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Simplified Bernoulli formula to predict flow limiting stenosis at coronary computed tomography angiography

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ABSTRACT

Objective: To compare the diagnostic performance of estimated energy loss (EEL) with diameter stenosis (DS) to estimate significant stenosis by fractional flow reserve (FFR).

Materials and methods: One hundred twenty-five patients were included. EEL was calculated using DS, lesion length, minimal lumen area and left ventricular volume. FFR ≤ 0.80 was determined significant.

Results: EEL improved the accuracy from 63% (95% confidence interval (CI): 55–72%) to 83% (95% CI: 75–89%, $p < 0.0001$). EEL increased the area under the receiver operating characteristics curve from 0.63 to 0.85 ($p < 0.0001$).

Conclusions: EEL improved the diagnostic performance to detect functionally significant stenosis than DS.

1. Introduction

Coronary computed tomography (CT) angiography is an established modality to detect obstructive coronary stenosis with a high accuracy [1]. However, percutaneous coronary intervention (PCI) would not reduce the risk of cardiovascular events compared with optimal medical therapy alone when therapy is decided based on anatomical stenosis [2]. Fractional flow reserve (FFR) has become a golden-standard to diagnose functionally significant stenosis [3]. FFR-guided PCI resulted in better prognosis compared with angiography-guided PCI [4]. Recent advancement in computational fluid dynamics allowed to estimate FFR using coronary CT angiography data with a high diagnostic performance [5]. However, real-time on-site diagnosis of ischemia is difficult because complicated calculation is necessary to derive FFR from CT angiography data.

Simplified Bernoulli formula allows to estimate pressure loss across a stenosis by measuring the lesion length (LL), minimal lumen area (MLA) and diameter stenosis (DS) [6]. Although only a rough estimation could be performed, pressure loss could be calculated on-site without a supercomputer. Thus, the purpose of the present study was to investigate the diagnostic performance of simplified Bernoulli method to estimate functionally significant stenosis assessed by invasive FFR.

2. Materials and methods

This study was approved by the local ethics committee, and the requirement for informed consent to participate this study was waived.

2.1. Patients

The records of 133 consecutive patients without renal dysfunction (effective glomerular filtration rate $< 40\,\text{ml}\,\text{min}^{-1}$) who underwent FFR evaluation during coronary angiography because coronary artery disease was suspected by CT angiography from March 2013 to December 2016 were retrospectively examined. FFR was performed when at least one stenosis had diameter reduction between 30 and 80% at coronary angiography. The following patients were excluded: severe motion artifact at coronary CT angiography (n = 4), FFR only performed in a vessel with previous stent placement (n = 3) and caffeine intake before coronary angiography (n = 1). We did not exclude patients with a history of prior stent placement but FFR performed in a vessel without a stent (n = 6). Thus, the final study group included 125 patients and 134 vessels were evaluated. The pretest probability of coronary artery disease was estimated by a previously described method [7]. In summary, this risk score was calculated based on age, sex, hemoglobin A1c, systolic blood pressure, high-density lipoprotein and smoking status of the patient with a maximum score of 24.

2.2. CT data acquisition

All patients underwent CT angiography with a 64-row CT (Brilliance 64; Philips, Eindhoven, Netherlands). Each patient first underwent

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unenhanced prospectively electrocardiogram-gated axial scan with 120 kVp, 196 mA and 2.5 mm collimation for calcium scoring. Images were acquired at 40% or 70% of the R-R interval depending on the heart rate and were reconstructed with a slice thickness of 2.5 mm and increment of 2.5 mm. Coronary CT angiography was performed by electrocardiogram-gated helical scan with dose modulation technique. The scanning parameters were as follows: detector configuration, 64 × 0.625 mm; tube potential, 120 kVp; tube current-time product, 800–1050 mAs, depending on the body weight; gantry rotation time, 420 ms; and helical pitch, 0.2.

A 20-gauge catheter was placed at the right antecubital vein. Patients received 40–90 ml of iopamidol 370 mg iodine/ml (Iopamiron 370; Bayer, Osaka, Japan) depending on the body weight. Contrast medium was injected for acquisition duration plus 7 s, followed by a 30 ml saline flush. Bolus tracking method was performed to determine the scan timing. The scan started 6 s after the descending aorta reached 100 Hounsfield unit (HU).

Patients with heart rate > 65 beats per minute at the outpatient department were told to take an oral β-blocker (20 mg of metoprolol) 1 h prior to CT angiography. If the heart rate was over 65 beats per minute on site, a maximum dose of 12.5 mg of landiolol (Corebeta; Ono Pharmaceutical, Tokyo, Japan) was given intravenously [8]. All patients received 0.3 mg sublingual nitroglycerin (Nitropen; Nippon Kayaku, Tokyo, Japan) before imaging.

For each patient, a senior technologist determined the phase with minimum artifacts at the CT console. Multiple phases were reconstructed when artifacts appeared in the image. The reconstructed slice thickness was 0.67 mm, and the increment was 0.33 mm. Images were reconstructed using a cardiac sharp kernel. For processing, images were transferred to a workstation (Synapse Vincent Ver 4.6; Fujifilm Medical, Tokyo, Japan).

2.3. Calcium scoring

Calcified lesions with a minimum area of three pixels and a minimum CT number of 130 HU were scored by using the algorithm developed by Agatston et al. [9] Lesion scores from the left main, left anterior descending, left circumflex and right coronary arteries were summed to determine a total calcium score. Calcium score was not calculated in patients with stents.

2.4. Stenosis analysis

The stenosis analysis software of the workstation automatically identified coronary lumen and vessel border based on the attenuation. The border was manually corrected when necessary. One experienced cardiovascular interpreter defined the start and end of a stenotic lesion. DS, LL and MLA were automatically obtained (Fig. 1a). The most severe stenosis was selected for analysis when multiple lesions were present on a vessel. Plaque features such as total plaque volume (TPV), non-calcified plaque volume (NCPV) and low-density plaque volume (LDPV) were also recorded. The criteria for NCPV and LDPV were plaque volume with an attenuation < 130 HU and < 30 HU, respectively. The left ventricular volume of the stenosis-related territory ($LV_{stenosis}$) was estimated using the Voronoi method [10] (Fig. 1b).

Using a simplified Bernoulli formula, pressure loss across a stenosis can be estimated as follows [6].

$$\Delta P = Q\frac{8\pi\mu LL}{MLA^2} + Q^2\frac{\rho}{2}\frac{(1-(1-DS/100)^2)^2}{MLA^2}$$

where ΔP is the pressure drop, Q is the blood flow, μ is the blood viscosity ($0.004\ kg\ m^{-1}\ s^{-1}$) and ρ is the blood density ($1000\ kg\ m^{-3}$). The first term accounts energy loss due to viscous friction between laminar layers of fluid and the second term reflects energy loss when normal arterial flow is transformed first to high-velocity flow in the stenosis and then to the turbulent nonlaminar distal flow eddies at the exit from the stenosis. We defined estimated energy loss (EEL) as log ΔP. The flow at the hyperemic state was estimated as $4.0\ ml\ min^{-1}\ g^{-1}$ [11], hence the blood flow at the stenotic site was calculated as: $Q = 4.0 \times LV_{stenosis}$.

2.5. FFR measurement by coronary angiography

FFR was performed using a pressure wire (PressureWire Cetrus, St Jude Medical Systems, St. Paul, MN) when the stenosis was between 30 and 80% at invasive coronary angiography. The pressure wire was positioned distal to the stenosis of interest under intravenous infusion of adenosine at $140\ \mu g\ kg^{-1}\ min^{-1}$ for 3 min. FFR was derived as the ratio of the mean coronary pressure distal to the stenosis over the mean aortic pressure at maximal hyperemia. An FFR value of ≤0.80 was determined as hemodynamically significant. The cardiologists performing angiography had total access to the coronary CT data. However, they were not aware of EEL because this value was calculated for research use and not mentioned in the radiology report.

2.6. Statistical analysis

Continuous variables were shown as mean ± standard deviation and categorical variables as number (%) unless otherwise described. The Student's *t*-test was used to compare continuous variables. The Chi square (χ^2) test and Fisher's exact test were used to compare categorical variables and skewed variables. Pearson correlation analysis was used to investigate the relationships of EEL and CT stenosis with FFR.

Receiver-operating characteristics (ROC) curve analysis was used to compare the diagnostic performance of DS and EEL to predict hemodynamically significant stenosis. Anatomically significant stenosis was defined as DS ≥ 50%. We determined the optimal cutoff value of EEL at the point with the largest Youden's index (sensitivity + specificity − 1). The diagnostic accuracy of DS and EEL to predict ischemic stenosis was assessed by the McNemar test. The net reclassification index (NRI) and the integrated discrimination improvement (IDI) was used to determine whether EEL improved vessel classification to be hemodynamically significant compared with DS. Subgroup analysis of the diagnostic performance of EEL to predict ischemia was performed by the following variables: proximal (segments 1, 5, 6 and 11) or distal, mild calcification (Agatston score < 400) or heavy calcification (Agatston score ≥ 400).

The difference in area under the curve (AUC) was assessed by the DeLong method [12] using R (The R Foundation for Statistical Computing). R software was also used to calculate the NRI and IDI. The remaining statistical analyses were performed using JMP software (version 12.2.0; SAS, Cary, NC). A *p*-value < 0.05 was deemed to indicate significance.

3. Results

3.1. Patient demographics and lesion characteristics

Of the 125 patients, 34 patients (27%) had a positive FFR (≤0.80) in at least one vessel (Table 1). Among the 134 vessels analyzed, 37 vessels (27%) included ischemic stenosis (Table 2). The majority of analyzed vessel was the left anterior descending (77%), followed by right coronary (16%) and left circumflex (7%). Patients with ischemic stenosis were more often male and more calcified than patients without ischemic stenosis, but the difference was marginal (Table 1). Other characteristics such as age, body habitus, disease status, smoking status, family history and medication were similar between patients with and without ischemia.

3.2. Relationship of CT-derived parameters and FFR

DS and FFR showed a negative correlation ($r^2 = 0.087$, $p < 0.001$,