
<td>1,309 (32.0)</td>
<td>193 (18.9)</td>
<td>281 (27.5)</td>
<td>345 (33.7)</td>
<td>490 (47.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>231.1 ± 38.8</td>
<td>226.1 ± 37.0</td>
<td>233.4 ± 38.7</td>
<td>232.9 ± 38.7</td>
<td>232.0 ± 40.2</td>
<td>0.002</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dl</td>
<td>146.8 ± 36.1</td>
<td>138.2 ± 35.4</td>
<td>149.2 ± 36.7</td>
<td>149.9 ± 34.8</td>
<td>150.0 ± 36.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dl</td>
<td>59.0 ± 17.2</td>
<td>66.9 ± 17.9</td>
<td>60.9 ± 16.1</td>
<td>56.4 ± 16.0</td>
<td>51.7 ± 15.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lipid-lowering medication use</td>
<td>366 (8.9)</td>
<td>64 (6.3)</td>
<td>86 (8.4)</td>
<td>111 (10.8)</td>
<td>105 (10.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>508 (12.4)</td>
<td>40 (3.9)</td>
<td>77 (7.5)</td>
<td>167 (16.3)</td>
<td>224 (21.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>Current</td>
<td>947 (23.1)</td>
<td>225 (22.0)</td>
<td>214 (21.0)</td>
<td>251 (24.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Former</td>
<td>1,357 (33.2)</td>
<td>269 (26.3)</td>
<td>313 (30.6)</td>
<td>355 (34.7)</td>
<td>420 (41.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Never</td>
<td>1,789 (43.7)</td>
<td>529 (51.7)</td>
<td>495 (48.4)</td>
<td>418 (40.8)</td>
<td>347 (33.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CAC score</td>
<td>12.6 (0.0–116.0)</td>
<td>1.0 (0–37.9)</td>
<td>4.1 (0–62.4)</td>
<td>21.9 (10–129.7)</td>
<td>58.8 (77–246.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epicardial fat volume, cm³</td>
<td>85.9 (61.4–120.9)</td>
<td>47.6 (38.9–54.6)</td>
<td>73.1 (67.4–79.6)</td>
<td>101.2 (94.0–110.6)</td>
<td>150.5 (133.7–178.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fatal or nonfatal coronary event</td>
<td>130 (3.2)</td>
<td>9 (0.9)</td>
<td>22 (2.2)</td>
<td>51 (5.0)</td>
<td>48 (4.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are mean ± SD, n (%), or median (interquartile range). CAC = coronary artery calcification; HDL = high-density lipoprotein; LDL = low-density lipoprotein.
Epicardial fat volume and coronary events. During a mean follow-up period of 8.0 ± 1.5 years, fatal or nonfatal coronary events occurred in 130 subjects (3.2%; 39 fatal, 91 nonfatal). Coronary events were more prevalent in men than in women (91 vs. 39 events, p < 0.001). Subjects with incident coronary events were older and had higher systolic and diastolic blood pressure, higher waist circumference, lower HDL-cholesterol levels, and a higher frequency of antihypertensive medication use, diabetes, and smoking compared with event-free subjects (all p < 0.05). Total cholesterol levels and frequency of lipid-lowering medication use were not different between both groups (all p > 0.15). Epicardial fat volume was higher in subjects with events (121 ml vs. 95 ml, p < 0.001) (Fig. 1). Likewise, frequencies of incident coronary events increased with the amount of EAT, with subjects in the highest quartile of EAT having a 5-fold higher risk compared with subjects in the lowest quartile (Table 1,Fig. 2). In univariate analysis, doubling of EAT was associated with more than 2-fold increase of the HR for coronary events (Table 3). After adjustment for cardiovascular risk factors, EAT volume remained independently associated with coronary events. In addition, the HR remained unchanged after further adjustment for CAC score (Table 3). Using tertiles of CAC instead of CAC as a continuous variable showed similar results (HR [95% CI]: 1.55 [1.10 to 2.19], p = 0.01). Stratifying by sex, we observed a trend towards a stronger association of EAT with coronary events in female compared with male subjects (HR [95% CI]: 2.85 [1.76 to 4.63] vs. 1.55 [1.11 to 2.16]). When further stratifying by the amount of coronary calcification using a CAC score of 100 as the threshold, we observed higher HRs for subjects with no or mild calcification compared with subjects with CAC scores >100 (HR [95% CI]: 2.50 [1.27 to 4.92] and 2.80 [1.44 to 5.45] for CAC <100 vs. 1.11 [0.76 to 1.62] and 1.91 [0.94 to 3.88] for CAC >100 for male and female subjects, respectively) (Fig. 3). For subjects with CAC = 0,
similar HRs as for CAC <100 were observed; however, analysis was limited by the low number of events in these subgroups (detailed data not shown).

Of the 91 subjects with nonfatal coronary events, 60 subjects received initial revascularization of a single coronary artery for acute treatment (the left anterior descending coronary artery in 24 cases, the left circumflex in 16 cases, and the right coronary artery in 20 cases). Within this subgroup, mean pericoronary fat area was 324 ± 158 mm². Coronary arteries that developed a culprit lesion during follow-up causing a coronary event had significantly higher pericoronary fat area at baseline (378 ± 183 mm² vs. 297 ± 138 mm², respectively, p = 0.001).

When investigating the ability of EAT in discriminating persons with events from those without, we observed a trend for improvement of Harrell’s C by EAT over traditional cardiovascular risk factors, but not, however, reaching statistical significance (increasing from 0.720 to 0.730 when adding EAT to traditional risk factors, p = 0.10). Likewise, Harrell’s C slightly improved when adding EAT to traditional cardiovascular risk factors in combination with the CAC score (0.781 to 0.786 for traditional risk factors and CAC score, alone and with EAT added, respectively, p = 0.137). To confirm these results, we investigated the explanation of variance for development of coronary events by risk factors and observed a trend of EAT increasing the explained variance over traditional risk factors (R² = 2.73% to R² = 2.92% for traditional risk factors alone and with EAT added, IDI(t) = 0.196%), indicating that EAT may improve risk discrimination above traditional cardiovascular risk factors, while overall effect sizes were low. Consistently, risk discrimination slightly improved when adding EAT to cardiovascular risk factors and CAC score (R² = 5.09% to R² = 5.37% for traditional risk factors and CAC, alone and with EAT added, IDI(t) = 0.279%).

**Discussion**

In this study, we examined the association of epicardial fat volume with traditional cardiovascular risk factors, CAC scores, and incident fatal and nonfatal coronary events in the population-based Heinz Nixdorf Recall cohort study. We found a significant association of EAT volume with cardiovascular risk factors in univariable and multivariable analyses. By contrast, although CAC scores increased with quartiles of EAT volume, this effect did not hold when adjusting for traditional cardiovascular risk factors, indicating that the association of EAT with CAC is ultimately

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**Table 3**

<table>
<thead>
<tr>
<th>Model</th>
<th>Hazard Ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>2.24 (1.74–2.88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age and sex adjusted</td>
<td>1.63 (1.23–2.17)</td>
<td>0.001</td>
</tr>
<tr>
<td>+ Traditional cardiovascular risk factors*</td>
<td>1.54 (1.09–2.19)</td>
<td>0.01</td>
</tr>
<tr>
<td>+ CAC score, log(CAC + 1)</td>
<td>1.50 (1.07–2.11)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*Traditional cardiovascular risk factors included waist circumference, systolic blood pressure, hypertensive medication, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, lipid-lowering medication, diabetes, and smoking.

Abbreviations as in Tables 1 and 2.
explained by shared risk factors. EAT volume was significantly associated with coronary events, independent of traditional cardiovascular risk factors. This effect remained unchanged after further adjustment for the CAC score, which itself is a strong predictor for coronary events. Notably, the association of EAT volume with coronary events was more distinct in subjects with no or mild CAC, which—together with the lack of association of EAT with CAC—may support the hypothesis that EAT may be linked with future coronary events through a mechanistic pathway different from that of coronary calcification, such as early and noncalcified plaque burden. Our finding of increased pericoronary fat at the coronary vessel causing a coronary event during follow-up may suggest that local visceral adipose tissue supports the development of atherosclerosis in the underlying coronary vasculature.

Several studies have demonstrated a strong association between EAT and coronary plaque burden, as well as with the presence of coronary heart disease (CHD) (8,12,25). In part, this is explained by a strong association of EAT with cardiovascular risk factors (6). However, there is growing evidence that the correlation of EAT with CHD may not be fully explained by shared risk factors. A potential explanation is that the endocrine activity of EAT, as with visceral adipose tissue, secretes pro- and anti-inflammatory mediators and cytokines such as adiponectin, interleukin-6, and tumor necrosis factor alpha (1,3,26,27). Increased CD45 mRNA expression in the EAT of subjects with coronary artery disease, representing elevated macrophage infiltration, and an increase of mast cells in the adventitia of coronary lesions have been observed (3,5,26). The hypothesis of a mechanism of EAT in the development of CHD different from that of traditional risk factors is supported by our findings.

The observed association of EAT with incident coronary events in our study was independent of coronary calcification. This finding is in good agreement with a recent report by Ito et al. (28), who described an association of epicardial fat with overall plaque burden even in subjects with zero CAC. Moreover, Alexopoulos et al. (10) showed that EAT volume was significantly larger in patients with mixed or noncalcified plaques compared with patients with calcified plaques or no plaques, which supports the hypothesis that EAT may be linked to early plaque components. Likewise, we and others (8,10,25) have described a significant association of epicardial and pericoronary fat with the presence also of noncalcified plaque burden in the underlying coronary artery. Together with our results, these findings indicate that EAT as quantified from noncontrast cardiac CT may complement prognostic information drawn from the CAC score without the need of any extra radiation exposure or administration of contrast media.

Our finding of a lack of a link between EAT and CAC scores in a multivariable model is in contrast to the current literature. Ding et al. (29) described a significant association of EAT with the presence of coronary calcification independent of traditional risk factors in a subgroup of MESA (the Multi-Ethnic Study of Atherosclerosis). Likewise, Framingham investigators (6) found EAT to be associated with the CAC score when adjusting for risk factors and visceral abdominal fat, whereas no significant link was found when adjusting for traditional risk factors only.
Although several studies demonstrated an association of EAT with prevalent CHD, data on incident CHD are limited (12,30). In a recent case-control study based on the Multi-Ethnic Study of Atherosclerosis cohort, an increase of CHD probability by quartile of EAT volume as well as a significant association of epicardial fat with incident CHD was described that remained statistically significant after adjustment for body mass index and cardiovascular risk factors (14). Similar results were observed in a case-control analysis drawn from a registry of asymptomatic subjects undergoing cardiac CT, where EAT was associated with incident cardiac events (31). These findings are confirmed by our results in a large population-based cohort with EAT, providing prognostic information and improving risk prediction for first coronary events.

**Implications.** Our results indicate that increased amounts of EAT volume are associated with excessive risk for fatal or nonfatal coronary events, independent of traditional cardiovascular risk factors. The finding of a strong correlation of EAT with coronary events independent of CAC and the lack of association of EAT with CAC suggest that EAT may be linked with future coronary events through a mechanistic pathway different from that of coronary calcification, such as early and noncalcified plaque burden. Therefore, EAT volume may complement prognostic information derived from calcium scoring and increase the predictive value of noncontrast cardiac CT, which can be quantified without additional radiation exposure or contrast administration.

Overall, subjects with high EAT may qualify for intensified risk factor modification. Because physical activity and weight changes have a major impact on visceral adiposity in general and EAT in specific (32,33), lifestyle changes may be of particular importance in preventing myocardial infarction in subjects with increased EAT volume.

**Study strengths and limitations.** Strengths of our study include the population-based design without selection of the cohort to adiposity-related traits. Traditional cardiovascular risk factors were measured using highly standardized protocols, and EAT was quantified using a reproducible, volume-based method. However, different definitions of pericardial and epicardial fat volume are established in the literature, and other measures of thoracic adipose tissues, such as intrathoracic fat or pericoronary fat quantification as described in the literature (7,8), were not tested in comparison. Because our study was conducted in a predominantly Caucasian population, generalization to other ethnic groups remains uncertain.

**Conclusions**

Epicardial fat is independently associated with fatal or nonfatal coronary events in the general population independent of traditional cardiovascular risk factors and the CAC score. Our results suggest that EAT complements information derived from the CAC score and therefore may increase the value of noncontrast cardiac CT examinations.

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**REFERENCES**


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