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REVIEW

Angiography-Derived Fractional Flow Reserve in Coronary Assessment: Current Developments and Future Perspectives

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Abstract

Coronary physiology assessment is an important factor in guiding myocardial revascularization. A growing body of research highlights the value of using fractional flow reserve, FFR and other pressure-based indicators for functional assessment of stable coronary stenoses. Invasive functional coronary assessment techniques have evolved from intracoronary wire-based to wire-free approaches as a result of technological advancements. In addition, several software programs on the market have been thoroughly investigated and validated against invasive FFR, and have shown good accuracy and correlation. However, use of FFR remains modest. Hence, this review provides an overview of angiography-based FFR solutions and compares their technologies. Additionally, a systematic scoping review was performed to understand the research landscape in wire-free coronary physiology assessment, to complement the narratives of existing FFR trials on wire-free FFR. Furthermore, future developments and strategies that could expand the use of wire-free computed coronary functional assessment in the Asia Pacific region are discussed.

Keywords: Angiography-based FFR; wire-free FFR; Percutaneous coronary intervention; Coronary physiological assessment

Overview and Progress in Wire-Free Coronary Physiology Assessment

Conventionally, myocardial ischemia is attributed to “flow-limiting” epicardial coronary artery stenoses of >70% that are identified angiographically. However, in addition to the severity of stenoses, the area of the myocardium being supplied affects the functional significance of coronary artery lesions. Percutaneous coronary intervention (PCI), for instance, is a contemporary procedure to relieve flow-limiting stenosis, thus enhancing perfusion to the myocardium in patients with stable angina who are unresponsive to medication. According to recent studies, the presence of ischemia in

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intermediate-severity coronary lesions remains the most critical factor determining the clinical benefits of revascularization in the context of stable coronary artery disease (CAD), and an initial invasive strategy of functionally non-significant lesions does not confer any additional benefits over optimal medical therapy [1, 2]. PCI of non-flow limiting lesions has also been associated with major adverse cardiac events and the need for repeat revascularization [1]. Overall, clinical trial data support a primary pharmacological approach in this clinical scenario and recommend delaying revascularization in coronary artery stenoses without functionally significant ischemia [3–5]. Hence, recommendations have suggested identifying and quantifying ischemia before considering revascularization for stable angina [6, 7]. Nonetheless, no standard approach exists for performing physiological assessment of all coronary stenoses with intermediate severity before revascularization.

Before the development of an invasive wire-based technology that objectively measures pressure gradient differences across a coronary lesion (driving pressure for microcirculatory flow distal to the stenosis (Pd) in relation to the coronary pressure available in the absence of stenosis, aortic pressure ratio (Pa)), visual assessment of intermediate-degree stenoses remained the standard approach for revascularization decision-making [8]. Fractional flow reserve (FFR), a technique pioneered 30 years ago, is based on Poiseuille's law, in which the distal coronary driving pressure measured in maximal hyperemia is directly proportional to the maximum vasodilated perfusion. To quantify the percentage contribution of coronary stenosis to cardiac flow limitation, the downstream arteries with resistance must be dilated with pharmaceutical drugs [9].

The acceptance of FFR is limited, although FFR assessment is increasingly used in interventional cardiology, and abundant scientific evidence supports its prognostic ability and cost-effectiveness. This limited acceptance is associated with perceptions that FFR is associated with additional procedure costs, time, and pressure wire instrumentation, as well as patient discomfort from the pharmacological medicines used to induce hyperemia [10]. Consequently, non-hyperemic pressure ratios (NHPR) or diastolic-only pressure ratios (dPR) have been developed in the search for simpler patient-friendly methods to increase the use of physiologically guided revascularization. These methods do not require hyperemia and avoid concerns regarding the best time to measure FFR during hyperemia or how to handle the adverse effects of hyperemia-inducing drugs such as adenosine. However, landmark studies of these applications have varied in their use of wire-based modalities and their assessment of various types of lesions in a heterogeneous population, thus yielding a range of results [11–14]. Different delivery techniques for NHPR, such as instantaneous wave-free ratio (iFR), have been demonstrated to be non-inferior to FFR and to provide a straightforward assessment of resting Pd/Pa in the diastolic period. The diastolic hyperemia-free ratio, resting full-cycle ratio and diastolic pressure ratio (DPR/dPR) are other diastolic indices from various vendors that have been validated with FFR [11–14].

Given that the adoption of wire-based coronary physiology assessment remains low, numerous groups have begun to develop wire-free angiography-based procedures using artificial intelligence to assess the functional importance of intermediate lesions, even in the absence of hyperemia induction. This review provides an overview and scientific background for various angiography-based FFR technologies, current evidence supporting their use in clinical practice and perspectives on future directions.

Concept of Angiography-Based FFR

Wire-free image-based FFR is software-based and has been enabled by the development of three-dimensional quantitative coronary angiography (3-D QCA) and computational fluid dynamics (CFD). Most programs use paired two-dimensional angiograms to reconstruct the three-dimensional vascular anatomy of the arteries. Because the Navier-Stokes equation, which uses CFD to explain fluid motion, can be time- and resource-intensive, simplified assessments using equations based on the pioneering work of Young, Tsai and Gould have been suggested [15, 16]. The Gould formula estimates the pressure drop for each stenosis segment by using geometry and the mean hyperemic flow velocity, by modelling a range of flow rates