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Editorial

Angiography based quantitative flow ratio in coronary artery disease: Mimic of FFR – Ready for clinical use?

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Invasive fractional flow reserve (FFR) is defined as the ratio of the pressure distal to a stenosis (Pd), relative to the pressure in aorta (Pa) during maximal hyperemia, typically induced with adenosine. When FFR is utilized to guide percutaneous coronary intervention (PCI) using a threshold of ≤0.8 to define ischemia, it is associated with improved outcomes, when compared with angiography guided PCI. However, the intracoronary instrumentation and systemic vasodilatation during FFR interrogation requires expertise, add extra procedural time, and is associated with patient discomfort during vasodilator stress and a small risk of serious complications [1]. Resting indices such as instantaneous wave-free ratio (iFR) and resting Pd/Pa ratio obviate the need for hyperemia and two recent multicenter studies have demonstrated that iFR guided PCI is associated with equivalent 1-year outcomes as invasive FFR. However, similar to FFR, these techniques still require intracoronary manipulation, which together with issues related to costs and lack of reimbursement may present a barrier for the universal adoption of these tests [1]. Accordingly, several blood flow simulation strategies based on either invasive coronary (ICA) or computed tomography angiography (CTA) have been introduced over the past decade. FFRct is based on a 3-D model of the coronary arteries derived from standard acquired CTA data using complex segmentation techniques, and assumptions regarding hyperemia and flow based on tissue perfusion requirements and computational fluid dynamics (CFD) analysis to estimate FFRct along the entire coronary tree. FFRct demonstrates in stable coronary artery disease (CAD) high diagnostic performance against FFR, and knowledge about FFRct may favorably change clinical practice and outcomes [2]. More recently, various methodological strategies have been introduced for ICA derived physiological evaluation. The most validated being the Quantitative Flow Ratio (QFR) technique which is based on a 3-dimensional reconstruction of a stenotic vessel, rendered from 2 ICA projections, and the contrast flow frame count or assumption of a fixed inflow velocity. Since QFR is based on geometry, and not complex CFD assessments, it may be computed within a few minutes. Multicentre diagnostic performance studies have evaluated the technique in patients with intermediate coronary lesions, and have reported short computational times of approximately 7 min, high feasibility, and favorable overall diagnostic accuracy against FFR between 80 and 93% [3–6].

In this issue of Int. J Cardiol. Stähli B.E. and colleagues reported the diagnostic performance of QFR, resting Pd/Pa ratio, and percent diameter stenosis in a total of 436 single-center real-world patients in whom FFR was measured in 516 vessels with intermediate predominantly non-complex lesions [7]. Both continuous contrast flow and fixed flow vessel QFR ≤ 0.80 had higher discrimination for identifying lesion-specific ischemia than both resting Pd/Pa ratio ≤ 0.91, and >50% diameter stenosis with AUCs 0.86, 0.84, 0.76, and 0.63, respectively. The diagnostic accuracy, sensitivity, and specificity of QFR ≤ 0.80 was 93.4%, 75%, and 97.8%. This study adds to previous studies by demonstrating overall high diagnostic accuracy of QFR in a large real-world cohort of patients (vessels) with intermediate lesions comparable to the multicenter Wifi II and FAVOR studies [3–6]. QFR analysis could be performed in 90% of the vessels. Notably, QFR demonstrated a higher diagnostic performance than resting Pd/Pa ratio. This may be of importance, particularly when resting Pd/Pa ratio and iFR have been demonstrated to have comparable associations with anatomic and hemodynamic stenosis severity, and risk of adverse clinical outcomes [8]. However, there are several issues that should be considered. First of all, this is a retrospective study, and the findings may be subject to selection bias. Moreover, 40% of the vessels in this study had stenosis <40% when assessed by 3D-QCA. Accordingly, the prevalence of FFR ≤0.8 vessels in this cohort is lower than in previous studies (19% as compared to 33% and 34% in the FAVOR II Europe-Japan and China studies), which may have contributed to the reported high diagnostic performance. Importantly, while focusing the diagnostic accuracy around the diagnostic threshold (0.75–0.85) comprising 40% of the total cohort, diagnostic accuracy of QFR was reduced to 81%, for which the sensitivity and specificity was not

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presented. Turnaround times for QFR computation is of crucial importance such that timely results for decision-making in the catheterization laboratory can be provided. Unfortunately, time taken for analysis, observer experience and inter-observer reproducibility of the technique was not reported in this study.

We still have much to learn about QFR, -e.g. how it performs in ostial, bifurcation and tandem lesions; vessels with stents; tortuous vessels; severe diffuse disease, and in patients with microvascular dysfunction or arrhythmias. Moreover, future head to head comparisons between QFR and other ICA derived FFR modalities with regards to accuracy and on-site interobserver reproducibility will be required, especially in the FFR 0.75–0.85 range. Recently, the multi-centre FAST-FFR trial reached a diagnostic accuracy of 92.2% (both sensitivity and specificity >90%) by using the FFRangio tool [9]. While previous ICA based FFR methods consider a single artery, the FFRangio method (similar to FFRct) allows calculation of FFR in the entire coronary tree including side branches, which may be an advantage for its utility in real-world practice.

In our enthusiasm for new wire-free FFR surrogates and the abundance of new information we should not forget that these tests provide information on a “lesion-specific” level. While mitigating stenosis by FFR guided PCI offers alleviation of anginal symptoms, we don't have solid evidence that this strategy leads to improved hard outcomes when compared with optimum medical therapy. In order to prevent hard events we must focus on parameters also beyond ischemia causing lesions such as plaque morphology and burden, which may be best managed by present and future disease modifying medical therapy.

We will undoubtedly see further refinement and sophistication of blood flow simulation techniques in the future, including use of machine learning algorithms, and application of anatomical and CFD based indices of plaque vulnerability in software packages [10]. The clinical adoption of these modalities will be driven by test accuracy, reproducibility, applicability in existing diagnostic workflows, costs, and data on clinical outcomes. The initial experience demonstrates QFR closely mimics invasive FFR on diagnostic performance, but before clinical use, we need more research to determine its diagnostic and outcome value relative to other pressure-wire free FFR surrogates and for replacement of invasive FFR in more complex CAD.

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