Routine Fractional Flow Reserve Combined to Diagnostic Coronary Angiography as a One-Stop Procedure

Episode 3

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R3F (Registre Français de la FFR) was the first study to investigate and demonstrate the clinical relevance of a new diagnostic concept based on the routine performance of fractional flow reserve (FFR) at the time of diagnostic angiography in patients suspected of coronary artery disease to define the optimal and individualized therapeutic option. The RIPCORD (Does Routine Pressure Wire Assessment Influence Management Strategy at Coronary Angiography for Diagnosis of Chest Pain) study, published a few months later, investigated the same idea and provided additional weight to the concept. It also gave us the opportunity to discuss several aspects of the concept and to further elaborate on its benefits. In short, this new diagnostic concept proposes to combine diagnostic angiography and FFR as a single one-stop procedure and intend to make it the ultimate tool for clinical decision making in patients suspected of coronary artery disease. The key benefit of such an approach is to allow to discharge the patient from the catheterization laboratory with a clear, detailed, and definitive therapeutic plan. This is of major importance at a time where the appropriateness of therapeutic decision is more than ever the ultimate goal of patients’ care and in a context where noninvasive tests have been shown to be often insufficient. Indeed as demonstrated many times, only 50% of patients are referred to coronary angiography with a noninvasive ischemic test performed before, and when they have been performed, their add-on diagnostic value—on top of a careful medical examination and history—has been challenged.

The POST-IT (Portuguese Study on the Evaluation of FFR Guided Treatment of Coronary Disease) study including >1000 patients and published in this issue of Circulation: Cardiovascular Interventions provides additional fuel to this emerging concept. Altogether, R3F, RIPCORD, and POST-IT are combining >2000 patients while sharing a similar prospective design to investigate the role of routine FFR at time of angiography on the therapeutic decision process. In addition, as R3F, POST-IT is providing prospective information on 1-year clinical outcome. These 3 studies established clearly that routine performance of FFR allow the reclassification of the initial therapeutic decision in more than one third of the patient population (26% in RIPCORD, 43% in R3F, and 44% in POST-IT). R3F and POST-IT further demonstrated that it is also safe to use FFR to reclassify the treatment decision.

A key addition of the POST-IT study is the demonstration that the implementation of routine FFR during angiography as the potential to reduce drastically the use of noninvasive tests. In this study, physicians requested the performance of a noninvasive test to clarify the patient management after coronary angiography in 22% of cases. The request of a noninvasive test after angiography may seem surprising but make sense when considering that, as reported many times and as also observed in the present study, only half of the patients are referred to coronary angiography with an ischemic test performed before. The key finding of the POST-IT study is that among these 22% of patients initially referred to a noninvasive test after angiography, every single one of them was reallocated to a therapeutic option by FFR—coronary artery bypass surgery, percutaneous coronary intervention (PCI), or medical treatment—without any more need for a noninvasive test. This important observation is an important addition to the previous findings of the R3F study demonstrating that reclassification by FFR occurs at the same high rate (>30%) irrespective of whether a noninvasive test has been performed or not before angiography and also whether this noninvasive test was positive or not. Combined with those previous R3F results, the observation made by POST-IT investigators reinforces the one-stop-shop concept aiming to a shortening of the decision process at the patient’s benefit and to a reduction of the additional costs related to the performance of these “postprocedural” noninvasive tests.

Another key contribution of the POST-IT study is to help to elucidate an important misconception about FFR. Since the results of the DEFER study, demonstrating that performing FFR in patients referred for PCI prevents the need of angioplasty in about 50% of them, most of the interventionists think that an extensive use of this technology will unequivocally lead to a drastic reduction in the number of PCI performed. Interestingly in POST-IT, after FFR, the total number of patients referred to coronary angioplasty did not decrease but actually increase by 10% (Figure). Similarly, R3F and RIPCORD reported only a slight decrease in the number of
patients referred to PCI after routine FFR (−5%; Figure). The pooled analysis of the 2193 patients included in the 3 studies demonstrates that routine use of FFR reclassifies treatment allocation in as many as 42% of the patients but remains neutral on the number of those referred to PCI (+1%; Figure). Can we reconcile the apparent discrepancy between the DEFER findings and the observation made in these 3 studies? A key difference in study design is providing the answer. Unlike DEFER, in those studies, FFR was not applied only to patients considered for PCI but to a much broader population including also those considered for medical treatment or bypass surgery. When focusing on patients initially considered for PCI, the findings were consistent with those made in DEFER with a large proportion of patients referred to a medical treatment by FFR (R3F=48%; POST-IT=25%; RIPCORD=27%). More important was the observation that >20% of patients considered for a different option than PCI were referred to PCI by FFR (R3F=25%; POST-IT=29%; RIPCORD=15%), counterbalancing the deferral observed in patients considered for PCI. Taking all these information together, it is clear that the ultimate goal and ultimate effect of routine FFR combined with angiography is not to decrease the number of PCI but rather to define the appropriate treatment to each individual patient.

A third important observation of the POST-IT study is the demonstration of the safety of FFR-based deferral to medical treatment in a contemporary population. The seminal DEFER study was conducted in 1997, a time when drug-eluting stents were not available, and in a selected population excluding any type of acute coronary syndrome (ACS). Therefore, validity of the DEFER findings to our patients could be questioned, and it is reassuring to observe that the safety of FFR-based deferral is preserved in a population including 35% of ACS and use of drug-eluting stents.

Taken together, the findings of POST-IT, RIPCORD, and R3F are remarkably consistent, reinforcing each other. They also demonstrate that in cardiovascular research, there is space for nonrandomized studies pending that they are prospective with an appropriate design. In that context, the POST-IT study is an important addition to the long series of evidence supporting the use of FFR and in particular to the case of implementing routine FFR as the default approach to all patients referred to coronary angiography. This case is not fully close however because 2 important subpopulations have not been fully investigated yet. The first is the group of patients with multivessel coronary artery disease. This population is of peculiar importance because in theory the range of reclassification of the management strategy may be wider (ie, patients could be reclassified from coronary artery bypass surgery to medical treatment or the opposite). However, this group represented only one third of the patients included in the POST-IT study, and no dedicated analysis was performed. Studies focusing on multivessel coronary artery disease patients are needed and will have to clarify how often patient’s management is modified by the use of FFR and also whether selective FFR evaluation in some vessels is sufficient or whether a full vessel evaluation is required.

The second important population in which more information is needed before recommending performing FFR routinely is the one sustaining an ACS. This group is currently making up the majority of patients considered for coronary revascularization. However, concerns about microcirculatory responsiveness during the acute setting have undermined the use of FFR in this subset. Clinical evidence supporting its use, particularly in the setting of non–ST-segment–elevation myocardial infarction, are based on the results of relatively small clinical outcome studies and subgroup analysis. In addition, there is currently no report of the impact of routine use of FFR in the decision-making process in ACS patients. Large studies, powered for clinical outcomes, are therefore needed to assess the integration of routine FFR measurement into the management of patients with ongoing or recent ACS and further refine the role of FFR-based management of patients with ACS undergoing invasive management. Some of these studies (Define-FLAIR, ifr-Swedheart) should be released later this year. These studies will also provide information on the benefit of an alternate pressure wire index, the instantaneous wave free ratio, which does not require hyperemia.

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Dr Van Belle is consultants for St. Jude Medical and received Speaker’s fees from Volcano. Dr Rioufol is consultant for St. Jude Medical and Boston Scientific. He received Speaker’s fees from Volcano and received grants from Boston Scientific and Medtronic. Dr Dupouy has no potential conflicts of interest to disclose.

References
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