Atherosclerosis 268 (2018) 127–137

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Additional prognostic value of brachial-ankle pulse wave velocity to coronary computed tomography angiography in patients with suspected coronary artery disease

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ARTICLE INFO

Article history:
Received 6 April 2017
Received in revised form
17 November 2017
Accepted 22 November 2017
Available online 1 December 2017

Keywords:
Arterial stiffness
Coronary artery disease
Coronary CT angiography
Prognosis

ABSTRACT

Background and aims: Increased arterial stiffness is associated with a higher risk of future cardiovascular events. We aimed to investigate whether information about arterial stiffness provides additional prognostic value to coronary computed tomography angiography (CCTA) findings.

Methods: A total of 523 consecutive patients (mean age, 58.0 ± 10.3 years; male, 60.6%) with suspected coronary artery disease (CAD), who underwent CCTA and brachial-ankle pulse wave velocity (baPWV) measurement within a month, were retrospectively analyzed. A composite of cardiovascular death, nonfatal myocardial infarction (MI), coronary revascularization, nonfatal stroke, and hospitalization for cardiovascular causes was assessed.

Results: During a median 43.9 months of follow-up (interquartile range, 11.6–66.9 months), the composite endpoint occurred in 66 patients (3 cardiovascular deaths, 1 nonfatal MI, 35 coronary revascularizations, 16 nonfatal strokes, and 45 hospitalizations for cardiovascular causes). After adjustment for clinical risk factors and CCTA findings, higher baPWV was an independent prognostic factor for the composite endpoint (adjusted hazard ratio, 4.717; 95% confidence interval, 2.675–8.319; $p < 0.001$). The addition of baPWV to clinical risk factors and CCTA findings significantly improved the prediction of cardiovascular events (global χ^2 score, from 132 to 154; $p = 0.005$).

Conclusions: Arterial stiffness provides additional prognostic information to CCTA findings in patients with suspected CAD. The baPWV can serve as a useful clinical tool for risk stratification in this population.

1. Introduction

Coronary artery disease (CAD) is the leading cause of death worldwide, and disability from CAD is expected to increase in next several decades [1]. Therefore, there is a growing need for the appropriate use of noninvasive tests for early detection of CAD, risk stratification, and timely management. To this purpose, coronary computed tomography angiography (CCTA), an emerging technique, has received attentions and expanded its clinical indications from the detection of obstructive CAD to the risk stratification of patients with suspected CAD [2]. Although CCTA provides highly accurate anatomical information of coronary arteries, there remains a limitation that it does not provide the functional aspects of atherosclerosis, which include not only myocardial ischemia but also the overall vascular function and non-coronary cardiovascular disease [3]. Several approaches have attempted to compensate this limitation through combining information from other diagnostic imaging modalities [4–8], inflammatory markers such as C-reactive protein (CRP) [9], and measures of vascular function [10–13].

Artery stiffens is the result of the aging process and arteriosclerosis [14,15]. Measurement of arterial stiffness provides some

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https://doi.org/10.1016/j.atherosclerosis.2017.11.026
0021-9150/

unique prognostic information about future cardiovascular events [16–18]. Brachial-ankle pulse wave velocity (baPWV) has been established as a simple tool to measure arterial stiffness [19]. Numerous studies have reported the clinical usefulness of baPWV for diagnosis of CAD and prediction of cardiovascular events [19–22].

Combined use of coronary anatomical tests and arterial stiffness measurements has the potential to improve risk prediction, however, no study has investigated the combined use of CCTA and baPWV in predicting cardiovascular events. In this study, we aimed to assess the prognostic value of baPWV for the occurrence of cardiovascular events according to the results of CCTA, and to investigate the prognostic value of baPWV when added to CCTA findings.

2. Patients and methods

2.1. Study population

This single center study was performed at Boramae Medical Center (Seoul, Korea). From 2009 to 2013, we retrospectively reviewed a total of 614 patients with suspected CAD, undergoing CCTA and baPWV measurements within a month, on an out-patient basis. We excluded 91 patients with acute coronary syndrome (ACS) (n = 30), prior history of coronary revascularization, including percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) (n = 48), inadequate image quality of CCTA (n = 2), peripheral artery disease (ankle brachial index <0.9) (n = 7), malignancy (n = 1), and insufficient clinical information (n = 3). After these exclusions, 523 patients were included in the final analysis.

The baPWV is measured as part of the routine work-up protocol for stable patients with suspected CAD at the study hospital. Among the total study population, 312 patients (59.7%) underwent CCTA and baPWV measurement with intervals between 2 and 4 weeks. The other 211 patients (40.3%) underwent the 2 tests within 2 weeks: most of them (179 patients) underwent baPWV measurement as the initial test, and 32 patients (6.1%) underwent CCTA followed by baPWV measurement on the same day. Given the retrospective study design, the results of CCTA and baPWV measurement were communicated between the patients and attending physician, and were incorporated into the clinical practice.

The study protocol was approved by the Boramae Medical Center Institutional Review Board (IRB no. 16-2017-5). Given the observational nature of this study, the Institutional Review Board waived the need for written informed consent from the subjects. All clinical investigations were conducted according to the principles of the Declaration of Helsinki.

2.2. Clinical and laboratory data

Clinical data of comorbidities and laboratory test results were obtained from hospital records. Body weight, height, and blood pressure (BP) were measured on the day of the CT scan. Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg, diastolic blood pressure (DBP) ≥90 mmHg, or current use of antihypertensive medications. Diabetes mellitus (DM) was defined as fasting blood glucose ≥126 mg/dL, hemoglobin A1c ≥ 6.5%, or use of antidiabetic medications. Dyslipidemia was defined as total cholesterol ≥240 mg/dL, low-density lipoprotein cholesterol (LDL-c) ≥160 mg/dL, high-density lipoprotein cholesterol (HDL-c) <40 mg/dL in men and <50 mg/dL in women, or use of lipid-lowering medications. Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2. Obesity was defined as body mass index (BMI) ≥30 kg/m^2. Atrial fibrillation (AF) was defined as a history of paroxysmal, persistent, or permanent AF documented on electrocardiogram. Heart failure (HF) was defined based on the hospital records. Use of aspirin, clopidogrel or other P2Y12 inhibitors, diuretics, β-blockers (BB), calcium channel blockers (CCB), angiotensin-converting enzyme inhibitors (ACEi), angiotensin II receptor blockers (ARB), and statins was assessed at the time of baPWV measurement and CCTA evaluation.

All participants fasted for at least 8 h before the blood test, and blood levels of serum creatinine, fasting glucose, hemoglobin, total cholesterol, triglyceride, LDL-c and HDL-c were measured.

2.3. baPWV measurement

The baPWV was measured after patients were resting in a supine position for at least 5 min. Patients were allowed to take their regular medications but caffeine and cigarette smoking were prohibited on the day of the measurement. The baPWV measurement was performed using a noninvasive automated waveform analyzer (VP−1000; Colin Co. Ltd., Komaki, Japan), as previously described [22,23]. Cuffs were wrapped on both upper and lower extremities. Phonogram, pulse volume waveform, BP, and heart rate were recorded simultaneously, according to the manufacturer's recommendations. The baPWV was calculated by measuring the time for the pulse wave to travel between the brachial and posterior tibial arteries. The higher value between left and right baPWV was used for study analyses. All measurements were performed by a single experienced operator, who was blinded to all clinical data. The intra-observer coefficient of variation for baPWV was 5.1% [11].

2.4. CCTA image acquisition and analysis

CCTA was performed in a 64-slice CT scanner (n = 210) (Brilliance 64, Philips Medical Systems, the Netherlands) or a 128-slice CT scanner (n = 313) (Ingenuity, Philips Medical Systems, the Netherlands). We obtained both coronary artery calcium scoring CT scans and retrospectively electrocardiogram-gated CCTA for patients. To control heart rate, we have given bisoprolol 5–10 mg orally 1 h before the examination for patients with a heart rate of 65 beats/min or higher, if not contraindicated. Just before the start of CT scan, we routinely used sublingual nitroglycerin (0.6 mg). CT images were acquired in cranio-caudal direction covering the whole heart from tracheal carina to heart base. A bolus of 70 mL Iomeprol (Iomeron 400, Bracco, Milan, Italy) was administered to each patient, with an injection rate of 4–5 mL/s, followed by administration of a 40 mL mixture of iodine and saline (ratio 6:4). The scan parameters were as follows: 64 × 0.625 mm detector array, 420 ms rotation time, 120 kV tube voltage, and 800–1000 mAs tube current for the 64-slice CT scanner; and 64 × 0.625 mm detector array, 400 ms rotation time, 120 kV tube voltage, and 300–500 mAs tube current for the 128-slice CT scanner. Initial CT datasets were reconstructed using raw CT data at 75% of RR interval of the cardiac cycle (mid-diastolic phase). We reconstructed 2 axial datasets with slice thicknesses of 2.5 mm and 1.0 mm and increments of 2.5 mm and 1.0 mm, respectively. A filtered back projection algorithm was used for 64-slice CT images and an iterative reconstruction algorithm (iDose4, Philips Healthcare, Cleveland, OH, USA) was used for 128-slice CT images. Multiplanar reconstruction images were routinely reconstructed with short-axis, 2-chamber, and 4-chamber views. CACS was calculated with the Agatston method using a threshold of 130 Hounsfield units (HU). To estimate the radiation dose, dose-length product values provided on the CT scanner console were recorded. The effective dose of the CT scan was calculated as the product of the dose-length product multiplied by a conversion coefficient for the