Editorial

Borderline multivessel coronary artery disease assessed by fractional flow reserve—affecting practice?

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Invasive coronary angiogram is pivotal in the diagnosis of coronary artery disease (CAD). However, as ischemia is the most important factor related to outcome for patients with CAD (1), additional functional assessment of coronary artery stenosis is important to evaluate the physiological significance of a coronary stenosis and to guide treatment and management. Today the gold standard for functional assessment of a coronary artery stenosis is invasive fractional flow reserve (FFR). FFR expresses the ratio between the aortic pressure and the pressure distal to the stenosis during maximal hyperemia most frequently induced by adenosine and takes into account the severity of the stenosis, amount of viable myocardium supplied by the vessel downstream to the stenosis and collateral flow (2). A cut-off FFR value of 0.75 or below has been associated with inducible ischemia using non-invasive techniques (3). Accordingly, it was demonstrated safe to defer revascularization in patients with FFR ≥0.75 (4,5). Using a cut-off value of ≤0.80 for performing percutaneous coronary intervention (PCI) FFR-guided treatment was demonstrated superior to angiography guided treatment in patients with CAD and multivessel disease (6). The superiority of FFR-guided revascularization over angiography-guided has been confirmed in real world registries (7). Therefore, today FFR guided management of patients with CAD is recommended in professional guidelines.

A specific cut-off value for FFR makes it a clinical useful tool for every single stenosis, but in terms of predicting future clinical events, and the benefit from revascularization, FFR should be considered a continuum. Several publications have demonstrated an inverse relationship between the FFR value and the risk of a future event, thus FFR value acts as a continuum with lower FFR values bringing patients at higher risk and vice versa regarding higher values (7-9). Interestingly, there seems to be little difference in the outcome for patients with FFR value of 0.75–0.80 (gray zone) compared to 0.81–0.85 (borderline) (10). In the 3V-FFR-FRIENDS study Lee and colleagues did FFR in all 3 coronary vessels before and after revascularization. By adding the FFR values from all 3 vessels—using the post-revascularization FFR in case PCI were performed—they demonstrated that the summed FFR value is a strong predictor for future events even in the absence of FFR significant lesions (11). Adding to this, also using data from the 3V-FFR-FRIENDS study, Park and colleagues found that patients with functionally insignificant moderate multivessel CAD—defined as FFR 0.81–0.87 in more than one vessel—had a 3-fold increased risk for future events compared to either patients with no CAD or patients with functionally insignificant single vessel moderate CAD (12). However, the risk was mainly driven by an increased rate of new revascularization. Moreover, the annual risk for death or myocardial infarction among the patients with functionally insignificant moderate multivessel CAD was still <1% (12), which is similar to previous observations in patients with insignificant FFR (13). The increased risk for

patients with functionally insignificant moderate multivessel CAD may thus present the natural history of CAD as patients with more severe borderline disease are more likely to experience progression of the CAD. The findings by Park and colleagues are interesting as FFR is systematically done in all 3 vessels (12). However, the issue of how to deal with the increased risk for patients with borderline FFR values and multivessel disease still remains.

The introduction of FFR-guided treatment results in a change in strategy in around 40% of patients compared to angiography-guided treatment (14) and fewer lesions needing revascularization (6). In patients with stable CAD and functionally significant lesions (FFR ≤0.80) PCI is superior to medical management (15,16). Similar FFR-guided revascularization is superior to conservative management in patients with multivessel disease and ST-segment elevation myocardial infarction (17,18), especially in patients with more extensive CAD (19). However, the benefit from revascularization narrows in closer to the cut-off value (7,9) and the effect of PCI in the gray zone is questionable (20). As a matter of fact revascularization compared to deferral in patients with FFR ≥0.75 seems to be related to more events during follow-up until 15 years (21). In terms of coronary artery bypass graft the patency of the grafts depends greatly on the presence of functional significant stenosis using FFR in the native vessel as 9% of bypass grafts to vessels with functional significant lesions occlude after 1 year compared to 21% of bypass grafts to vessels with functional insignificant stenosis (22,23). Therefore, taken together a FFR value <0.75 is considered indicative for the need of revascularization and a FFR value >0.80 indicate that revascularization should be deferred. The decision of revascularization for FFR values in the gray-zone—between 0.75 and 0.80—should rely on symptoms, results from non-invasive test, risk related to revascularization, complex lesion and PCI-eligibility of the stenosis. Thus, in the light of the current evidence and low annual risk for a death or myocardial infarction (<1%) in patients with borderline FFR values (0.81–0.87) these patients should not undergo revascularization even in the presence of borderline FFR values in multiple vessels. Intensifying the medical treatment and watchful waiting should be sufficient.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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