A novel noninvasive method for measuring fractional flow reserve through three-dimensional modeling

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Coronary stenosis with lumen diameter reduction greater than 50% is recognized as coronary artery disease (CAD) [1-4]. Fractional flow reserve (FFR) is an epicardial lesion-specific parameter to determine the functional coronary stenosis, which is determined by pressure difference and resistance [5-8]. Previous studies have demonstrated that FFR guided percutaneous coronary intervention (PCI) could improve outcomes compared with anatomical invasive coronary angiography (ICA) guided PCI [6-10]. This study aims to overcome the deficiencies of invasive FFR and create a novel noninvasive FFR (FFR_{ni}).

A 70-year-old female patient, diagnosed with CAD, stable angina pectoris, cardiac function III, essential hypertension III (very high-risk group), with blood pressure of 140/85 mm Hg, was enrolled in as a pilot study.

Coronary computed tomography angiography (CCTA) was performed using multi-detector computed tomography scanners (Lightspeed 16 Pro). Original images were spilt into thin layers and directly exported into imaging control software MIMICS and processed to form an image sequence. Three-dimensional (3D) geometric models of the narrow coronary arteries including the right coronary artery (RCA), left anterior descending coronary (LAD) and left circumflex artery (LCX) were reconstructed and exported. Then, the geometric model was meshed with 3D Flotran elements in ANSYS software. Finite element analysis (FEA) was applied to analyze the velocity and pressure distribution of selected coronary arteries. Given boundary conditions including average velocity measured by transthoracic Doppler echocardiography with an ultrasound system (Sequoia C256) were applied in an inlet of 3D model. By setting the proper iteration time, the calculation went smoothly. ICA, as the "gold standard", was performed with standard techniques.

Invasive coronary angiography indicated that there was around 80% stenosis in the proximal RCA (Figure 1 A). Mild (about 30%) stenosis in the proximal LAD and a diffuse lesion of the LCX (the narrowest was 80%)

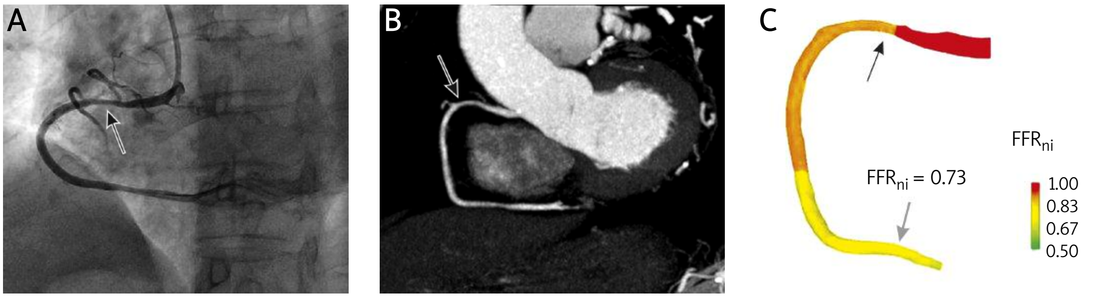

Figure 1. Anatomically obstructive stenosis of right coronary artery (RCA) with a lesion causing ischemia. **A** – Invasive coronary angiography indicates that stenosis is about 80% in the proximal RCA (black arrow). **B** – Multi-planar reformat of coronary computed tomography angiography demonstrates moderate (around 60%) obstructive stenosis (black arrow). **C** – FFR_{ni} indicates the lesion-specific functional ischemia with the value 0.73 of distal RCA

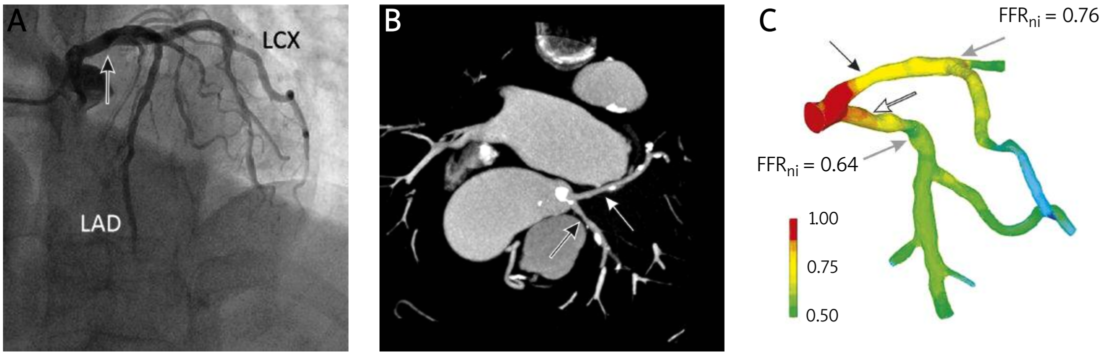

Figure 2. Anatomically obstructive stenosis of left anterior descending coronary (LAD) and left circumflex artery (LCX) with/without functional ischemia. **A** – Invasive coronary angiography indicates that there exist 30% stenosis in proximal LAD (black arrow) and a diffuse lesion (narrowest point around 80% stenosis) in LCX. **B** – Multi-planar reformat from coronary computed tomography angiography shows about 30% stenosis in proximal LAD (black arrow) and diffuse stenosis in LCX (white arrow). **C** – Lesion-specific functional ischemia is indicated with FFR_{ni} value 0.76, 0.64 in the distal stenosis of LAD and LCX, respectively

could also be quantified (Figure 2 A). Additionally, the coronal section of CCTA images demonstrated moderate (around 60%) obstructive stenosis in the proximal RCA (Figure 1 B). The cross-sectional images indicated 30% stenosis in the proximal and first branch segment of the LAD and diffuse patchy calcified plaques in the LCX leading to intermediate (50%) stenosis (Figure 2 B). The diagnostic performance of FFR_{ni} was generally consistent with the results of ICA and CCTA. The values of proximal RCA, LAD and distal LCX were 0.73, 0.76 and 0.64, respectively, which suggested the severity of lesion-specific functional ischemia in distal myocardium with 0.75 as the cutoff value (Figures 1 C and 2 C).

Recently, FFR computed from CCTA (FFR_{CT}) was reported. A good correlation between FFR_{CT} and invasive FFR was certified through a randomized clinical controlled trial on 159 vessels in 103 patients [11]. The differences in the calculation process of FFR_{CT} and FFR_{ni} in our study mainly reflect the following factors. During FFR_{CT} calculation, coronary flow and pressure are unknown. A method to couple lumped parameter models of the microcirculation to the outflow boundaries of the 3D model was adopted. As a result of the cumbersome workload, it takes approximately 5 h/exam. We utilized FEA of the Flotran CFD module to solve the hemodynamic calculation under given boundary conditions. Therefore, it can greatly reduce the computation time to 3 h/exam. The more relaxed equipment requirements and faster inspection time guarantee potential clinical application of FFR_{ni}.

Fractional flow reserve is a well-evaluated functional index to assess the ischemic significance of coronary lesions, helping making the decision of revascularization [12-14]. Nevertheless, the invasiveness and costliness are two major reasons restricting its further application. Finite element analysis and CFD over digital 3D modeling were applied in this pilot study and created a novel method to evaluate functional coronary stenosis by FFR_{ni}, which showed good consistency with ICA and CCTA. The superiority of no invasiveness and cost-effectiveness establishes the foundation of FFR_{ni} for its further applications in clinical practice. However, a large randomized clinical controlled trial assessed by FFR_{ni} compared with invasive FFR is urgently needed.

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