Journal of Clinical Lipidology (2016) 10, 1423–1430

Journal of Clinical Lipidology

Association of epicardial fat volume and nonalcoholic fatty liver disease with metabolic syndrome: From the CAESAR study

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KEYWORDS:
Metabolic syndrome;
Epicardial fat;
Epicardial adipose tissue;
Epicardial fat volume;
Fatty liver;
Nonalcoholic fatty liver disease

BACKGROUND AND AIMS: Epicardial adipose tissue or nonalcoholic fatty liver disease (NAFLD) can be one of putative risk factors for metabolic syndrome (MetS). However, there are no data assessing the associations of MetS with epicardial fat and NAFLD. The present study was performed to evaluate the combined effect of epicardial fat volume (EFV) and NAFLD on MetS in Korean adults.

METHODS AND RESULTS: Computed tomographic EFV and ultrasonographic fatty liver were measured in 1472 individuals (1242 men: mean age, 44 ± 8.6 years) among a total of 2277 individuals enrolled in the CArdiometabolic risk, Epicardial fat, and Subclinical Atherosclerosis Registry (CAESAR). Subjects were divided into 4 groups according to EFV and NAFLD (group I: low EFV and without NAFLD; group II: low EFV and with NAFLD; group III: high EFV and without NAFLD; and group IV: high EFV and with NAFLD). The overall prevalence of MetS was 24.2%. The EFV levels and prevalence of NAFLD in individuals with MetS was significant higher than those without MetS (81.0 cm^3 vs 57.3 cm^3, $P < .001$; 75.6% vs 36.5%, $P < .001$). The multivariate regression analysis including the five components of MetS showed that Group IV had significantly higher odds ratios (ORs) for the presence of MetS compared with Group I (OR [95% CI], 2.10 [1.11–3.98]). In the model, EFV was associated with MetS (2.03 [1.17–3.52]) but NAFLD was not (1.38 [0.88–2.12]).

CONCLUSION: This study showed that increased EFV and NAFLD are associated with the presence of MetS. However, EFV was more influenced by MetS than NAFLD despite NAFLD having more unfavorable metabolic and lipid profiles.

Introduction

Epicardial adipose tissue (EAT) located between the myocardium and visceral pericardium is an active endocrine organ with biochemical properties and reflects intraabdominal fat.[1,2] Previous studies reported that EAT is associated with metabolic syndrome and cardiovascular risk.[3–11] However, most are relatively small studies and are based on epicardial fat thickness (EFT) by echocardiography or computed tomography, which does not reflect total epicardial fat volume (EFV).[3–6] Studies about the relationship between EFV and MetS have also shown inconsistent results.[11–14]

Nonalcoholic fatty liver disease (NAFLD) is a common liver disease and manifests a various pathologic conditions

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Submitted March 16, 2016. Accepted for publication September 7, 2016.

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http://dx.doi.org/10.1016/j.jacl.2016.09.007

ranging from simple steatosis to cirrhosis, hepatic failure, and hepatocellular carcinoma. The prevalence of NAFLD continues to increase with growing obesity worldwide,[15] although the rates are relatively different according to ethnicity and the diagnostic modality used. NAFLD has been considered a hepatic manifestation of MetS and is frequently comorbid with type 2 diabetes, insulin resistance, dyslipidemia, and abdominal obesity. Although previous studies have reported that NAFLD is associated with MetS or its components, most of those studies did not include the multivariate confounders incorporating MetS components.[15–19] Furthermore, to our knowledge, there are no data comparing the relationship between MetS and epicardial fat or NAFLD.

Therefore, the present study was performed to assess the association between each EFV and NAFLD and MetS independently and to evaluate the combined effect of EFV and NAFLD on MetS in Korean adults.

Methods

Study population

The CArdiometabolic risk, Epicardial fat, and Subclinical Atherosclerosis Registry (CAESAR) study was designed to assess the relationship between cardiovascular risk, CACS, and epicardial fat in 2277 individuals who visited Kangbuk Samsung Health Promotion Center between 2010 and 2011 and who received nonenhanced CT and echocardiogram at baseline with follow-up every 3 to 5 years. Among the overall population (n = 2277), 1472 individuals were included in the final analysis. Eight-hundred five subjects were excluded from the analyses for the following reasons: 370 subjects were men or women who consumed alcohol in excess of 30 or 20 g/d, 312 were missing data on alcohol consumption, 61 were positive for viral hepatitis B antigen, 53 did not undergo viral hepatitis B antigen measurement, 4 were positive for viral hepatitis C antibody, 4 were missing abdominal ultrasonography data, and 1 was missing EFV data.

This study was approved by the Institutional Review Board of Kangbuk Samsung Hospital.

The methodology of questionnaires, anthropometric and blood pressure data, and laboratory data has been described previously.[7,9]

Measurement of total EFV

Nonenhanced images using a 64-slice multidetector CT scanner (Lightspeed VCT XTE, GE Healthcare, Tokyo, Japan) were acquired as electrocardiogram triggering was set at 70%–75% of the R-R interval with prospective ECG gating. The scanning protocol included section collimation of 16 × 2.5 mm, rotation time of 400 ms, tube voltage of 120 kV, current of 31 mAs (310 mA × 0.1 second), and tomographic slice thickness of 2.5 mm. Epicardial fat areas and volumes were measured with a dedicated semiautomated, offline workstation (Extended Brilliance Workplace and Easy Vision; Phillips Medical Systems, Best, The Netherlands). A density range of epicardial fat density was defined as −30 to −190 Hounsfield Units. The superior and inferior boundaries of epicardial fat using axial views were manually determined. The superior boundary was arranged at the level of bifurcation of the main pulmonary artery to the right pulmonary artery, and the inferior boundary was set at the last slice contacting the posterior descending coronary artery in the inferior atrioventricular groove. Total EFV was obtained as the sum of the epicardial fat area per slice on axial images. Total EFV measurements were performed by 1 cardiologist and 2 experienced cardiology technicians blinded to the clinical and echocardiographic data.

To minimize measurement error, 49 individuals for EFV measurement were randomly selected and re-measured from the same preselected images using the same method of measurement as the first iteration. Intraobserver and interobserver correlation coefficients were 0.99 and 0.97, respectively.

The definition of NAFLD

On the same day, abdominal ultrasonography (Logic Q700 MR; GE, Milwaukee, WI) using a 3.5-MHz probe was performed on all individuals by experienced clinical radiologists, blinded to clinical presentation and laboratory findings. Fatty liver was defined as the presence of a diffuse increase of fine echoes in the liver parenchyma compared with the kidney or spleen parenchyma.[20] NAFLD was defined after excluding other causes of fatty liver by laboratory data and questionnaires.

The definition of MetS

MetS was defined according to a previous joint interim statement for the definition of MetS, wherein 3 or more the following conditions were necessary for the presence of MetS: (a) elevated waist circumference (>90 cm in men and > 80 cm in women); (b) elevated triglyceride ≥ 150 mg/dL or drug treatment; (c) reduced high-density lipoprotein cholesterol (<40 mg/dL in men and < 50 mg/dL in women) or drug treatment; (d) elevated blood pressure (systolic ≥ 130 and/or diastolic ≥ 85 mmHg) or antihypertensive medication; (e) elevated fasting glucose ≥ 100 mg/dL or antidiabetic medication.[21]

Statistical analyses

Data are expressed as the mean ± standard deviation (SD) or as the median (interquartile ranges) for continuous variables and as percentages (%) for categorical variables. Fasting triglyceride, hsCRP, and epicardial fat volume were log-transformed for analysis to correct for skewed distributions. The values in tables are expressed as untransformed data for ease of interpretation. Statistical analyses