Does Routine Pressure Wire Assessment Influence Management Strategy at Coronary Angiography for Diagnosis of Chest Pain?: The RIPCORD Study
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According to current evidence base, the assessment of patients with suspected angina requires that 2 questions be addressed before an appropriate management plan (MP) can be formulated: (1) the presence and, ideally, locality of reversible myocardial ischemia and (2) the anatomic coronary stenosis(es) responsible for this ischemia. However, the optimal care pathway for patients with stable cardiac-sounding chest pain (CP) is uncertain. Conventional practice has been to undertake a noninvasive stress test to provide objective evidence of ischemia and refer patients with abnormal noninvasive assessment for coronary angiography (CA) with a view to percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) where appropriate. However, all noninvasive screening tests for ischemia have limitations that relate to, one or more of, diagnostic accuracy, cost, and availability.1–3 In the light of these limitations, recent NICE (National Institute for Health and Care Excellence) guidance recommends that a greater proportion of patients being investigated for stable angina undergo diagnostic angiography as a first-line investigation.4

Background—The use of coronary angiography (CA) for diagnosis and management of chest pain (CP) has several flaws. The assessment of coronary artery disease using fractional flow reserve (FFR) is a well-validated technique for describing lesion-level ischemia and improves clinical outcome in the context of percutaneous coronary intervention. The impact of routine FFR at the time of diagnostic CA on patient management has not been determined.

Method and Results—Two hundred patients with stable CP underwent CA for clinical indications. The supervising cardiologist (S.C.) made a management plan based on CA (optimal medical therapy alone, percutaneous coronary intervention, coronary artery bypass grafting, or more information required) and also recorded which stenoses were significant. An interventional cardiologist then measured FFR in all patent coronary arteries of stentable diameter (≥2.25 mm). S.C. was then asked to make a second management plan when FFR results were disclosed. Overall, after disclosure of FFR data, management plan based on CA alone was changed in 26% of patients, and the number and localization of functional stenoses changed in 32%. Specifically, of 72 cases in which optimal medical therapy was recommended after CA, 9 (13%) were actually referred for revascularization with FFR data. By contrast, of 89 cases in whom management plan was optimal medical therapy based on FFR, revascularization would have been recommended in 25 (28%) based on CA.

Conclusions—Routine measurement of FFR at CA has important influence both on which coronary arteries have significant stenoses and on patient management. These findings could have important implications for clinical practice.

Clinical Trial Registration—URL: http://www.clinicaltrial.gov. Unique identifier: NCT01070771.

(Circ Cardiovasc Interv. 2014;7:00-00.)

Key Words: angiography ■ coronary disease ■ physiology
WHAT IS KNOWN

- In patients with stable chest pain (CP), coronary angiography (CA) alone does not allow accurate assessment as to whether there is reversible myocardial ischemia.
- The use of pressure wire–derived fractional flow reserve (FFR) is an accurate and reproducible method for the detection of lesion-level ischemia.
- FFR predicts outcome and benefit from percutaneous coronary intervention (PCI) in patients with stable angina, but its value in patients at the stage of diagnostic angiography, who may be managed by medical therapy, PCI, or coronary artery bypass grafting (CABG), is not established.

WHAT THE STUDY ADDS

- FFR can be used at the stage of diagnostic CA to assess all epicardial coronary arteries of stentable diameter with a rate of important complication of 3 in 200 cases.
- When FFR data were added to information from CA alone in 200 patients with stable CP, the management plan (medical therapy alone, PCI, CABG, or more information required) changed in 26% of the population.

As a result, whether or not objective evidence for ischemia has been previously obtained, a large proportion of patients presenting with stable CP undergo a diagnostic coronary angiogram. Based on this test, the supervising cardiologist will then recommend a MP from 3 possible options: optimal medical therapy (OMT) alone, OMT plus PCI, or OMT plus CABG. Whether each coronary vessel requires revascularization is generally based on an eyeball assessment of the severity of any narrowing on the angiogram, and this process is flawed. First, the diagnostic accuracy of this form of assessment is subject to substantial variability. Second, the correlation between the perceived degree of stenosis and inducible ischemia in the myocardial territory beyond it is poor. In most cases, this leads to a successful MP with revascularization recommended where appropriate. However, in a substantial number of patients, the angiographic appearance of coronary arteries leads to diagnostic uncertainty. Observational data have consistently demonstrated that it is the presence and extent of reversible ischemia, rather than the coronary anatomy, that is most predictive of subsequent acute coronary events. This concept undermines traditional approaches that are dominated by angiography-derived management of this patient group.

In this context, the pressure wire is a well validated tool for the assessment of the functional severity of coronary stenoses and is associated with a low complication rate. Studies have demonstrated that the derivation of fractional flow reserve (FFR) by the translesion intracoronary pressure gradient can be used to predict clinical event rates with a robust binary cut-off value. Randomized study data demonstrate that PCI of coronary artery lesions with FFR ≥0.8 has no clinical outcome advantage compared with OMT alone, making the case for cost effectiveness of the pressure wire.

In real life clinical practice, routine access to FFR measurement at diagnostic angiography has the potential to tailor not just PCI but also medical and surgical revascularization management, according to the burden of ischemia. Furthermore, according to previous data, the ability of such a FFR-guided strategy to confirm which lesions are functionally significant might be expected to have a bearing on the nature of any revascularization recommended.

In this study, we tested the hypothesis that, in patients being investigated for stable cardiac-sounding CP, routine assessment of FFR in all the main coronary branches would modify the management strategy derived from diagnostic CA alone. The aims of this study were: (1) to determine whether the FFR data would influence the management strategy for patients on the basis of diagnostic CA (which represents routine clinical practice), and (2) to determine the degree of correlation between standard angiographic assessment of the coronary arteries and pressure wire assessment of the main arteries.

The RIPCORD (Does Routine Pressure Wire Assessment Influence Management Strategy at Coronary Angiography for Diagnosis of Chest Pain) study was designed to provide proof of concept that FFR assessment at the diagnostic angiography stage would have an important influence on the management of patients when compared with angiographic assessment without physiological data. It was designed with the expectation that data from this study would be used to inform a larger randomized strategy trial.

Methods

The study protocol was approved by the Southampton and South West Hampshire Research Ethics Committee A and was conducted in accordance with the Declaration of Helsinki. All patients provided written informed consent before FFR measurements were undertaken. Patients were screened and recruited at 10 cardiology centers in the United Kingdom.

Patient Population

Patients with stable cardiac-sounding CP who had been listed by their supervising cardiologist on clinical grounds for diagnostic CA were eligible for this study. There was, therefore, no absolute requirement that they had previous objective evidence of ischemia obtained by noninvasive testing because the decision to investigate the coronary anatomy was a clinical one determined solely by the supervising cardiologist based on a provisional diagnosis of angina in all cases.

All potential patients were provided with a study information sheet, and then the study process was discussed with them by a member of the local research team. Clinical exclusion criteria included failure to provide written informed consent, participation in other clinical studies, previous CABG, acute coronary syndrome at presentation, diagnostic angiography or PCI within the previous 12 months, contraindication to adenosine, severe valve disease, serum creatinine >180 μmol/L, and life-threatening comorbidity.

Investigational Sites

All the sites recruiting patients were centers with operators and catheter laboratory staff experienced in undertaking FFR measurements.

angiographic assessment and analysis

Patients underwent a diagnostic angiogram by the cardiologist who was supervising patient care (cardiologist 1) according to their routine
clinical practice (Figure 1). Angiographic inclusion criteria included the presence in any epicardial vessel of ≥2.25 mm diameter of a ≥30% stenosis by visual estimate. Thus, if the patient did not have any stenoses of ≥30% severity, they were not included in the study.

After the angiogram, cardiologist 1 analyzed the pictures and graded the outcome according to the criteria shown in Table 1 and then formulated an MP consistent with their routine clinical practice and independent of subsequent pressure wire data. Specifically, they recorded an overall plan for each patient, using the options (1) medical treatment alone, (2) PCI, (3) CABG, and (4) more information required. Specific vessels with a significant stenosis and which vessels were recommended for revascularization either by PCI or CABG were also recorded. This MP was documented in the case report form. Cardiologist 1 then left the catheter laboratory.

**Pressure Wire Assessment and Analysis**

An interventional cardiologist (in all cases different from the supervising cardiologist) then performed FFR assessment of all epicardial vessels or major branches of ≥2.25 mm diameter, which had Thrombolysis in Myocardial Infarction 3 flow, regardless of whether these other vessels had a stenosis of ≥30% severity or not. Patients were given 70 U/kg heparin systemically and intracoronary glyceryl trinitrate before FFR measurements. Before the first FFR measurements, an angiogram was encouraged in the protocol to document adequate engagement of the guiding catheter. All FFR readings were taken after maximal hyperemia was achieved using either intravenous infusion or intracoronary adenosine according to operator preference, except that the protocol mandated intracoronary adenosine infusion in cases with ostial disease of either the left or right coronary arteries. Where intracoronary adenosine was used, the minimum data set required by the protocol was a baseline FFR and then 2 intracoronary boluses of 50 mcg adenosine each. The minimum FFR reading was taken in each vessel, and FFR readings ≥0.8 were considered to represent hemodynamic significance. Chronic total occlusions were awarded an FFR value of 0.5.

The extra screening time and contrast used in each case as a result of FFR readings were recorded at the end of each case by the radiographer and committed to the case report form.

Thereafter, the FFR data were disclosed to cardiologist 1 who was then invited to consider and document a revised MP, using the same options. Once again, the vessels with a significant stenosis and recommended for revascularization either by PCI or CABG were recorded. After completion of the second MP based on FFR data, the patient was then managed at the discretion of their supervising cardiologist (cardiologist 1), who was therefore not obliged to use the FFR data. The study did not follow up patients for clinical outcome.

**Primary Study End Point**

At the end of each study, there were 2 MPs recorded in the case report form from cardiologist 1: (1) angiogram alone directed and (2) angiogram plus FFR directed. The primary end point for the study was the proportion of cases in which the angiogram-directed MP changed after FFR data were disclosed. The definition of a change in MP included (1) OMT alone to PCI or CABG, (2) PCI to OMT or CABG, (3) CABG to PCI or OMT, or (4) more information required to definitive management.

**Prespecified Secondary End Points**

1. The number of vessels in which there was a discrepant result in relation to angiographically and FFR-defined significance.
2. The difference in indication for revascularization of each major coronary artery territory (left anterior descending [LAD], circumflex, and right coronary artery [RCA]) as judged according to the angiogram alone compared with after FFR data were disclosed.

**Statistical Considerations**

From pilot data (and other evidence such as the Fractional Flow Reserve Versus Angiography for Multivessel Evaluation [FAME] study), it was estimated that a change in management would occur in 20% of patients, and we asserted at the outset that a change of ≤10% would not be deemed important. The number of patients required in this study is directed by p, the proportion of cases in which the decision is different after the intervention than it was before. The 95% confidence intervals for p are derived from the formula: $p-hat ± 1.96 sqrt(p-hat(1−p-hat)/n)$. A sample size of 200 provides 95% confidence intervals of 15% to 25% for this effect size.

All data are presented as mean±SD (normally distributed data) or median and interquartile range (nonnormally distributed data) for continuous variables. In addition, categorical variables are presented as number (percentage). The primary and secondary outcomes were compared using $\chi^2$ and McNemar tests as appropriate with a P value <0.05 considered as significant. All statistical analyses were performed using SPSS version 20.0 (IBM Corporation, Armonk, NY).

**Results**

Of 203 patients who were recruited into the study in a total of 10 UK centers, 200 were included in data analyses (see protocol for revascularization is your recommended strategy, which vessels are significant and therefore require either percutaneous coronary intervention or coronary artery bypass grafting?

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**Table 1. Criteria Required for Case Report Form Based on Angiogram Data Alone**

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Are there significant stenoses (≥70% by eyeball) in the major epicardial vessels (ie, main coronaries or any branch of ≥2.25 mm)?</td>
<td>Yes/No</td>
</tr>
<tr>
<td>2. What is your clinical management plan from the options (1) medical treatment alone, (2) percutaneous coronary intervention, (3) coronary artery bypass grafting, (4) more information required by noninvasive test for ischemia?</td>
<td>Option</td>
</tr>
</tbody>
</table>
violations below). Baseline demographics for the study population are shown in Table 2. The mean age was 64±10 years, and 75% of patients were men. Ninety-five percent of patients in the study had angina graded at between I and III according to the Canadian Cardiovascular Society classification. Only 111 (55.5%) patients had any noninvasive test of ischemia before angiography, and this was a conventional exercise tolerance test in 93 patients (84% of noninvasive tests).

From the population of 200 patients, FFR measurements were undertaken in LAD in 190 cases, in ≥1 branch of the circumflex coronary in 199 cases, in RCA in 138 cases, in a diagonal branch of LAD in 57 cases, in an intermediate artery in 14 cases, and in another vessel (typically a posterior descending or posterolateral branch) in 38 cases. There were 28 cases in which 1 chronic total occlusion was present. There was no case in which >1 chronic total occlusion was present.

### Adverse Events

Four serious adverse events were recorded in 3 patients. In 1 patient, the operator crossed a tightly stenosed RCA with the pressure wire, but this vessel subsequently occluded, leading to emergency PCI and a troponin rise to 5.88 mg/L. In a second case, pressure wire manipulation in LAD led to coronary artery dissection, and the patient underwent emergency CABG, which was subsequently complicated by a deep vein thrombosis. Finally, in 1 patient there was an episode of ventricular fibrillation during FFR assessment of RCA, and the operator decided not to proceed with further measurements.

### Protocol Deviations

#### Patients Withdrawn From the Study

In 1 patient, described above, FFR data acquisition was stopped after 1 vessel because of ventricular fibrillation. This patient’s data were, therefore, incomplete and could not be used in study analysis. In another patient, profound bronchospasm with adenosine led to withdrawal from the study before all FFR data could be acquired. In a third case, FFR was measured in RCA, and the cardiologist decided to perform follow-on PCI without obtaining any FFR data in other coronary arteries. Data obtained from this patient were also incomplete and not analyzed further.

#### Violations Without Patient Withdrawal

In 1 case, the patient had undergone a previous PCI 346 days before being enrolled in RIPCORD (protocol stated that they should not be included <1 year). A second patient had a serum creatinine at enrolment of 204 μmol/L (protocol stated <180 μmol/L). Both patients were included in study analysis.

#### Additional Fluoroscopy Screening Time and Contrast

Measurements of FFR in the study were associated with 70 mL (interquartile range, 140) of extra contrast and 342 seconds (526) of extra fluoroscopy screening time above and beyond the requirements for angiography alone.

### Primary Study End Point

In 147 (74%) of 200 cases, there was an agreement in MP between angiographic and FFR assessment. Thus, there was a change in MP after FFR data were provided in addition to angiographic data in 26% of the study population (P<0.001). A detailed breakdown of management choice distribution derived from angiographic data alone compared with after FFR data were available is shown in Table 3. The most important of management changes are described here. In 72 of 200 patients, medical treatment alone was recommended after the angiogram. However, in 9 of these 72 (12.5%) cases, revascularization was advised (6 PCI, 3 CABG) as a result of FFR data becoming available. By contrast, after FFR data were taken into account, OMT alone was recommended in 89 of 200 cases, of whom 25 had been recommended for revascularization after angiogram (24 PCI, 1 CABG).

### Table 2. Demographics for Study Population

<table>
<thead>
<tr>
<th>Patients, n</th>
<th>200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64±10</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>149 (74.5%)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>29±5</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>28 (14%)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>112 (56%)</td>
</tr>
<tr>
<td>Elevated cholesterol, n (%)</td>
<td>149 (74.5%)</td>
</tr>
<tr>
<td>Cholesterol level, mmol/L</td>
<td>4.4±1.3</td>
</tr>
<tr>
<td>History of smoking, n (%)</td>
<td>138 (68%)</td>
</tr>
<tr>
<td>Previous myocardial infarction, n (%)</td>
<td>39 (19.5%)</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L</td>
<td>127±85</td>
</tr>
<tr>
<td>Canadian Cardiovascular Society angina, n (%)</td>
<td></td>
</tr>
<tr>
<td>Class I</td>
<td>45 (22.5%)</td>
</tr>
<tr>
<td>Class II</td>
<td>104 (52%)</td>
</tr>
<tr>
<td>Class III</td>
<td>41 (20.5%)</td>
</tr>
<tr>
<td>Class IV</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>New York Heart Association heart failure status, n (%)</td>
<td></td>
</tr>
<tr>
<td>Class I</td>
<td>179 (89.5%)</td>
</tr>
<tr>
<td>Class II</td>
<td>13 (6.5%)</td>
</tr>
<tr>
<td>Class III</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Medications, n (%)</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>174 (87%)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>55 (27.5%)</td>
</tr>
<tr>
<td>Statin</td>
<td>167 (83.5%)</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>132 (66%)</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>65 (32.5%)</td>
</tr>
<tr>
<td>Oral nitrate</td>
<td>61 (30.5%)</td>
</tr>
<tr>
<td>Nicorandil</td>
<td>34 (17%)</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitor</td>
<td>76 (38%)</td>
</tr>
<tr>
<td>Angiotensin receptor blocker</td>
<td>24 (12%)</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>11 (5%)</td>
</tr>
<tr>
<td>Diuretic</td>
<td>32 (16%)</td>
</tr>
<tr>
<td>Noninvasive test for ischemia performed, n (%)</td>
<td>111 (55.5%)</td>
</tr>
<tr>
<td>Exercise tolerance test, n (%)</td>
<td>93 (46.5%)</td>
</tr>
<tr>
<td>Nuclear scintigraphy scan, n (%)</td>
<td>15 (7.5%)</td>
</tr>
<tr>
<td>Stress echocardiogram</td>
<td>9 (4.5%)</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD or number (percentage).
the FFR value was <0.8 in 33%, 33%, and 13%, respectively.

In 90 of 200 cases, angiographic assessment on its own led to the recommendation of PCI to ≥1 vessel, but in 24 (26.7%) of these cases, there was no physiologically significant stenosis detected by FFR.

Overall, after FFR data were available, revascularization was recommended in 110 of 200 patients (80 PCI, 30 CABG), and this included 9 patients in whom medical treatment was recommended and 13 in whom further stress test data were requested on the basis of angiogram alone. In total, there were 15 cases of 200 in whom further data were requested after angiogram, but this reduced to 1 case after FFR data were taken into account.

**Secondary Study End Points**
The relationship between the degree of angiographic stenosis and minimum FFR measurement for all vessels is shown in Figure 2. Table 4 provides a detailed breakdown of the distribution of significant coronary disease as determined by angiographic appearance alone and then when taking account of the physiological significance as well.

In a total of 64 cases (32%), the number of vessels considered as significant changed after FFR data were revealed compared with the assessment based on angiogram alone. In

Table 3. Management Plan for Population According to Angiogram Alone or FFR

<table>
<thead>
<tr>
<th>Post-Angiogram Decision</th>
<th>Medical</th>
<th>PCI</th>
<th>CABG</th>
<th>Further Info</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical</td>
<td>63</td>
<td>6</td>
<td>3</td>
<td>0</td>
<td>72</td>
</tr>
<tr>
<td>PCI</td>
<td>24</td>
<td>64</td>
<td>2</td>
<td>0</td>
<td>90</td>
</tr>
<tr>
<td>CABG</td>
<td>1</td>
<td>3</td>
<td>19</td>
<td>0</td>
<td>23</td>
</tr>
<tr>
<td>Further info</td>
<td>1</td>
<td>7</td>
<td>6</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>89</td>
<td>80</td>
<td>30</td>
<td>1</td>
<td>200</td>
</tr>
</tbody>
</table>

P<0.001 by McNemar test. CABG indicates coronary artery bypass grafting; FFR, fractional flow reserve; and PCI, percutaneous coronary intervention.

81 of 200 cases, patients were labeled as having no significant CAD after angiography alone, but in 18 of these 81 (22%), FFR was <0.8. By contrast, after FFR, there were 89 cases with no hemodynamically significant CAD, including 24 patients labeled as having single-vessel disease, 1 as 2-vessel disease, and 1 as 3-vessel disease after angiography alone. It is notable that in 1 of 9 cases with hemodynamically significant 3-vessel disease, angiographic assessment had reported no significant CAD.

An assessment was made of the indication for revascularization for individual coronary artery territories as determined by angiographic data alone compared with taking into account physiological assessment by FFR. In 63 of 200 cases, angiographic and FFR assessments were in agreement to suggest an indication for revascularization of LAD. However, in 15 cases, the angiographic indication for LAD revascularization was not confirmed by FFR, and in another 21 cases, FFR showed hemodynamically significant LAD requiring revascularization that was not detected by angiography alone (Figure 3A). Thus, in 36 of 200 patients (18%), the angiogram got the indication for LAD revascularization incorrect.

Similarly, angiographic assessment would have been inaccurate in suggesting an indication for left circumflex artery or RCA revascularization in 27 (13.5%) and 17 (8.5%) of 200 patients, respectively, as shown in Figure 3B and 3C.

**Discussion**
This study has shown that routine pressure wire assessment during diagnostic angiography in patients with stable cardiac-sounding CP leads to a change in MP in 26% of the study population. Furthermore, it demonstrated that the number of coronary arteries considered to be significant at angiography is incorrect in 32% of cases, using the generally accepted definition of physiological significance provided by pressure wire assessment as a reference. As a result of the latter data, we also found that the indication for revascularization of individual coronary territories is also erroneous when judged according to angiogram alone.

These data have important clinical implications. The extent to which FFR measurement changes the angiogram-derived assessment of the distribution of significant CAD is consistent with previous studies. The utility
and value of FFR assessment in determining the hemodynamic significance of coronary vessels has been robustly demonstrated and validated in a series of high-quality scientific studies, including Fractional Flow Reserve to Determine the Appropriateness of Angioplasty in Moderate Coronary Stenosis (DEFER),9 FAME,18 and FFR versus angiography for multivessel evaluation 2 (FAME-2).22 Importantly, in these large scale randomized studies, there is a close correlation between FFR-derived hemodynamic significance and clinical outcome. A recently published large observational study demonstrates reduced rates of death and myocardial infarction when comparing populations treated according to angiographic data compared with matched groups in whom FFR guidance was used.23 The wealth of data in favor of FFR has led to a class Ia indication for its use in decision making in the context of PCI revascularization.24

Despite these impressive data, the potential clinical utility of systematic FFR assessment of coronary arteries has probably not yet been fully exploited. As our study has demonstrated, there are potential advantages to using FFR as an adjunct to diagnostic angiography, rather than solely at the later stage of intervention. Furthermore, the potential value of FFR in the precise identification of hemodynamically significant coronary lesions is likely to be just as high for those not already labeled as requiring PCI, as was the case in DEFER, FAME, and FAME-2. Certainly, the data from RIPCORD indicate that routine application of FFR at the stage of diagnostic angiography would have a profound effect on the assessment and management of those patients in whom angiogram alone suggests medical therapy alone or CABG would be the optimal treatment plan. The potential value extends toward informing when not to revascularize as well as which revascularization modality is optimal for an individual patient.

As data accumulate to demonstrate that it is the presence and extent of myocardial ischemia that determines clinical outcome, the nascent logic that directing revascularization to patient-level and lesion-level ischemia becomes dominant. The envelope for the clinical application of FFR is likely to expand as a result of this change in the evidence base for targeting our interventions. The RIPCORD study offers proof of principle about the potential value of FFR at the diagnostic angiography stage, but a larger randomized trial is now needed whose aim should be to demonstrate both clinical and cost effectiveness for such a strategy. RIPCORD is a small proof-of-concept investigation that cannot in its own right be used to address some of the important questions that arise. Specifically, if these findings are reproduced in a large randomized strategy trial, it will raise the challenging question as to how routine FFR assessment at the stage of diagnostic angiography can be achieved in centers and by operators who

Figure 3. Indication for revascularization of named vessel based on angiogram, fractional flow reserve (FFR), or both modalities. The y axis represents the absolute number of cases in which the test in each category on the x axis indicated that there was disease of the specific vessel warranting revascularization: left anterior descending (LAD) in A, circumflex (Cx) in B, and right coronary artery (RCA) in C. In both, there was an indication for revascularization of the stated vessel from both angiographic appearance and because the FFR indicated hemodynamically significant disease; in angi, revascularization of the stated vessel was recommended on the basis of angiographic severity, but the FFR in the vessel was >0.8 and thus not hemodynamically significant; in FFR, the FFR was hemodynamically significant but the vessel was not thought to be angiographically severe enough to warrant revascularization. The angiogram would have got the indication for revascularization of LAD, Cx, and RCA wrong, using FFR as the reference, in 36 (18%), 27 (13.5%), and 17 (8.5%) of 200 cases, respectively.

![Figure 3](image-url)
currently perform angiography without intervention. Will such operators and centers be encouraged to use FFR as part of the diagnostic service they offer, or will diagnostic angiography for angina have to be performed only by trained interventional cardiologists experienced in FFR and with the technical ability to repair pressure wire–induced complications?

There are several limitations of this study. First, it was powered to detect a change in management and does not, therefore, take account of clinical outcome. Second, the protocol did not require any consideration as to why some patients were selected for the study and some were not. The primary end point did not require that question to be addressed because the comparison comprised internal paired samples. Furthermore, this is a study of stable patients only and takes no account of the potential benefit of routine FFR in an ACS population, a question that is being addressed by the Fractional Flow Reserve Versus Angiography in Guiding Management to Optimise Outcomes in Non–ST-Segment–Elevation Myocardial Infarction (FAMOUS) study.25 Therefore, we do not know from this study what effect FFR would have if used in this way in a consecutive all-comers group of patients. Third, several common patterns of CAD seen routinely at diagnostic angiography are poorly represented in this study population, including chronic total occlusions, left main stem lesions, and very diffusely diseased small vessels. Fourth, it is clear that the strategy of undertaking routine FFR measurement deployed here is associated with procedural complications. Specifically, there were 3 (1.5%) important procedural complications including 1 emergency CABG, 1 emergency PCI, and 1 case of recurrent ventricular arrhythmia. It is conceivable that in future FFR will not be deemed necessary for tight angiographic lesions, which would improve safety. A fifth limitation is that the number of individual coronary vessels (ie, LAD, circumflex, and RCA) is too small to perform a meaningful per-vessel assessment of the impact of FFR versus angiography in each territory. Finally, the acquisition of FFR data in this population is associated with important excess of both contrast agent and screening time compared with obtaining angiography alone. The potential for this to add to catheter laboratory time in an unpredictable fashion could be disruptive to scheduling. Furthermore, resource utilization modeling in a large-scale randomized trial will be essential to assess the overall financial burden introduced by routine FFR measurement.

In conclusion, the RIPCORD study has demonstrated that routine use of FFR at the time of diagnostic CA in patients with stable angina modifies the MP chosen for 26% of the patient population. FFR data resulted in a change in the number of vessels deemed significant and in need of revascularization in 32% of patients. These data may have important implications for routine clinical practice, and a larger randomized trial powered for resource utilization and clinical outcome is now warranted.

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