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ORIGINAL ARTICLE

# Ankle Brachial Index Intensifies the Diagnostic Accuracy of Epicardial Fat Thickness for the Prediction of Coronary Artery Disease Complexity

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**Objectives** Epicardial fat thickness (EFT) and Ankle brachial index (ABI) are associated with coronary artery disease (CAD). The SYNTAX score (SS) reflects the complexity of CAD. We aimed to evaluate the relation of EFT and ABI with CAD complexity.

**Methods** We enrolled 197 patients undergoing coronary angiography. In all patients, ABI and EFT were determined. SS was calculated. The relationship between EFT, ABI and SS was analysed.

**Results** ABI and EFT were significantly correlated with SS ($r = -0.525$, $p < 0.001$, and $r = 0.650$, $p < 0.001$, respectively) and found to be independent predictors of SS.
ABI<0.9 mm identified patients with SS>22 with a sensitivity of 45.28% and a specificity of %82.64 (AUC = 0.689, %95 CI = 0.619-0.763, p<0.001). The optimal cutoff value for EFT was 5 mm, yielding a sensitivity of 81.1% and a specificity of 90.3% (AUC = 0.859, 95% CI 0.802–0.904). In order to identify which parameters were the most accurate, we compared both AUC of ROC curves and there was no difference (p = 0.170).

**Conclusion** EFT and ABI enables the noninvasive prediction of CAD severity in patients with suspected CAD and combining ABI to EFT was additive for the prediction of coronary artery disease complexity.

**Keywords** Peripheral artery disease • Epicardial fat thickness • Coronary • Angiography • SYNTAX • Ankle brachial index

## Introduction

Increased visceral adipose tissue accumulation and peripheral artery disease (PAD) are associated with cardiovascular morbidity and mortality [1,2]. Lower extremity PAD affects a considerable percentage of the population. The ankle-brachial index (ABI), calculated by dividing the higher systolic blood pressure (SBP) of each ankle artery by the higher SBP of the upper limbs, is a simple and non-invasive tool with high specificity and sensitivity for the diagnosis of PAD [2]. Peripheral artery disease and coronary artery disease (CAD) are different manifestations of the same atherosclerotic process. Therefore ABI may reflect the CAD. Various studies reported that ABI is related to CAD severity and complexity [3,4].

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Epicardial fat has the same embryogenic origin as visceral adipose tissue, which plays an important role in the metabolic syndrome and reflects the visceral fat [5,6]. Secretion of inflammatory cytokines and release of bioactive molecules by epicardial fat tissue may promote coronary atherosclerosis [7,8]. Transthoracic echocardiography is a noninvasive tool for measuring epicardial fat thickness (EFT) [9]. The SYNTAX score (SS) is a widely accepted complexity score of coronary artery disease (CAD) based on lesion morphology. Previous studies have shown that increased CAD complexity is difficult to treat and related to unfavourable acute and long-term cardiovascular outcomes [10,11]. Using noninvasive methods which help to predict CAD complexity, patients at high risk for adverse cardiovascular events can be discerned before treatment initiation. ABI and EFT, which are noninvasive and safe methods, may be valuable in the prediction of the severity and complexity of coronary atherosclerosis [12,13]. The association of CAD complexity with ABI and EFT has not been adequately evaluated. Hence, we studied the relation of EFT and ABI with CAD complexity, which was assessed by SS in patients undergoing coronary angiography for suspected CAD. Additionally we compared the diagnostic accuracies of ABI and EFT for detecting intermediate-high SS; to our knowledge there is no study evaluating this in the literature.

# Patients and Methods

## Study Design

This was a single-centre, prospectively enrolled, cross-sectional study conducted between August and November 2013. We enrolled 197 consecutive patients undergoing coronary angiography for the assessment of suspected CAD. Patients with heart failure, chronic renal failure, acute coronary syndrome, uncontrolled hypertension, poor echocardiographic imaging, prosthetic heart valve, pericardial effusion, moderate to severe valvular disease, prior coronary artery bypass graft surgery and previous percutaneous coronary intervention were excluded from the study. Additionally we excluded patients with peripheral vascular surgery or intervention and noncompressible vessels. Informed consent was obtained from all subjects, and the investigation conforms to the principles outlined in the Declaration of Helsinki. The study protocol was approved by ethics committee.

Weights of the patients, in light clothes and without shoes, were measured in kilograms, and their heights were also measured. Body mass index (BMI) was calculated by dividing body weight in kilograms by the square of body height in metres. Waist circumference (WC) was measured between the last rib and iliac crest on the midline while the patient was standing. Hip circumference (HC) was measured by using the line between the right and left great trochanter of the femur.

Blood pressure was measured, in compliance with World Health Organization guidelines, by using a mercury sphygmomanometer (ERKA, Germany) with a cuff appropriate to the arm circumference, in patients at rest for 20 minutes (Korotkoff phase I for SBP and V for diastolic blood pressure (DBP)) at least three times and the average of the measurements was calculated. Hypertension was defined by a previous diagnosis of hypertension or the presence of SBP$\geq$140 mmHg or DBP $\geq$90 mmHg (mean of two consecutive measurements). Diabetes was defined as fasting plasma glucose $\geq$126 mg/dl or plasma glucose level $\geq$200 mg/dl 2 hours after the 75 mg oral glucose tolerance test or symptoms of hyperglycaemia accompanied by casual plasma glucose $\geq$200 mg/dl or HbA1C $\geq$6.5% or patients using antidiabetic medications.

Pulse pressure = systolic blood pressure – diastolic blood pressure

Patients who self-reported as having smoked during the previous six months were classified as smokers. Venous blood samples were drawn after a 12-hour overnight fast. Serum glucose, total cholesterol and triglycerides were determined using standard automatic enzymatic methods. HDL cholesterol was determined after specific precipitation and low density lipoprotein (LDL) cholesterol was determined by the Friedewald formula.

## Measurement of Echocardiographic Parameters and EFT

Comprehensive echocardiography, including M-mode, two dimensional and Doppler echocardiography, was performed by two operators blinded to ABI measurements, using a Vivid-5S GE instrument with 3.6-MHz transducer. Echocardiographic examinations were performed in left lateral decubitus position according to the guidelines of American Society of Echocardiography. Epicardial fat was defined as an echo-free space between the outer wall of the myocardium and the visceral layer of the pericardium. The largest diameter of epicardial fat located on the right ventricular free wall was determined. EFT was measured in the parasternal long axis view at end-diastole in three cardiac cycles. The average of three cardiac cycles was used for statistical analysis.

Left ventricular mass was calculated according to Devereux formula:

LV mass: $0.8 \times 1.04 \times [(LVEDD+IVS+PW)^3 - LVEDD^3]+0.6$

LV mass index (LVMI): LV mass/body surface area

## ABI Measurements

Ankle brachial index (ABI) was measured using a VaSera 1000 instrument (Fukuda Denshi Co Ltd, Tokyo). ABI was measured in the morning after 12 hour fasting before coronary angiography. Briefly, cuffs were applied to both upper arms and ankles, with the participant supine and the head in the midline position. After resting for 15 minutes, measurements were performed. This device provides both left and right ABI automatically. We chose the lowest ABI in cases of difference between left and right ABI.