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Original article

Association between epicardial adipose tissue volume and myocardial salvage in patients with a first ST-segment elevation myocardial infarction: An epicardial adipose tissue paradox

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ABSTRACT

Background: Epicardial adipose tissue (EAT), defined as the adipose tissue between the visceral pericardium and the outer margin of the myocardium, is associated with coronary artery disease in the general population. However, the clinical implications of EAT in patients with ST-segment elevation myocardial infarction (STEMI) remain unclear.
Methods: A total of 142 patients with a first STEMI, who received reperfusion therapy within 12 h from symptom onset, were enrolled. All patients underwent cardiac magnetic resonance imaging to evaluate infarct core (Core), area at risk (AAR), and EAT volume. Myocardial salvage index (MSI) was defined as AAR minus Core divided by AAR. Patients in the lower tertile of EAT volume were classified as the low EAT group (group L) and the other two-thirds as the high EAT group (group H).
Results: The mean MSI was lower in group L than in group H (0.43 ± 0.13 vs 0.49 ± 0.13, $p = 0.01$), and the mean extent of Core was higher in group L than in group H ($25 \pm 10\%$ vs $19 \pm 10\%$, $p < 0.01$). Multivariate linear regression analysis including coronary risk factors and previously reported predictors of infarct size demonstrated that EAT volume was an independent predictor of MSI (β coefficient = 0.002 per 1 mL, $p = 0.002$).
Conclusions: A lower EAT volume is associated with less myocardial salvage and larger infarct size in patients with a first STEMI.

Introduction

Epicardial adipose tissue (EAT), defined as the adipose tissue between the visceral pericardium and the outer margin of the myocardium, can be considered an endocrine organ that secretes pro-inflammatory and anti-inflammatory cytokines and chemokines including adiponectin [1]. EAT volume is associated with coronary calcification as advanced atherosclerosis, cardiovascular risk factors, the incidence of myocardial infarction, and the severity of coronary artery disease in the general population [2–5]. Thus, EAT volume may reflect the stage of coronary atherosclerosis, resulting in cardiovascular events. However, in some patients, ST-segment elevation myocardial infarction (STEMI) is not caused by advanced atherosclerosis, but by early atherosclerosis, as represented by positive remodeling with plaque rupture [6], resulting in a large infarct size even after early successful reperfusion [7].

Cardiac magnetic resonance imaging (CMR) is the gold standard for evaluating infarct size and myocardial salvage (MS) in patients with acute myocardial infarction (AMI) [8–10]. We can also evaluate EAT volume on cine-CMR [11,12].

We prospectively investigated the associations of EAT volume with myocardial salvage index (MSI) and infarct size in patients with a first STEMI.

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Materials and methods

Patients

From January 2012 through September 2014, we screened 267 consecutive patients with a first STEMI who received reperfusion therapy within 12 h of symptom onset in Yokohama City University Medical Center. STEMI was defined as chest pain lasting for at least 30 min, accompanied by ST-segment elevation [13] and an increase in the serum creatine phosphokinase (CPK) level to more than twice the upper limit of normal. We excluded patients with any of the following characteristics: informed consent was not obtained, history of previous myocardial infarction or coronary-artery bypass surgery, stent thrombosis, clinical instability precluding CMR, estimated glomerular filtration rate (eGFR) of less than 30 mL/min/1.73 m^2, or contraindications to CMR. A total of 142 patients met the eligibility criteria and were enrolled (Fig. 1).

After admission, 5000 U of heparin was given. All patients received aspirin (a 200-mg loading dose, followed by 100 mg/d) and clopidogrel (a 300-mg loading dose, followed by 75 mg/d). Glycoprotein (GP) IIb/IIIa inhibitors were not used, because they have not been approved for use in Japan. All patients had a final Thrombolysis in Myocardial Infarction (TIMI) flow grade of 2 or 3. The study protocol was approved by the Yokohama City University Medical Center Institutional Review Board, and all patients gave written informed consent (UMIN-CTR ID: UMIN000012027).

Blood sampling

Biochemistry data including CPK, creatine kinase MB (CK-MB), and high-sensitivity C-reactive protein (hs-CRP) were evaluated on admission and at 3-h intervals during the first 24 h and then daily until discharge. Brain natriuretic peptide (BNP) was evaluated on admission, 6 h after admission, and daily until discharge. The high molecular weight adiponectin level was evaluated on admission by a commercial laboratory (SRL, Tokyo, Japan) in a randomly chosen group of 45 (32%) of the 142 subjects.

CMR protocol

All patients underwent CMR on day 10 ± 4 using a 1.5-T CMR system with an 8-element phased-array cardiac coil (MAGNETOM Avanto, Siemens Medical Solutions, Inc., Erlangen, Germany). Black-blood T2-weighted CMR images were acquired in 3 short-axis views, and typical parameters were as follows: repetition time (TR) 2 R–R intervals, echo time (TE) 78 ms, flip angle (FA) 180°, and 10-mm slice thickness. After scout imaging, cine true fast images with steady precession (True-FISP) sequences were obtained. Cine images were acquired in 6–8 short-axis views and 1 long-axis view at rest (TR 39.2 ms, TE 1.94 ms, FA 80°, 10-mm slice thickness). An infusion of 0.1 mmol/kg gadolinium–diethylenetriamine pentaacetic acid (Gd-DTPA) (Magnevist, Bayer Schering Pharma, Berlin, Germany) was given, and late gadolinium enhancement (LGE) images were acquired 10–15 min later using a phase-sensitive inversion recovery method; the images included 6–8 short-axis views at rest (TR 943.2 ms, TE 1.33 ms, FA 40°, 10-mm slice thickness). All images were acquired during breath-holding at end expiration.

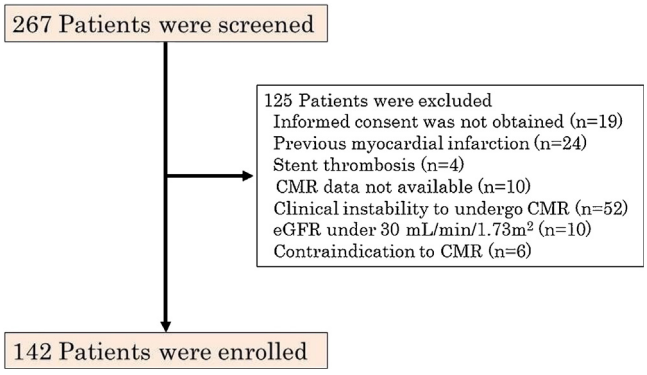

Fig. 1. Study flow chart. Of 267 screened patients, 142 were enrolled in the present study. CMR, cardiac magnetic resonance imaging; eGFR, estimated glomerular filtration rate.

CMR analysis

All CMR images were independently interpreted by 2 experienced observers blinded to the angiographic and clinical data using Q-MASS MR 7.5 imaging system (Medis, Leiden, The Netherlands). After review of the cine images, left ventricular (LV) volumes (end-diastolic volume index, EDVI; end-systolic volume index, ESVI) and ejection fraction (EF) were calculated by manually tracing the LV endocardial and epicardial borders on the short-axis images at end-diastole and end-systole. EAT was defined as the adipose tissue between the visceral pericardium and the outer margin of the myocardium. EAT area was calculated from consecutive short-axis images at end-diastole (Fig. 2), and EAT volume was calculated by the disk method, as described previously [11,12].

This manual tracing was also performed on LGE and T2-weighted images. The myocardial segment containing the region of high signal intensity (SI) myocardium was then outlined, and the maximum SI within this region was determined. A region of interest (ROI) was placed at the remote non-infarcted myocardium with uniform myocardial suppression. We used the full-width at half-maximum method (FWHM) to define the infarct core (Core) on LGE images, as described previously [14]. Core was defined as the myocardium with SI equivalent to >50% of the maximal SI. Microvascular obstruction (MVO) was defined as a dark area within the hyperenhanced area on LGE images. MVO was manually traced and considered as part of Core. The infarct size was defined as the extent of Core. On T2-weighted images, myocardial tissue with an SI of at least 2 SD above the mean SI obtained in the remote non-infarcted myocardium was considered the area at risk (AAR) [15]. MS and MSI were then estimated by the following formulae [16]:

MS = AAR minus Core
MSI = MS divided by AAR

Intramyocardial hemorrhage was defined as a dark area within the hyperenhanced area on T2-weighted images that was considered to belong to the AAR. All measurements were calculated by the planimetric method and expressed as grams of myocardium. The values were normalized to LV mass and represented as % of LV mass.

We divided the 142 patients into 2 groups according to their EAT volume. Patients belonging to the lower tertile of EAT volume were categorized into the low EAT group (group L) and the other two-thirds into the high EAT group (group H).

Coronary artery findings on coronary angiography

The extent index

The extent index was evaluated as described previously [17] and considered as a marker of advanced atherosclerosis (Supplemental method 1).

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