One-Dimensional Mathematical Model-Based Automated Assessment of Fractional Flow Reserve in a Patient with Silent Myocardial Ischemia

Patient: Male, 58
Final Diagnosis: Coronary artery disease • silent myocardial ischemia
Symptoms: Silent myocardial ischemia
Medication: —
Clinical Procedure: Noninvasive assessment of fractional flow reserve • left descending artery revascularization
Specialty: Cardiology

Objective: Unusual setting of medical care

Background: Noninvasive assessment of the fractional flow reserve (FFR) in patients with coronary artery disease plays an important role in determining the need for revascularization. It is particularly relevant for patients with a borderline stenoses and painless myocardial ischemia. Our article describes the first clinical experience in the Russian Federation of using an automated method of noninvasive assessment of the fractional flow reserve (FFR\textsubscript{ct}) with a one-dimensional (1-D) mathematical model in a patient with painless myocardial ischemia.

Case Report: A 58-year-old male patient who underwent stent implantation in the left circumflex coronary artery (LCX) due to an acute non-ST-elevation posterior myocardial infarction had borderline stenoses of the left anterior descending artery (LAD). After stent implantation, there were no relapse angina symptoms on drug treatment, and according to our examination guideline for patients with borderline stenoses, a treadmill test was performed. The test was positive; therefore, FFR assessment was recommended, with coronary multi-slice CT being performed. The following results were obtained: FFR\textsubscript{LAD} – 0.57; FFR\textsubscript{LCX} – 0.88. An invasive assessment of FFR was also performed as a reference standard and revealed: FFR\textsubscript{LAD} – 0.6; FFR\textsubscript{LCX} – 0.88, and simultaneously a LAD percutaneous coronary intervention (PCI) was performed. Three months later, the patient underwent a stress test, which revealed no evidence of induced ischemia.

Conclusions: Our method of noninvasive assessment of FFR has shown encouraging results, but we believe that larger-scale studies are needed to establish it as common clinical practice.

MeSH Keywords: Coronary Artery Disease • Fractional Flow Reserve, Myocardial • Models, Theoretical

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/908449
Background

In 2015, for the first time in the Russian Federation, specialists from the Institute of Numerical Mathematics in collaboration with specialists of the I.M. Sechenov First Moscow State Medical University developed software allowing the noninvasive assessment of FFR by a 1-D mathematical model construction using routine coronary computed tomographic angiography (CCTA) data.

The world’s first fully automated algorithm for processing CT data was applied [1–5].

This article reports the Russian Federation’s first clinical case with the automated method of noninvasive assessment of FFR with 1-D mathematical model construction using the routine CCTA data in a patient with silent myocardial ischemia.

Case Report

We report the case of a 58-year-old male patient who had no severe comorbid somatic pathologies or family history of coronary artery disease (CAD) and no tobacco use, who denied angina symptoms, and had no subjective decrease in tolerance to physical activity.

In 2016, the patient had CAD, class III angina, under Canadian Cardiovascular Society classifications. On 16 April 2016, the patient had an acute non-ST-elevation posterior myocardial infarction. An emergency coronary angiography was performed, which revealed: a balanced type of coronary circulation; up to 40% proximal segment stenosis in the left anterior descending artery (LAD); up to 50% mid-segment stenosis; up to 60% ostium stenosis in the diagonal branch; and up to 99% extended stenosis in the left circumflex coronary artery (LCX). The patient underwent PCI with bare metal stent (Driver, 2.75×24 mm). The patient was discharged with the following treatment: clopidogrel (75 mg once daily), acetylsalicylic acid (100 mg once daily), metoprolol (50 mg once daily), lisinopril (5 mg once daily), and atorvastatin (20 mg once daily). While being treated, the patient did not have any angina symptoms. On 12 May 2016, a treadmill test was performed according our protocol for borderline stenoses, with 7.6 METs being achieved. At the peak (HR 146 beats/min), inverted T waves in leads II, III, AVF, V5, and V6 were detected. At the third minute of the recovery period, there was horizontal ST depression in leads V2–V4, with an absence of chest pain symptoms. The test result was positive, and FFR assessment was recommended with further possible LAD revascularization.

During the physical examination, no significant abnormalities were found. Laboratory testing revealed no significant deviations, and total cholesterol and low-density lipoproteins values were within the normal range. The electrocardiographic study revealed signs of the previous myocardial infarction, and scar changes of the posterior wall on the left ventricle myocardium. According to the echocardiography, there were no local contractility abnormalities, the ejection fraction was 59%, mitral valve insufficiency with regurgitation was up to grade 1, and there was a slight increase of the left atrium.

Taking into consideration the anamnesis and the results of the physical examination, the patient was diagnosed with CAD, silent myocardial ischemia, and postinfarction cardioclerosis (non-ST-elevation posterior myocardial infarction from 16.06.2016). The patient had no other comorbidities.
Coronary multi-slice CT was performed with a 640-slice CT scanner (Toshiba Aquilion ONE) for noninvasive FFR assessment. The patient was given oral beta-blockers to target a heart rate of <60 beats/min, and sublingual nitrates to ensure coronary vasodilation. CT images (Figure 1) were derived and processed by the working group of the Institute of Numerical Mathematics, which was responsible for blood flow and cardiovascular pathology models construction. CT images were processed in the following order: a) preprocessing; b) segmentation of aorta, the search for ostium image and segmentation of coronary arteries; c) artery skeletonization; d) artery graph construction. In the first stage, the initial CT images, with narrowed visibility scope, were deleted and the lung vessels were shadowed by means of mathematical morphology. In the second stage, 3-D models of the aorta and coronary arteries were constructed (Figure 2), but in our patient’s case, a few artery segments were selected manually. In the third stage, the vessel centerlines were extracted from the 3-D model, and in the last stage, the artery graph was built containing information on the vessel topology, length, and diameter. Specific edges were introduced to the graph, which corresponded to the regions of the FFR\(_{ct}\) computing. Then, the numerical experiments were performed. All the algorithms are described in a previous study [6] and have previously been used in other studies [1–3]. The following results were obtained: FFR\(_{ct}\), LAD – 0.57; FFR\(_{ct}\), LCX – 0.88 (Figure 3A). An invasive assessment of FFR was also performed as a reference standard and revealed: FFR LAD – 0.6; FFR LCX – 0.88 (Figure 3B).

Simultaneously, the LAD PCI with drug-eluting stent (DES) (Synergy, 3.00×48 mm) was performed. After post-surgery control, the measurement of the invasive FFR LAD was 0.86 (Figure 4).

The patient was discharged with the following treatment: clopidogrel (150 mg once daily for 1 month, then 75 mg once daily for 11 months), acetylsalicylic acid (100 mg once daily for...
life), metoprolol (25 mg once daily), lisinopril (5 mg once daily), atorvastatin (20 mg once daily), and pantoprazole (40 mg once daily).

During the whole follow-up period, including the invasive and the noninvasive stages, no adverse and/or unanticipated events were witnessed. Three months after the stent implantation, the patient underwent a functional stress test, which revealed no evidence of induced ischemia.

Discussion

Both in Russia and abroad, the application of the invasive FFR assessment is limited, as it is only performed at major clinical diagnostic centers due to the high cost of material and the invasiveness of the procedure. A search for alternative methods for the noninvasive assessment of functional significance of coronary stenoses has led to the development of new software solutions that allow the construction of a 3-D mathematical model of coronary blood flow using the routine CT angiography data without modifying image acquisition protocol, additional radiation, or added medications for vasodilation.

The recently conducted DISCOVER, DEFACTO, and NXT studies have revealed the high diagnostic efficiency of this method [7–13]. Nevertheless, one of the disadvantages of a 3-D model building is its high computational complexity, and to assess the noninvasive FFR, time-consuming calculations need to be done on costly computers. Many 3-D models also require the input data to be processed manually. All these factors make the implementation of this approach difficult in clinical practice.

Our method allows the calculations to be made even when computing power is limited, as a typical FFR calculation run on a laptop takes no longer than 20 minutes. CTTA data are processed automatically if there is sufficient image quality. Even so, there are several limitations:

Automated processing requires a DICOM format of source data. Only images captured with contrast dye in the arterial phase are suitable. Image processing is complicated when contrast dye enters coronary veins and heart chambers (except for the LV). Shaded arteries, where the contrast dye has not entered, are not visible when the $FFR_{10}$ model is constructed. DICOM images should contain cross-sections of the aorta above the Valsalva sinus, and the DICOM file should contain information on voxel size. More studies on the evaluation of diagnostic accuracy, sensitivity, and specificity of the described approach with a larger cohort of patients are needed for this become normal clinical practice.

Conclusions

Our method of noninvasive FFR assessment has shown encouraging results. The advantages are its noninvasiveness and the low cost of the procedure, as well as the ability to jointly get information about the anatomical and functional significance of the stenoses. Moreover, this method is simple to use due to the fully automated algorithm of data processing. All these factors should allow clinicians to be able to quickly determine whether revascularization is needed. It is of particular relevance for patients with borderline stenoses, with or without atypical angina symptoms, and in those cases where, for whatever reasons, stress testing cannot be performed or its results seem to be unreliable.

Conflict of interest

None.
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