Next Generation FFR Microcatheter Technology


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Next Generation FFR Microcatheter Technology


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Abstract
Fractional flow reserve (FFR) is the mainstay of functional haemodynamic assessment of coronary artery lesions, guiding decisions in percutaneous coronary interventions (PCI). The RXi® rapid exchange FFR system, featuring an ultrathin monorail pressure microcatheter (Navvus™) has the potential to simplify PCI procedures. Data from two studies sponsored by ACIST Medical Systems evaluating the clinical utility of the microcatheter system were presented at EuroPCR, which took place over 16–19 May 2017 in Paris. Early data from the FFR-Stent Evaluated at Rotterdam Cardiology Hospital (FFR-SEARCH) registry have indicated that post-PCI, almost half of patients have FFR values below 0.90 even when stent placement appears fine on angiography. This registry is noteworthy for including a high proportion of unstable patients. The Assessment of Catheter-based Interrogation and Standard Techniques for Fractional Flow Reserve measurement (ACIST-FFR) study has shown that the microcatheter system provides a modestly lower FFR value compared with the traditional pressure wire, and an independent predictor of a difference between the two is the physiological severity of the lesion as measured by the Navvus microcatheter, meaning that the clinical impact of the difference is minimal for most measurements. These findings add to the growing body of evidence in support of the microcatheter FFR system and have prompted further research into optimising procedures.

Keywords
Fractional flow reserve, microcatheter, coronary artery disease


Fractional flow reserve (FFR) assesses the reduction in flow resulting from a coronary artery stenosis. It is an essential tool in the evaluation of the physiological significance and proper treatment of coronary stenosis in the catheterisation laboratory since many stenotic lesions identified at angiography are of intermediate severity, and their impact on myocardial perfusion cannot be determined accurately from angiography alone. Multiple studies have demonstrated the efficacy and safety of FFR, including the 2009 Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) study. However, the technique is underutilised: a 2012 report of the National Cardiovascular Data Registry reported that only 6.1% of patients in the US underwent FFR assessment prior to percutaneous coronary intervention (PCI) for intermediate coronary stenosis (40–70% stenosis).

Most FFR measurements are performed using a 0.014" guidewire incorporating a distal pressure sensor. This is more difficult to guide through tortuous lesions. In addition, assessment of diffuse disease or multiple lesions requires wire pullback, which results in the loss of wire position. As the use of FFR is increasing worldwide and increasingly complex lesions are being treated, there is a need for improved technologies to improve speed, accuracy and ease of use. In addition, post-stenting FFR has been proposed as an effective tool to assess the effect of treatment on coronary flow. However, FFR wiring after stenting requires additional time and could lead to wire placing behind the stents struts.

The ACIST RXi® rapid exchange system (ACIST Medical Systems) features an ultrathin monorail microcatheter (Navvus™, ACIST Medical Systems) with an optical pressure sensor located close to the distal catheter tip (see Figure 1). This system allows the use of any 0.014" coronary guidewire appropriate for the patient’s anatomy. It enables repeated pullbacks and advancements, as well as the ability to move the sensor up and down the artery to determine the site of change in pressure gradient, without losing wire position. Furthermore, it allows an easy and fast assessment of post-stenting FFR.

However, the larger diameter of the catheter (0.022" mean diameter, compared with the 0.014" guidewire) could influence FFR measurement. The ACIST Diagnosis of Coronary Arterial Disease with a Rapid Exchange Monorail Pressure Sensor for the Measurement of Fractional Flow Reserve (ACCESS-NZ) study compared the Navvus/RXi system with a conventional pressure wire and found that fewer patients had clinically significant (>±0.03) drift with the Navvus catheter (13%) than with the pressure wire (33%) when FFR was measured with both systems.

On-going studies are evaluating the clinical utility of the Navvus microcatheter systems, including the FFR-Stent Evaluated at Rotterdam Cardiology Hospital (FFR-SEARCH) registry and the Assessment of Catheter-based Interrogation and Standard Techniques for Fractional Flow Reserve measurement (ACIST-FFR) study. This article describes two presentations given at EuroPCR (16–19 May 2017, Paris) that discussed the latest findings of these studies.
Routine Fractional Flow Reserve Measurement after Percutaneous Coronary Intervention: The FFR-SEARCH Study

Presented by Roberto Diletti
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Intracoronary measurement of myocardial FFR is a simple, reliable and reproducible index of the physiological significance of coronary stenosis. In addition, FFR assessment can be used to guide PCI, improving procedural outcomes. However, the impact of FFR values after PCI on clinical outcomes remains unclear.

The FFR-SEARCH study aimed to determine the impact of post-PCI FFR values on long-term clinical outcomes in a prospective all-comer registry study. All patients who underwent successful PCI were enrolled. An FFR assessment using the ACIST RXi system and Navvus microcatheter was performed after each PCI when the angiographic result was considered acceptable by the operator. Wire access to the vessel was maintained and a pressure sensor FFR microcatheter was inserted over the previously used coronary guide-wire. The Navvus microcatheter allows FFR assessment after crossing the lesion with any 0.014" guideewire of choice. A platinum marker band is located 2.5 mm from the tip and a fibre-optic sensor 2.5 mm from the marker band (5 mm from the tip). This gives a profile comparable to 0.022" diameter at the lesion site (see Figure 1).

The study screened 1,512 patients undergoing PCI. Of these, 512 patients were excluded: 156 because of unstable disease, 148 because of operator decision, 129 because vessels were too small and 79 for other reasons. Of the 1,000 patients who underwent assessment using the Navvus microcatheter, the wire did not cross the lesion in 28 cases, equipment failure occurred in 11 cases and two patients had an adverse response to adenosine. Of the remaining patients, 1,165 lesions had a successful post-PCI FFR measurement. Failure to cross the lesion was reported in 14 procedures, nine patients were not assessed because of unstable disease, 22 lesions were not measured because of operator decision and 28 for other reasons. In 109 lesions the vessel was too small and there was one case of equipment failure. The baseline characteristics were reported on 1000 patients and procedural results were reported on 959 patients with 1,165 lesions. The average age at baseline was 64.6 ± 11.8 years and patients were predominantly male (72.5 %). Of note, clinical presentations were evenly distributed between stable angina (30.4 %), unstable angina/non ST-elevation MI (36.7 %) and acute MI (32.9 %), i.e. >60 % of the patients involved were unstable.

Where possible, FFR was performed at least 20 mm from the most distal stent then a pullback was performed to obtain pressure gradients on the distal and proximal stent edge border as well as to assess overall drift at the ostium. The average drift value was low, 0.011 ± 0.015, and the average procedural time per lesion was 5.0 ± 1.4 minutes, which included the full duration of the adenosine infusion, showing that FFR can be used quickly to evaluate PCI results. Failure to cross the post-PCI lesion occurred in 42 of 1,207 (3.5 %) attempted lesions, mostly because of tortuosity and calcification, and there were no Navvus-related complications reported.

Dr Diletti presented preliminary outcome data from this study. Patient-level analysis showed that almost half (48 %) of patients had an FFR below 0.90. Lesion level assessment showed that in 43.3 % of cases, the FFR was ≤0.90. In 7.7 % of lesions post-stenting FFR was below the threshold for ischaemia (≤0.80). The number of lesions per 0.01 FFR increment was 660 lesions (57 %) with FFR >0.90, 505 lesions (43 %) ≤0.90; 231 lesions (19.8 %) ≤0.85 and 90 lesions (8 %) ≤0.80 (see Figure 2). The cut-off of 0.90 could help guide procedural optimisation.

The primary outcome measure was major adverse coronary events (MACE), including all-cause mortality, Q-wave MI, target lesion revascularisation, target vessel revascularisation, stent thrombosis and any revascularisation at 30 days. Of 798 (89 %) patients with complete 30-day follow-up, MACE occurred in only 15 (1.9 %). The MACE rate for
The use of FFR guidance to identify and treat functionally significant coronary lesions has been shown to reduce the risk of MACE and save healthcare resources compared with angiographic guidance alone. Two types of FFR technologies are commercially available. Pressure wire technology involves a specially constructed 0.014” wire. Microcatheter technology employs a low-profile catheter with a pressure sensor incorporating fibre-optic technology into the distal end, giving a profile comparable to a 0.022” diameter at the lesion site. The latter is more convenient and may overcome some of the limitations associated with conventional pressure wire systems, but the larger profile may influence coronary haemodynamics, an effect that might also depend on lesion and vessel characteristics. There is a need to investigate these unresolved issues in a large, multicentre, prospective study including a wide range of vessel and lesion types and utilising an independent core laboratory.

The ACIST-FFR prospective, open label study aimed to assess the differences between FFR measured by a microcatheter and commercially available 0.014” pressure wires in the setting of clinically relevant vessel diameters and lesion lengths. A Navus microcatheter was used and compared to two different commercially available pressure wire systems: Abbott-St. Jude Medical and Philips-Volcano. The primary endpoint was the difference in agreement between microcatheter and pressure wire FFR as assessed by Bland-Altman analysis. The core laboratory (Cardiovascular Research Foundation, New York) assessed FFR and provided quantitative coronary angiography. Independent analyses were performed by Stanford University.

The inclusion criteria were patients with stable ischaemia; a vessel with a Thrombolysis in Myocardial Infarction flow of 3; a de novo lesion that a physician has considered to have a clinical indication for FFR measurement; and operator-assessed reference vessel diameter (RVD) of the target lesion ≥2.25 mm. Exclusion criteria were acute ST-elevation or non-ST-elevation MI, New York Heart Association Class 4 severe heart failure; a target vessel with an angiographically visible or suspected thrombus; a target lesion within a bypass graft; angiographic evidence of a dissection prior to initiation of pressure wire measurements and a target vessel containing excessive tortuosity or calcification. The inclusion criteria were patients with stable ischaemia; a vessel with a Thrombolysis in Myocardial Infarction flow of 3; a de novo lesion that a physician has considered to have a clinical indication for FFR measurement; and operator-assessed reference vessel diameter (RVD) of the target lesion ≥2.25 mm. Exclusion criteria were acute ST-elevation or non-ST-elevation MI, New York Heart Association Class 4 severe heart failure; a target vessel with an angiographically visible or suspected thrombus; a target lesion within a bypass graft; angiographic evidence of a dissection prior to initiation of pressure wire measurements and a target vessel containing excessive tortuosity or calcification. The baseline patient characteristics were typical of PCI study populations: average age was 68 years and 37 % had a history of diabetes. Baseline angiographic characteristics were as follows: mean diameter stenosis was 47 %, i.e., angiographically indeterminate lesions. The average lesion length was 15.3 mm and the average RVD of the target lesion was 2.1 mm. Of the enrolled target lesions, 30 % were <2.5 mm in diameter. Therefore small vessels were well represented in this study – prior microcatheter FFR clinical studies had only included vessels with RVD ≥2.5 mm. The mean pressure wire FFR was 0.83, again representative of a patient population with a clinical indication for FFR.

Compared with the pressure wire, the microcatheter gave consistent and modestly lower FFR measurements with an average bias of −0.022 (see Figure 4). In terms of the secondary endpoint, the difference in pressure wire FFR with and without the microcatheter on the pressure wire, the average bias was −0.03. A sensitivity analysis of all reported data (i.e., all patients with paired FFRs) showed that the bias was similar to that of the primary analysis cohort (−0.025). A strong correlation was seen between the microcatheter and the pressure wire FFR (Pearson

In the subsequent audience discussion, some experts at EuroPCR questioned whether the FFR was detecting suboptimal stent placement, or if other factors such as microcirculatory problems might be contributing. Others questioned the next step to optimising procedures. The upcoming FFR REACT randomised study aims to evaluate the clinical impact of intravascular-ultrasound-directed FFR optimisation of PCI.
The increased use of FFR – particularly in multivessel disease and tandem lesions – has necessitated more efficient and accurate techniques, and it is increasingly important to understand the benefits and limitations of available FFR technologies. The use of microcatheter-based FFR technology can overcome the limitations of pressure wire technology such as accessibility in challenging anatomy, maintaining wire position, pressure-measurement drift and ease of obtaining post-intervention FFR. The microcatheter system can thus simplify PCI procedures as well as avoid technical errors. Preliminary data from the FFR-SEARCH registry has indicated that post-PCI, almost half of patients have FFR values below 0.90 even when stent placement appears adequate on angiography. The ACIST-FFR trial has shown that the clinical impact of the difference between microcatheter and conventional pressure wire FFR measurements is minimal in most cases. These data have added to the body of clinical evidence supporting the use of microcatheter FFR.

In summary:

- A pressure-monitoring microcatheter provides a modestly lower FFR value compared with a traditional pressure wire, with an average bias of −0.02.
- Using univariate analysis, smaller RVD and greater lesion length tend to predict a lower FFR measured by the microcatheter.
- Using multivariate analysis, lower FFR as measured by the microcatheter is the only predictor of a greater difference between the two measurements.
- Since the bias is less at higher FFR values (e.g., the grey zone and above), the clinical impact of this difference for those scenarios is likely minimal.

This study confirms and expands previous findings and provides robust evidence for the diagnostic capabilities of microcatheter FFR.

Summary and Concluding Remarks

The increased use of FFR – particularly in multivessel disease and tandem lesions – has necessitated more efficient and accurate techniques, and it is increasingly important to understand the benefits and limitations of available FFR technologies. The use of microcatheter-based FFR technology can overcome the limitations of pressure wire technology such as accessibility in challenging anatomy, maintaining wire position, pressure-measurement drift and ease of obtaining post-intervention FFR. The microcatheter system can thus simplify PCI procedures as well as avoid technical errors. Preliminary data from the FFR-SEARCH registry has indicated that post-PCI, almost half of patients have FFR values below 0.90 even when stent placement appears adequate on angiography. The ACIST-FFR trial has shown that the clinical impact of the difference between microcatheter and conventional pressure wire FFR measurements is minimal in most cases.

These data have added to the body of clinical evidence supporting the use of microcatheter-based FFR. Furthermore, while FFR has previously been considered a diagnostic tool to assess whether a lesion has to be treated or not, these studies have led to an expanded view of FFR as a tool to understand and evaluate the results of PCI procedures. These studies have stimulated further research into optimising procedures and should facilitate the more widespread use of FFR.


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