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Research paper

Coronary CT angiography derived fractional flow reserve: Methodology and evaluation of a point of care algorithm

Adriaan Coenen [a, b, *], Marisa M. Lubbers [a, b], Akira Kurata [a], Atsushi Kono [a], Admir Dedic [a, b], Raluca G. Chelu [a, b], Marcel L. Dijkshoorn [a], Robert-Jan M. van Geuns [a, b], Max Schoebinger [c], Lucian Itu [d], Puneet Sharma [e], Koen Nieman [a, b]

[a] *Department of Radiology, Erasmus University Medical Center, Rotterdam, The Netherlands*
[b] *Department of Cardiology, Erasmus University Medical Center, Rotterdam, The Netherlands*
[c] *Siemens Healthcare, Forchheim, Germany*
[d] *Corporate Technology, Siemens SRL, Brasov, Romania*
[e] *Medical Imaging Technologies, Siemens Medical Solutions USA, Inc., Princeton NJ, USA*

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ABSTRACT

Background: Recently several publications described the diagnostic value of coronary CT angiography (coronary CTA) derived fractional flow reserve (CTA-FFR). For a recently introduced on-site CTA-FFR application, detailed methodology and factors potentially affecting performance have not yet been described.
Objective: To provide a methodological background for an on-site CTA-FFR application and evaluate the effect of patient and acquisition characteristics.
Methods: The on-site CTA-FFR application utilized a reduced-order hybrid model applying pressure drop models within stenotic regions. In 116 patients and 203 vessels the diagnostic performance of CTA-FFR was investigated using invasive FFR measurements as a reference. The effect of several potentially relevant factors on CTA-FFR was investigated.
Results: 90 vessels (44%) had a hemodynamically relevant stenosis according to invasive FFR (threshold ≤0.80). The overall vessel-based sensitivity, specificity and accuracy of CTA-FFR were 88% (CI 95%:79–94%), 65% (55–73%) and 75% (69–81%). The specificity was significantly lower in the presence of misalignment artifacts (25%, CI: 6–57%). A non-significant reduction in specificity from 74% (60–85%) to 48% (26–70%) was found for higher coronary artery calcium scores. Left ventricular mass, diabetes mellitus and large vessel size increased the discrepancy between invasive FFR and CTA-FFR values.
Conclusions: On-site calculation of CTA-FFR can identify hemodynamically significant CAD with an overall per-vessel accuracy of 75% in comparison to invasive FFR. The diagnostic performance of CTA-FFR is negatively affected by misalignment artifacts. CTA-FFR is potentially affected by left ventricular mass, diabetes mellitus and vessel size.

1. Introduction

Coronary CT angiography (coronary CTA) can effectively rule out coronary stenosis.[1–4] However, overestimation of stenosis severity by coronary CTA has been reported, potentially leading to unnecessary invasive angiography referrals.[5,6] For decades, classification of CAD severity has predominantly been based on angiographic findings. Over the past years, functional parameters of CAD severity have become more important. Fractional flow reserve (FFR) is now the clinical standard for assessment of the hemodynamic relevance of coronary atherosclerotic lesions and it is recommended for

Abbreviations: Coronary CTA, coronary CT angiography; CAD, coronary artery disease; FFR, fractional flow reserve; CTA-FFR, coronary CT angiography derived fractional flow reserve; 3D, 3 dimensional; LV, left ventricle; CAC, coronary artery calcium; RCA, right coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery.

* Corresponding author. Erasmus Medical Center, The Netherlands, Rotterdam, 's-Gravendijkwal 230, 3015 CE, ca-207.
E-mail address: a.coenen@erasmusmc.nl (A. Coenen).

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making treatment decisions.[7,8]

By applying computational fluid dynamics to coronary CTA data, coronary blood flow can be numerically computed, which allows for functional assessment of coronary stenosis severity.[9–11] CT-derived FFR (CTA-FFR) correlates well with invasive FFR and can improve the diagnostic performance of cardiac CT.[12–14] Reproducibility of CTA-FFR is good[15]

More recently, a new CTA-FFR algorithm has been introduced that allows for on-site computation of CTA-FFR.[16–18] This requires the clinician to generate an accurate 3 dimensional (3D) coronary artery model from the coronary CT angiogram. As the 3D coronary model is crucial for reliable CTA-FFR results, the process of generating this 3D coronary model is described in detail in this paper.

The application of computational fluid dynamics from anatomical coronary CTA data relies on several assumptions: primarily, the relationship between total heart mass and resting total coronary blood flow, adequate myocardial perfusion in rest, and simulation of hyperemic state by reducing the peripheral coronary microvascular resistance. In this paper we describe the methodological background of an on-site CTA-FFR algorithm, and evaluate how potentially influencing factors such as left ventricular (LV) mass, coronary artery calcium (CAC) deposits, location of the stenosis of interest, vessel size, mode of CT data acquisition, reconstructed cardiac phase, several coronary CTA image artifacts and presence of a bifurcation CTA-FFR performance in comparison to invasive FFR measurements.

2. Methods

2.1. Population

From the hospital records, we identified 122 consecutive patients who, between 2007 and 2013, had undergone both coronary CTA and invasive FFR measurements within a period of 50 days. After exclusion of six patients (four due to non-diagnostic coronary CTA quality and two due to incomplete coronary coverage), the study population consisted of 116 patients, in whom 203 vessels had been interrogated by invasive FFR (Table 1). CTA-FFR was computed using a dedicated prototype software (cFFR version 1.4, Siemens Healthcare, Forchheim, Germany; not commercially available). The institutional review board at our hospital provided a waiver based on the retrospective observational study design. This study includes patients previously described in a report on the diagnostic performance of on-site CTA-FFR.[17]

Table 1
Demographics of included patients.

Number of patients (*n*)	116
Age (years)	62 ± 9.4
Male gender (*n*)	91 (78%)
Body mass index (kg/m^2)	27.2 ± 3.9
Heart rate (beats per minute)	66.3 ± 12.9
Cardiovascular risk factors (*n*)	
Hypertension	70 (60%)
Dyslipidemia	65 (56%)
Diabetes mellitus	24 (21%)
Family history of CAD	53 (46%)
Smoking within the last year	28 (24%)
Typical angina (*n*)	83 (72%)
Prior myocardial infarction (*n*)[a]	16 (14%)
Prior PCI (*n*)[a]	11 (9%)
Hematocrit (volume percentage)	42 ± 4
Creatinine (μmol/l)	85 ± 14
Total Agatston score[b]	541 (160–1053)

Values are reported as mean and ±standard deviation or absolute number *n* and percentage (%). CAD, coronary artery disease; PCI, percutaneous coronary intervention.
[a] Not in the vessel territories interrogated by invasive FFR.
[b] Median and quartiles, in two patients, no CAC score scan was performed.

2.2. Coronary CT angiography

The first 39 (34%) coronary CTA examinations were performed on a first generation dual-source 64-slice CT, the remaining 77 (66%) patients on a second generation dual-source 128-slice CT scanner (Somatom Definition and Definition Flash, Siemens Medical Solutions, Forchheim, Germany). Sublingual nitroglycerin was routinely given, beta blockers were administrated in patients with a fast heart rate. Prospectively ECG triggered axial acquisition was applied in 97 patients, with a mean dose-length product of 366 ± 301 mGycm (estimated effective dose 5.1 mSv, using k = 0.014). In the remaining 19 patients, CT data were acquired in retrospectively ECG-gated spiral mode with a mean dose-length product of 694 ± 280 mGycm (9.7 mSv). All CT image data sets were reconstructed using a slice thickness of 0.75 mm and an increment of 0.4 mm. In 68 CTA data sets, a medium/soft kernel was used, while in the remaining 48 datasets a sharp reconstruction kernel was applied. The sharper reconstruction kernel was selected in the presence of large amounts of calcified coronary plaque. The locations of the stenoses of interest were recorded following the Society of Cardiovascular Computed Tomography (SCCT) 18-segment coronary artery model.[19] For each vessel, the lesion of interest was defined as the most severe stenosis proximal to the invasive FFR sample location. Calcification of the stenosis of interest was defined as any calcification within the plaque causing stenosis. Reference vessel size and coronary lumen attenuation were measured in a cross-sectional view, at the invasive FFR sample location. Lesions within 5 mm of the carina of a coronary artery bifurcation were defined as bifurcation lesions.[20,21] Image quality was scored per segment on a 4-point scale: 1 non diagnostic; 2 poor impaired image quality, differentiation of the coronary artery wall possible with reduced confidence; 3 adequate, reduced image quality due to artifacts without limiting coronary artery wall differentiation; 4 excellent, no artifacts present and clear differentiation of the coronary artery wall. The mean coronary CTA image quality score was calculated by adding the score for each segment and dividing this by the total number of segments scored for each scan. For each coronary segment, commonly encountered image artifacts were recorded including motion, misalignment, and low contrast.

2.3. Invasive angiography and fractional flow reserve

Invasive coronary angiography was performed following local standards. Invasive FFR was performed for clinical indications, or in the context of research projects unrelated to the CTA-FFR study. By protocol, an FFR pressure wire (PressureWire Aeris/Certus, St. Jude Medical, St. Paul, USA or Prime/Combo Wire, Volcano, San Diego, USA) was positioned distal to the stenosis of interest, after which hyperemia was induced by intravenous infusion of adenosine at 140 μg/kg/min. FFR values ≤ 0.80 were considered hemodynamically significant. To co-register the location of invasive FFR measurement and CTA-FFR, an independent reviewer (K.N.) without knowledge of angiographic or functional results identified the invasive FFR sample location on fluoroscopy images and registered the corresponding location on coronary CTA images using anatomical landmarks.

2.4. Coronary CTA derived FFR

2.4.1. Coronary CTA derived 3D coronary model

The CTA-FFR algorithm relies on a detailed 3D coronary model,