Noninvasive Fractional Flow Reserve Derived from Coronary Computed Tomography Angiography for the Diagnosis of Lesion-specific Ischemia

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KEYWORDS

• Fractional flow reserve • Coronary CT angiography • FFR_{CT} • Coronary artery disease

KEY POINTS

- Fractional flow reserve derived from coronary computed tomography angiography (FFR_{CT}) has emerged as a powerful tool for the assessment of flow-limiting coronary stenoses.
- To date, FFR_{CT} is the only noninvasive imaging modality for the depiction of lesion-specific ischemia and large prospective multicenter studies have established its high diagnostic value.
- The nature of FFR_{CT} allows the prediction of functional outcome of coronary stenting, which will expand the role of cardiac CT in the evaluation and management of coronary artery disease.

INTRODUCTION

Coronary computed tomography angiography (CCTA) is a noninvasive alternative for the evaluation of coronary anatomy. An array of studies have established its high sensitivity and negative predictive value (NPV),[1,2] rendering it an excellent tool for the rule out of obstructive coronary artery disease. Yet, CCTA tends to overestimate the degree of stenosis when compared with invasive coronary angiography (ICA),[2] which may prompt more downstream testing and unnecessary referrals to the catheterization laboratory.[3] In addition, CCTA is a purely anatomic imaging modality unable to determine the physiologic severity of coronary lesions, and even amongst CCTA-identified significant lesions confirmed by ICA, approximately half of them are found to be flow-limiting.[4,5] Therefore, functional testing of coronary stenoses deemed significant by CCTA is mandatory, not only to improve diagnostic accuracy, but also to enhance clinical decision-making on the need for a coronary revascularization. Fractional flow reserve (FFR) is considered the gold standard for determining the functional repercussion of angiographically intermediate stenosis.[6,7] It has been demonstrated that FFR-based guidance of coronary revascularization relieves symptoms and improves outcomes.[8–10] However, the

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invasive nature of FFR limits its application to broad populations as an initial diagnostic test. For the noninvasive diagnosis and management of coronary artery disease (CAD), detection of myocardial ischemia is indicated, and nuclear imaging modalities, such as single-photon emission computed tomography (SPECT) and PET have traditionally been assigned to this task. Importantly, detection of myocardial perfusion with these techniques comes at a cost of patient inconvenience and radiation exposure. Recently, a novel method has been described that applies computational fluid dynamics to derive FFR from traditional CCTA images (FFR_{CT}), obviating the need of additional imaging, modifications of computed tomography (CT) acquisition protocols, or administration of medications.[11] Notably, prospective multicenter studies demonstrated FFR_{CT} to exhibit high diagnostic accuracy for identification of flow-limiting CAD.[11–13] As such, FFR_{CT} may become a method that provides complementary information on coronary anatomy and the physiologic implications of coronary stenoses in patients evaluated for CAD.

FRACTIONAL FLOW RESERVE FOR THE ASSESSMENT OF LESION-SPECIFIC ISCHEMIA

FFR measurements in the presence of coronary stenoses have proved to yield useful information on the functional severity of coronary lesions.[14] FFR is an index and is defined as the ratio of hyperemic maximum coronary flow in a stenotic artery to maximum coronary flow in the same artery if it was hypothetically completely normal. The ratio of the 2 flows is expressed as the ratio of 2 pressures, namely the pressure proximal and distal to the stenosis (Fig. 1). The relationship between coronary flow and FFR was investigated in the early 1990s by Pijls and colleagues[15] in animal models, providing the basis for the concept of pressure measurements as a derivative of coronary flow and subsequent pathophysiologic severity of coronary artery stenoses. As such, normal myocardial blood flow is considered a prerequisite for the absence of hyperemic intracoronary pressure gradients.[15] Interestingly, the clinical feasibility of FFR was shown in 22 patients with an isolated stenosis in the left anterior descending artery, whereby FFR was compared against a background of quantitative [^{15}O]H_2O PET.[16] De Bruyne and colleagues[16] demonstrated that FFR was closely related to the relative flow reserve obtained by [^{15}O]H_2O PET (r = 0.86); however, coronary pressure and myocardial blood flow are not interchangeable and discrepancies between these 2 parameters do not imply the failure of either technique, but merely reflect the heterogeneous nature of coronary atherosclerosis spanning the gamut from focal obstructive CAD to coronary microvascular dysfunction.[17–19] However, to date, FFR is the only technique for the detection of ischemia that has been prospectively validated against multiple reference standards,[14] using the so-called Bayesian approach, rendering it a robust and reliable tool. The importance of FFR measurements for the evaluation of CAD has been demonstrated by the landmark FAME (Fractional Flow Reserve vs Angiography for Multivessel Evaluation) trial, which showed that FFR-guided stenting improved patient outcome

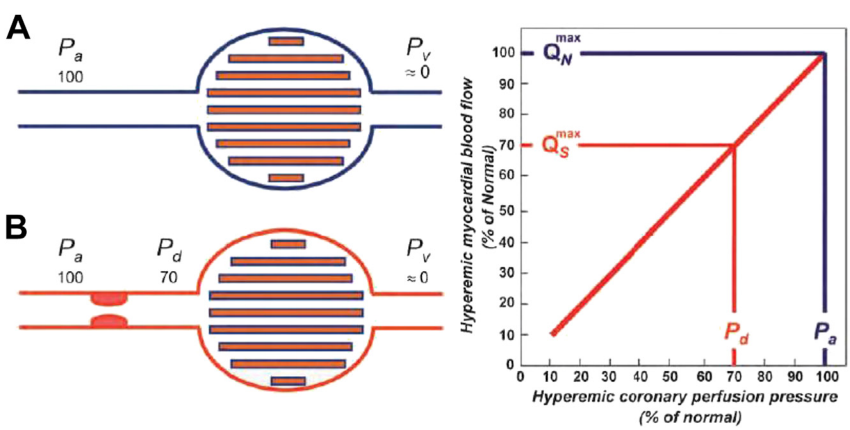

Fig. 1. Concept of fractional flow reserve. (*A*) If no coronary stenosis is present, the driving pressure reflects maximum coronary flow (100%). In the presence of a given epicardial stenosis (*B*), driving pressure in this example is no longer 100%, but only 70%. As such, myocardial blood flow is only 70% of maximum and FFR (Pd/Pa) = 0.70. *From* Pijls NH, Tanaka N, Fearon WF. Functional assessment of coronary stenoses: can we live without it? Eur Heart J 2013;34(18):1335–44; with permission.