CASE REPORT

Noninvasive Fractional Flow Reserve for the Diagnosis of Lesion-specific Ischemia: A Case Example

Jesper Møller Jensen, Lars Christian Gormsen[1], Henning Mølgaard, Bjarne Linde Nørgaard

Departments of Cardiology and [1]Nuclear Medicine, Aarhus University Hospital, Aarhus, Denmark

Address for correspondence:
Dr. Jesper Møller Jensen,
Department of Cardiology, Aarhus
University Hospital, Skejby,
Brendstrupgaardsvej 100, Aarhus
N - 8200, Denmark.
E-mail: jespje@rm.dk

ABSTRACT

A physically active 52-year-old male with atypical chest pain was referred to our department. A coronary computed tomography angiography (CCTA) showed a stenotic plaque in the mid left anterior descending coronary artery (LAD). A rest–stress Rubidium-82 myocardial perfusion was normal. One year later the patient sustained a cardiac arrest and percutaneous coronary intervention of the mid-LAD was successfully performed. The original CCTA data were submitted for noninvasive determination of fractional flow reserve (FFR_{CT}) revealing an ischemia-producing lesion in the mid-LAD. This case demonstrates the inherent limitations of assessing lesion-specific ischemia. FFR_{CT} shows promise as a new method for future selection of patients for coronary angiography.

Key words: Coronary artery disease, fractional flow reserve, nuclear medicine

INTRODUCTION

Recently, a new method for assessing the functional significance of coronary computed tomography angiography (CCTA) has become available.[1-4] This method uses patient-specific anatomic data from CCTA, mathematic modeling of coronary physiology, and computation of coronary pressure and blood flow utilizing computational fluid dynamics[1] to provide a noninvasive measure of fractional flow reserve (FFR_{CT}), which can identify ischemia-producing stenoses.[2-4] The present case demonstrates the potential role of this new method as a gatekeeper to the catheterization laboratory.

CASE REPORT

A 52-year-old male was referred for evaluation of atypical chest discomfort after strenuous exercise and occasional stabbing pain in the left thorax not associated with physical activity. The patient exercised daily and he had competed in 39 marathons without any chest symptoms. He had familial hypercholesterolemia but no history of diabetes, hypertension, or smoking. The patient had discontinued cholesterol-lowering medication. The patient's blood pressure, electrocardiogram, and echocardiogram were normal. Total cholesterol and low

density lipoprotein were 7.1 and 5.5 mmol/L, respectively. Due to the uncharacteristic nature of the patient's symptoms, a CCTA was performed. The calcium score was 140 and CCTA revealed calcified and noncalcified coronary atherosclerosis with a mixed, stenotic plaque in the mid left anterior descending coronary artery (LAD) [Figure 1]. Functional testing was scheduled with a rest–stress Rubidium-82 myocardial perfusion scan. Myocardial perfusion and coronary flow reserve were normal during adequate stress response to adenosine (140 µg/kg/min) [Figure 2]. Atorvastatin was prescribed and the patient continued his high level of daily physical activity.

One year later, following strenuous running, the patient sustained a cardiac arrest. Cardiopulmonary resuscitation was started immediately with successful electrical cardioversion of ventricular fibrillation and return of spontaneous circulation 6 min after the alarm. The electrocardiogram showed ST-elevation [Figure 3]. Acute

invasive angiography revealed occlusion of the mid-LAD. Normal coronary flow was restored after recanalization and stenting [Figure 4]. Ten days later, transthoracic echocardiography showed left ventricular ejection fraction of 40–45% with apical hypokinesis. The patient was advised cardiac rehabilitation.

As a blind study, we submitted the patient's CCTA data, which had been obtained one year earlier and had revealed a highly significant ischemia-producing lesion in the mid-LAD, for FFR$_{CT}$ analysis [Figure 5]. FFR$_{CT}$ analysis was performed at HeartFlow (Redwood City, CA, USA) utilizing updated proprietary software. Computation of noninvasive FFR$_{CT}$ from CCTA image data requires a physiologic model of coronary blood flow. The physiologic model is based on three underlying principles as described in detail by Taylor et al.,:[1] (i) The total resting coronary blood flow can be quantified relative to the myocardial mass, (ii) The

Figure 1: 52-year-old male with atypical chest pain. Coronary computed tomography angiography curved planar reformation image of the mid left anterior descending coronary artery. The white arrow marks an area suspicious for significant stenosis (>70%).
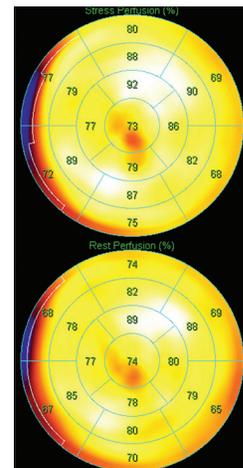
Figure 2: 52-year-old male with atypical chest pain. Static rubidium-82 perfusion images (17 segment polar maps) demonstrates no difference between stress (top) and rest perfusion (bottom). Images were acquired 150 s after injection of 1110 MBq Rb82. Total acquisition time was 270 s.
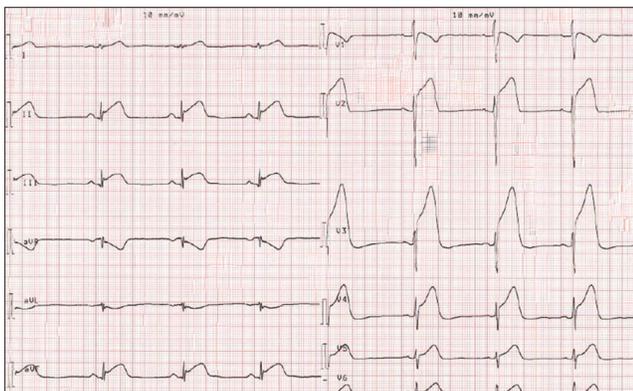
Figure 3: 53-year-old male presenting with severe chest pain and cardiac arrest, which was successfully treated with resuscitation and cardioversion. 12-lead electrocardiogram shows massive ST-elevation consistent with anterior ST-elevation myocardial infarction.

Figure 4: 53-year-old male presenting with severe chest pain and cardiac arrest, which was successfully treated with resuscitation and cardioversion. Invasive angiography shows present image of left anterior descending coronary artery occlusion marked by the white arrow (left side, angiography projection: 4° right anterior oblique and 24° cranial) and poststent image of re-perfused left anterior descending coronary artery with the white arrow marking the point of previous occlusion (right side, angiography projection: 6° right anterior oblique and 30° cranial).
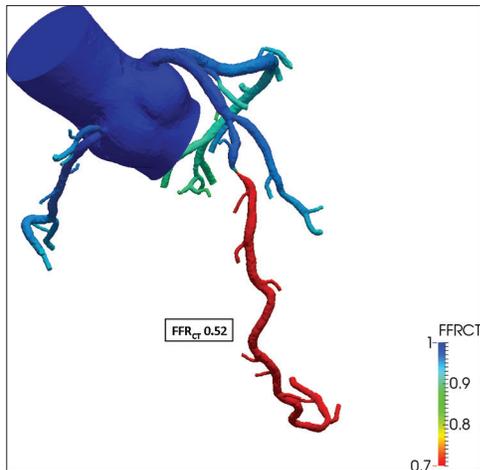
Figure 5: 52-year-old male with atypical chest pain. Fractional flow reserve (FFRCT = 0.52) derived from coronary computed tomography images and based on a physiologic model of coronary blood flow using three principles: (1) The total resting coronary blood flow can be quantified relative to the myocardial mass, (2) The microcirculatory vascular resistance at rest is inversely proportional to the size of the supplying coronary arteries, and (3) The vasodilatory response of the coronary microcirculation to adenosine can be predicted, allowing computational modeling of maximal hyperemia. The integration of the physiological model into 3-dimensional computational models allows computation of coronary flow and pressure under hyperemic conditions.

microcirculatory vascular resistance at rest is inversely proportional to the size of the coronary arteries supplying the myocardium, and (iii) The vasodilatory response of the coronary microcirculation to adenosine infusion can be predicted, allowing computational modeling of the maximal hyperemic state. The integration of the model of coronary physiology to 3-dimensional computational models allows computation of coronary flow and pressure at each point in the coronary arteries under hyperemic conditions.

DISCUSSION

This case demonstrates the inherent limitations of assessing lesion-specific ischemia utilizing currently available noninvasive imaging modalities. While CCTA can reliably identify coronary stenoses, it cannot assess their functional significance.[5] A coronary stenosis ≥50% detected by conventional angiography has a significantly lower diagnostic accuracy when compared with FFR_{CT} in detecting significant coronary artery disease as defined by FFR.[4] Myocardial perfusion imaging can detect perfusion abnormalities, but cannot assess the hemodynamic significance of individual coronary lesions.[6] Moreover, myocardial perfusion imaging misclassifies up to 58% of ischemic myocardial territories when compared with FFR in multivessel disease.[7] The prospective, randomized Fractional Flow Reserve versus Angiography for Multivessel Evaluation (FAME 2) study[8] has demonstrated reduced mortality and myocardial infarction from revascularization

of lesions with FFR <0.80 when compared with standard practice. One putative mechanism for this benefit is identification of stenoses at high risk for plaque rupture. Noninvasive FFR_{CT} values compare well with measured FFR,[2-4] thus FFR_{CT} may play a major role for selection of patients for coronary angiography. Large-scale prospective studies comparing the effect of FFR_{CT} versus standard diagnostic evaluation are ongoing.[9]

CONCLUSION

FFR_{CT} shows promise as a new method to identify lesion-specific ischemia noninvasively and, thus, FFR_{CT} may play a role in the selection of patients for coronary angiography.

REFERENCES

1. Taylor CA, Fonte TA, Min JK. Computational fluid dynamics applied to cardiac computed tomography for noninvasive quantification of fractional flow reserve: Scientific basis. J Am Coll Cardiol 2013;61:2233-41.
2. Koo BK, Erglis A, Doh JH, Daniels DV, Jegere S, Kim HS, et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. Results from the prospective multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) study. J Am Coll Cardiol 2011;58:1989-97.
3. Min JK, Leipsic J, Pencina MJ, Berman DS, Koo BK, van Mieghem C, et al. Diagnostic accuracy of fractional flow reserve from anatomic CT angiography. JAMA 2012;308:1237-45.
4. Nørgaard BL, Leipsic J, Gaur S, Seneviratne S, Ko BS, Ito H, et al. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease: The NXT trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps). J Am Coll Cardiol 2014;63:1145-55.
5. Rossi A, Papadopoulou SL, Pugliese F, Russo B, Dharampal AS, Dedic A, et al. Quantitative computed tomographic coronary angiography: Does it predict functionally significant coronary stenoses? Circ Cardiovasc Imaging 2014;7:43-51.
6. Yokota S, Ottervanger JP, Mouden M, Timmer JR, Knollema S, Jager PL. Prevalence, location, and extent of significant coronary artery disease in patients with normal myocardial perfusion imaging. J Nucl Cardiol 2014;21:284-90.
7. Melikian N, De Bondt P, Tonino P, De Winter O, Wyffels E, Bartunek J, et al. Fractional flow reserve and myocardial perfusion imaging in patients with angiographic multivessel coronary artery disease. JACC Cardiovasc Interv 2010;3:307-14.
8. De Bruyne B, Fearon WF, Pijls NH, Barbato E, Tonino P, Piroth Z, et al. Fractional flow reserve-guided PCI for stable coronary artery disease. N Engl J Med 2014;371:1208-17.
9. ClinicalTrials.gov A service of the U.S. National Institutes of Health. Available from: https://clinicaltrials.gov/ct2/show/NCT01943903?term = PLATFORMandrank = 2. [Last accessed on 14-11-2014].