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Editorial

To FFR, or Not to FFR an IRA, That Is the Question

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Fractional flow reserve (FFR) has been utilized extensively since its advent in the contemporary cardiac catheterization laboratory. FFR-guided percutaneous coronary intervention (PCI) is associated with superior clinical outcomes, and FFR-based deferral to medical therapy is safe.[1] FFR interpretation in an infarct-related artery (IRA) is more challenging compared with chronic coronary syndromes. During an ST-elevation myocardial infarction (STEMI), the coronary microcirculation undergoes several changes because of in situ inflammation, vasoconstriction, and microvascular occlusion. Acute plaque rupture and distal embolization may contribute to preexisting microvascular dysfunction. FFR may be underestimated across an IRA stenosis in the acute setting due to transient coronary microvascular dysfunction that impedes maximal hyperemia.[2] Coronary microcirculatory recovery begins at 24 hours following infarction and can recover completely by 6 months in some cases.[3] Hoole et al[4] found a large proportion of culprit lesions during STEMI were hemodynamically significant (FFR <0.80) at baseline and after treatment with thrombectomy despite an abnormal index of microcirculatory resistance (IMR). Over 2 decades ago, De Bruyne et al[5] evaluated the value of FFR in 57 patients who had sustained a myocardial infarction a week prior. Myocardial perfusion imaging and FFR were undertaken before and after angioplasty. An FFR value of 0.75 was able to precisely differentiate abnormal perfusion imaging from a negative study. The FFR was proportional to the mass of viable myocardium for a similar degree of coronary stenosis. These findings have been reproduced consistently.[6] However, the safety of FFR-based deferral of intervention in an IRA is the subject of debate, and long-term outcomes following this strategy are lacking.

In this context, we read the report by Ohashi et al[7] with great interest. These authors report a post hoc analysis from the long-term outcome of Japanese patients with deferral of coronary intervention based on fractional flow reserve in multicenter registry (J-CONFIRM) registry that includes patients with chronic coronary syndromes who did not undergo PCI irrespective of the FFR value. The authors extend their previous analysis[8] to include both IRAs (138 lesions) and non-IRAs (1309 lesions). The IRAs were identified using multimodality cardiac investigations including electrocardiogram, echocardiography, coronary angiography, and intravascular imaging. More than half of the cohort was asymptomatic, and less than 2% of the cohort had Canadian Cardiovascular Society IV angina. The overall cohort was mostly comprised of men with a median age of nearly 70 years, and just over 8% of the IRA cohort had a left ventricular ejection fraction <40%. The median duration from the index acute myocardial infarction was 716 days. Most of the IRA lesions were relatively short, with a median length of nearly 12 mm, and just over a third of the vessels had a reference vessel diameter of less than 2.5 mm. The IRAs were mostly comprised of functionally nonsignificant non-left main/noncomplex lesions, although 16% of the IRAs had FFR values between 0.75 and 0.80. No differences were observed in either the prevalence of visual-functional mismatch between lesions in IRA or non-IRA. Importantly, the 5-year incidence of target vessel failure across the IRA and non-IRA cohorts was similar. These findings suggest that the FFR measurement can be used to defer revascularization safely in IRAs. However, these findings should be interpreted in context of a few considerations.

First, this is a retrospective observational post hoc analysis, which is subject to inherent selection bias. Second, the relatively small sample size of the IRA cohort limits statistical power, making it more challenging to draw firm conclusions about the differences between the 2 cohorts. ^{18}F-sodium fluoride positron emission tomography has demonstrated that in acute coronary syndromes, there are multiple inflamed plaques across the coronary vasculature, making it at times challenging to identify the IRA and raising the question of the validity of physiologic analysis in this setting.[9] This could potentially result in misclassification bias. High IMR post-STEMI predicts poor long-term outcomes, and the addition of IMR measurement from the IRA distribution would have provided interesting data.[10] Functionally insignificant thin-cap fibroatheromas are associated with poor outcomes long term and unfortunately, this registry does not include intravascular imaging information.[11] Lastly, the population is similar to the

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Ischemia trial, consisting of mostly asymptomatic individuals with non-left main lesions, and irrespective of the FFR, they may have done well with medical therapy.[12]

This study by Kuramitsu et al certainly adds important information to the existing data regarding FFR in IRAs. The findings suggest that patients with a negative FFR can be safely treated medically long term. Ideally, FFR should be performed once the microcirculation has recovered. When possible, the combination of symptoms, lesion severity, pathological characteristics based on intravascular imaging, IMR, viability, the subtended area of myocardium at risk, and patient preference should all be taken into consideration in addition to the epicardial coronary physiology when deciding on deferral of revascularization. Further prospective randomized controlled trials assessing the safety of coronary physiology-based deferral of PCI in IRA would be welcomed to confirm the important findings in this study.

Declaration of competing interest

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