To define the most appropriate therapeutical management plan in patients suspected of having coronary artery disease is becoming the ultimate goal in this population. Accumulated evidence suggests that our current practice has major flaws. The use of a noninvasive test as the key information to plan a coronary angiography can be questioned. Patel et al. indeed demonstrated that the performance of such noninvasive test before angiographic evaluation provides little added value to the usual clinical parameters to predict the presence of coronary artery disease. The results of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) study suggest also that our current approach of deciding on revascularization based on the angiographic severity of coronary artery disease does not allow us to identify a population in which revascularization will provide a substantial clinical benefit. These recent observations have created much confusion among physicians and have increased their difficulties to decide on the most appropriate management plan to choose the best treatment for their patients. The implementation of the appropriate use criteria approach for coronary revascularization is an attempt to provide such guidance for the physician. Although meritorious, this approach is largely based on consensus of experts and could be seen by some physicians as relatively complex. In addition, the key objective of the appropriate use criteria approach is more to avoid a gross misuse of revascularization than to provide a refined decision tailored for each patient. Considering all these issues, there is a critical need of a better approach to decide on the most appropriate treatment option for each patient.

The elegant RIPCORD (Does Routine Pressure Wire Assessment Influence Management Strategy at Coronary Angiography for Diagnosis of Chest Pain) study by Curzen et al. in this issue of *Circulation: Cardiovascular Interventions*, together with the recently published Registre Français de la FFR (R3F) study by our group, provides important evidences in that context. DEFER, Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME), and Fractional Flow Reserve Versus Angiography for Multivessel Evaluation 2 (FAME2) have demonstrated that pressure wire assessment of the fractional flow reserve (FFR) is helpful to tailor the percutaneous coronary intervention (PCI) strategy in patients already preselected for PCI, allowing both a reduction in the number of stents implanted and an improvement in clinical outcome. Despite this evidence, the role of FFR in patients referred for a diagnostic angiography, although of potential critical importance for patient management, was unknown before the publication of the RIPCORD and R3F studies.

The RIPCORD study was conducted in 10 centers in the United Kingdom and included 200 patients referred for a coronary angiography. The core of the study design was similar to the R3F study performed in France in 20 centers and included 1075 patients. In both studies, investigators were asked to define prospectively their patient revascularization strategy a priori based on angiography alone before performing the FFR measurement and then again after FFR measurement was performed. The impact of FFR on patient management was investigated by comparing the 2 therapeutic proposals. Beside the number of patients included, the main design differences between the 2 studies were the following: (1) In RIPCORD, no post-acute coronary syndrome patients were included although they represented 20% of the R3F population; (2) In RIPCORD, all patients with ≥1 lesion >30% without any upper limit could be included, whereas in the R3F, patients with ≥1 ambiguous lesion (30%–65%) were included; (3) In RIPCORD, the investigators were asked to perform FFR assessment in all major coronary vessels, whereas no specific recommendations were provided to the R3F investigators, leading to a higher number of lesions investigated in each patient in RIPCORD than in R3F (2.9 versus 1.4); (4) In RIPCORD, the additional fluoroscopy time and extra contrast media related to the FFR assessment were recorded, which was not the case in R3F; (5) Although no long-term follow-up was available in RIPCORD, a 1-year clinical follow-up was part of R3F; (6) The number of patients included in R3F allowed for a multivariable analysis of the predictors of the FFR value and of the changes of the therapeutical plan.

The major findings of the 2 studies are consistent. First, the use of FFR during diagnostic angiography allowed
reclassification of individual management in a large proportion of patients: 26% in RIPCORD\(^2\) and 47% in R3F. Second, reclassification of the treatment strategy was achieved in all groups of treatment. Third, reclassification was independent of whether a noninvasive stress test was performed or not, and when performed, whether the test was positive or not, as demonstrated in R3F.\(^6\) Finally, adaptation of individual patient management by FFR only slightly modified the proportion of patients referred to each treatment modality. This was also the case for PCI. Indeed, the proportion of patients referred to PCI decreased only marginally from 45% to 40% in RIPCORD and from 38% to 32% in R3F.\(^6\)

Unfortunately, the RIPCORD study does not provide any information on the potential clinical benefit of reclassification by FFR during diagnostic angiography. Some information can, however, be derived from the DEFER, FAME, and FAME2 studies. They demonstrated clearly that in patients considered for PCI, which represents 45% of the population included in RIPCORD, FFR assessment was associated with an improved clinical outcome.\(^1,3\) The R3F study also provided meaningful information on clinical outcome, particularly for patients initially considered for medical management or coronary artery bypass graft as decided based on the analysis of the angiography. It demonstrated in particular that it remained safe, both in term of ischemic events and symptoms, to take the final decision of revascularization in contradiction with the one suggested by angiography pending that it was supported by FFR.\(^4\) Despite all these evidences, randomized studies comparing the clinical outcome of patients managed based on angiography without FFR assessment or angiography combined to FFR assessment are needed. It is in this context that the Functional Testing Underlying Coronary Revascularisation (FUTURE) trial (NCT01881555) was designed and recently started in France. This randomized trial, coordinated by Gilles Rioufol, is intended to include >1700 patients with multivessel coronary artery disease and will compare the benefit of angiography alone versus angiography+FFR on the risk of a composite end point (death, myocardial infarction, coronary revascularization, stroke) at 1 year.

When performing FFR evaluation during diagnostic angiography, should we focus only on the ambiguous lesions, as done in R3F, or perform a pan-vessel evaluation, as done in RIPCORD?\(^7\) Because the RIPCORD study demonstrated that 47% of the lesions graded as >70% were FFR negative and 13% of lesions graded as <30% were FFR positive, it suggests that a systematic pan-vessel FFR evaluation could be required. However, RIPCORD demonstrated also that there is a price to pay for such an extensive evaluation including the use of 70 mL of extra contrast media and the need of 6 minutes of extra fluoroscopy time per patient. On the contrary, the results of R3F may suggest that a more selective approach is also valid. The results of the multivariable analysis performed in R3F further suggest that some angiographic parameters could help to identify some FFR-positive or FFR-negative lesions, thus possibly obviating the need for an FFR evaluation in those lesions. Indeed, although the percent stenosis is only a weak predictor of the FFR value, other angiographic characteristics need to be considered to recognize an FFR-positive (typically a long and complex lesion of the proximal left anterior descending artery) from an FFR-negative lesion (typically a short smooth lesion of the distal right coronary artery). To define whether a selective or pan-vessel FFR evaluation is the best approach still needs to be determined. Unless instantaneous wave-free ratio,\(^10\) because it allows pressure wire assessment in all vessels without the need for hyperemia, demonstrates being the ultimate functional approach.

Accumulated evidences, including the results of the RIPCORD trial, suggest that routine FFR assessment at time of diagnostic angiography is close to be prime time. The implementation of such an approach could modify drastically both patient care and medical organization. Does the demonstration that reclassification by FFR is independent of the performance and results of noninvasive tests mean that there is no longer the need to perform such test before referring a patient to a diagnostic angiography+FFR evaluation? This remains to be seen. Currently, FFR is only performed in centers with PCI facilities. If the benefit of the angiography+FFR approach is confirmed, does this mean that all catheterization laboratories without PCI facilities should close? Or that these centers should be trained to perform FFR? Finally, it is important to remember that contrary to the fear of most interventionalists since the results of the DEFER study,\(^7\) a broad use of FFR during angiography will not translate in an important reduction of the number of patients undergoing PCI.

**Disclosures**

Dr Van Belle is a consultant for St Jude Medical and received Speaker’s fees from Volcano. Dr Rioufol is a consultant for St Jude Medical and Boston Scientific. He received Speaker’s fees from Volcano and received grants from Boston Scientific and Medtronic. The other author reports no conflicts.

**References**


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