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Renal sinus fat volume on computed tomography in middle-aged patients at risk for cardiovascular disease and its association with coronary artery calcification

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Objective: Renal sinus fat (RSF) behaves as one of the perivascular fats, however RSF volume (RSFV) is considerably affected by visceral adipose tissue volume (VTAV). The ratio of RSFV to VATV (RSFV/VATV ratio) can be an index of regional perivascular fat accumulation corrected for the influence of VATV. The aim of this study was to investigate the relation between RSFV/VATV ratio and coronary artery calcium (CAC) in patients with suspected coronary artery disease.
Methods: One hundred and eighty-nine patients (mean age 66.7 ± 10.2; 72% men) underwent ECG-gated cardiac computed tomography (CT) and unenhanced abdominal CT. CAC score (CACS) was assessed using axial CT images. RSFV was measured by partially manipulated segmentation of the right kidney. VATV was automatically quantified in the upper abdomen. Logistic and correlation analyses were performed to examine the correlations between CAC, RSFV/VATV ratio, and risk factors of cardiovascular diseases in total and subgroups classified by the patients' age.
Results: Log-transformed RSFV/VATV ratio was associated with CAC presence in 112 middle-aged patients less than 69 years of age as well as total. This association remained significant after multivariate adjustment only in the middle-aged patients (OR 15.9, 95% CI 1.15–218.8). In total, RSFV/VATV ratio ($r = 0.228$, $p = 0.002$) and age ($r = 0.316$, $p < 0.001$) correlated with CACS on univariate analyses, but only age correlated on multivariate analyses. RSFV/VATV ratio correlated with CACS in the middle-aged patients ($r = 0.418$, $p < 0.001$), as well as on multivariate analyses.
Conclusions: We demonstrated that RSFV/VATV could be an independent risk indicator of CAC in the middle-aged patients.

1. Introduction

The association of obesity with increased risk in cardiovascular disease (CVD) has been demonstrated in many epidemiological studies and is now generally accepted [1,2]. Its association, however, greatly varies and is not always straightforward; some metabolically obese subjects with normal range of body weight can develop CVD, whereas some obese subjects remain metabolically healthy; with the risks of cardiovascular morbidity and mortality being lower in the latter than in former group [3–5]. One third of individuals with metabolically healthy obese (MHO) phenotype changed to high-risk phenotype during the follow-up term.

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Therefore, maintaining MHO status appears to be beneficial to prevent future cardiovascular risk [6]. Body mass index (BMI) is a component of the MHO definition, but does not always represent fatty groups. Actually, no apparent difference in both BMI and fat mass was demonstrated between MHO and metabolically high-risk CVD groups [7]. Difference in the risk of CVD between high-risks groups and healthy group regardless of the extent or severity of the obesity is linked with metabolic health, which may in part be related to the paracrine function of dysfunctional adipose tissue. In addition to ideal prevention of both age-associated loss in fitness and increase in fatness, incorporating exercise efforts for improving fitness into weight reduction strategy seems to be beneficial for preventing the change to high-risk group from healthy group [8].

Regional fat deposits in specific organs or body compartments, such as pericardial fat and perivascular fat, were found to directly affect adjacent anatomical organs and have been implicated in the development of coronary atherosclerosis [9–12]. In addition to pericardial and perivascular fat, fat in renal sinus, a region of the kidney in which low pressure venous and lymphatic vessels are present, partly constitutes visceral adipose tissue (VAT), and has recently been focused on as a new index of the ectopic fat depots [13–16].

In one of the Framingham Heart studies, renal sinus fat (RSF) with a provision of stimulus to increase renal size and activation of the rennin angiotensin aldosterone system, thereby promoting insulin resistance and other adverse physiological effects related to obesity [17,18], was reported to be associated with hypertension and the severity of renal functional impairment in chronic kidney disease (CKD) [19]. RSF volume (RSFV) measured on unenhanced computed tomography (CT) images was found to be highly reproducible and influenced by age, while the study populations were mostly composed of healthy cases or patients with minimally impaired renal function [20,21]. Many past researches focused on the relationship between VAT and coronary artery calcium score (CACS) [9,22,23], whereas few have measured RSFV in patients with suspected coronary artery disease. As described above, RSF consists of VAT in some part, which has been supported by positive correlations between RSF and VAT in experimental rabbits model and human subjects [17,24]. VAT consists of various fat compartments, such as RSF, retroperitoneal fat, and intraperitoneal fat. However, these relationships are not linear. The ratio of RSFV to VATV can reflect regional fat distribution in renal sinus independent of total fat mass volume or body height. On the other hand, RSF constitutes perivascular adipose tissue from anatomical point of view, and actually was shown to be associated with urine micro-albuminuria [25,26]. In other words, RSF may function as one of the perivascular fats, at least to some extent, and is considerably affected by the amount of VAT. Therefore, the proportion of RSFV to VATV can distinguish the importance of RSF as an extension of VAT versus its perivascular effects. To put it the other way around, it might be also a metric of regional perivascular fat accumulation in the renal sinus corrected for the influence of VAT.

The aim of the present study was to evaluate the ratio of quantitatively-measured right RSFV to VAT volume (RSFV/VATV ratio) and correlation of CACS with the RSFV/VATV ratio and cardiovascular disease risk factors in patients suspected of coronary artery disease.

2. Materials and methods

2.1. Enrollment

Our institutional review board approved the study protocol and waived the need for informed consent given the retrospective nature of the research. We initially enrolled 712 patients who underwent 320-row ECG-gated computed tomography coronary angiography (CTCA) (Aquilion ONE, Toshiba Medical Systems, Otawara, Japan) in routine clinical practices during a 10-month period from August 2011 to March 2012. Among the 712 patients, we selected 281 patients who were subjected to both unenhanced abdominal CT examination and blood sample examination within 30 days (range 0–28, mean 4.5, median 0) of the CTCA examination date and of these 281 patients, clinical data was unavailable for 24 patients and 68 patients were excluded. The remaining 189 patients were assessed in this study (Fig. 1 data in Brief [27]).

The mean age of the 189 patients was 66.7 ± 10.2 years (range: 40–88). VATV, RSFV and CACS were markedly influenced by age [16,21]. Therefore, 189 patients were divided into middle-aged and elderly groups in order to conduct an additional sub-group analysis by age; the middle-age group consisted of 112 patients with an age of 69 or less, and the elderly group consisted of 77 patients with an age of 70 or more (Table 1 data in brief [27]).

2.2. Clinical assessment

Pack-years were calculated by the formula: (years smoked) × (number of cigarette packs consumed per day). Patients were classified as diabetic if diabetes mellitus was diagnosed by a medical doctor according to the guidelines of diabetes mellitus or if the current use of medications for diabetes mellitus was recorded. Medication for dyslipidemia was defined as the use of cholesterol-lowering drugs. Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg, diastolic blood pressure (DBP) ≥ 90 mmHg, or the current use of antihypertensive medication. Total serum cholesterol, serum high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, and serum triglycerides (TG) were obtained from the clinical examination of a fasting blood sample within thirty days of the CTCA examination. Body Mass Index (BMI) was calculated as the individual's body weight (kg) divided by their height squared (m^2). The estimated glomerular filtration rate (eGFR) was determined using the abbreviated Modification of Diet in Renal Disease Study Equation [28]. Brachial-ankle pulse wave velocity (BaPWV) was defined as the speed at which the forward pressure wave was transmitted PWV from the brachium to the ankle through the arterial tree, and can serve as an indicator of the severity of vascular damage [29]. In this study, measured right side baPWV was generally used.

2.3. Image data acquisition

Non-contrast scans for CACS were done prior to CTCA for the evaluation of coronary vascular diseases in a single visit. Scanning parameters were as follows: prospective ECG-gating; 120 kV, 200 mA, gantry rotation 350 milli-seconds. Image reconstruction parameters were 3-mm slice thickness, 3-mm increment, and 240-mm field of view (FOV).

VATV, RSFV, VAT area, subcutaneous adipose tissue area (SAT area) and kidney volume were obtained from the identical non-ECG gated abdominal CT images without contrast media. Scanning parameters were 120 kV, 250–400 mA and their image reconstruction parameters were 5-mm slice thickness, 5-mm increment, and 320–380 mm FOV.

2.4. Quantitative measurements of calcified lesions in the coronary arteries

CACS was obtained by the method described by Agatston et al. [30] with a dedicated computer workstation (ZAIO server, ZAIO software, Tokyo, Japan). CAC was defined as an area with CT