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Utilizing Post-Intervention Fractional Flow Reserve to Optimize Acute Results and the Relationship to Long-Term Outcomes

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ABSTRACT

OBJECTIVES This study sought to evaluate the impact of fractional flow reserve (FFR) after percutaneous coronary intervention (PCI) on subsequent in-lab interventional management vessels that had undergone pre-PCI FFR and its prognostic value in predicting long-term (>1 year) outcomes.

BACKGROUND Post-PCI FFR has been shown to be a predictor of intermediate-term (6 months) adverse events. However, its impact on immediate post procedure clinical decision making and long-term outcomes is not known.

METHODS Consecutive patients undergoing PCI who had pre- and post-PCI FFR evaluations were followed for major adverse cardiovascular events (MACE).

RESULTS In the study 574 patients (664 lesions) were followed for 31 ± 16 months. PCI led to significant improvement in FFR from 0.65 ± 0.14 to 0.87 ± 0.08 ($p < 0.0001$). Despite satisfactory angiographic appearance, 143 lesions (21%) demonstrated post-PCI FFR in the ischemic range (FFR ≤0.81). After subsequent interventions, FFR in this subgroup increased from 0.78 ± 0.08 to 0.87 ± 0.06 ($p < 0.0001$). Final FFR cutoff of ≤0.86 had the best predictive accuracy for MACE and ≤0.85 for TVR. Patients who achieved final FFR >0.86 had significantly lower MACE compared to the final FFR ≤0.86 group (17% vs. 23%; log-rank $p = 0.02$). Final FFR ≤0.86 had incremental prognostic value over clinical and angiographic variables for MACE prediction.

CONCLUSIONS Post-PCI FFR reclassified 20% of angiographically satisfactory lesions, which required further intervention thereby providing an opportunity for complete functional optimization at the time of the index procedure. This is particularly important as FFR post-PCI FFR was a powerful independent predictor of long-term outcomes. (J Am Coll Cardiol Intv 2016;9:1022–31) © 2016 by the American College of Cardiology Foundation.

Fractional flow reserve (FFR) has become the gold standard for establishing ischemia in the angiographically intermediate lesion and the use of percutaneous coronary intervention (PCI). Pre-PCI FFR holds a Class IA indication in the European (1) and IIa in the American College of Cardiology/American Heart Association guidelines (2) in this clinical scenario. Even though FFR in addition to angiography has been shown to be a valuable tool in improving long-term outcomes, a significant proportion of FFR-guided PCI patients continue to experience significant major adverse cardiac events (MACE). In the FAME (Fractional Flow Reserve versus Angiography for Guiding PCI in Patients with Multivessel Coronary Artery Disease) trial, MACE at 1 year in the FFR group was 13.2% and 20% at 2 years (3,4).

While angiography is considered limited in its ability to assess the functional severity of coronary lesions, the adequacy of PCI results is still largely assessed based on angiographic appearance alone. Presumably, this approach has been adopted in view of data showing the greatest variation between FFR and angiography is in the intermediate lesion range, with much less variation in general between

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FFR and angiography in the severe and mild lesion categories (5). Thus, the use of angiography alone after PCI is an extrapolation of available pre-PCI FFR data without empiric supporting evidence. In fact, studies evaluating post-PCI FFR have shown a wide variation of FFR values in angiographically satisfactory PCI results, reinforcing the notion that angiography is limited in determining the ischemic burden of a lesion even after intervention. The level of the FFR value post-PCI has shown a direct relationship to long-term outcomes (6–13). Thus, attempts to "functionally optimize" PCI results while the patient is in the cath lab might lead to improvement in long-term outcomes.

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Despite hints of the clinical value of post-PCI FFR, it is rarely performed and clinical guidelines and expert consensus documents are silent on the use of using post-PCI FFR (1,2). In this regard it should be emphasized that previous studies are limited by including relatively low-risk patient population, angiographically simple lesions, single-vessel disease, small sample size (10,11), short duration (6 months) of follow-up (7,8), or use of bare-metal stents (BMS) (7,8) or balloon angioplasty (10). No study has described the impact of post-PCI FFR results on clinical decision-making while the patient was still in the catheterization laboratory (6–17). Hence, our objectives were to evaluate the frequency of unacceptably low or ischemic FFR after angiographically successful PCI, subsequent treatment in the catheterization laboratory and the long-term (>1 year) prognostic utility of post-PCI FFR in predicting MACE in a contemporaneous, large, real-world complex patient population utilizing predominantly drug-eluting stents (DES).

METHODS

STUDY POPULATION. Consecutive patients undergoing PCI who had pre- and post-PCI FFR measurements between January 2009 and September 2014 at the Central Arkansas VA Health systems were studied. The study was approved by the institutional review board.

MEASUREMENT OF FFR. FFR was performed using either the Volcano [San Diego, California] or St. Jude Medical [St. Paul, Minnesota] pressure wire placed in the distal artery. FFR wire was balanced, pressures normalized, and advanced distal to the lesion, after therapeutic anticoagulation. After administration of intracoronary (IC) nitroglycerin, baseline pressure gradient was recorded. FFR was then measured under maximal hyperemic condition with either intravenous adenosine (140 μg/kg/min) or intracoronary adenosine (at least >60 μg). After obtaining angiographically satisfactory PCI result as determined by the operator, baseline pressure gradient and FFR were repeated. In the presence of a residual gradient, manual pullback was performed to localize the area of pressure drop.

In the presence of a persistently ischemic, or if not ischemic, "unsatisfactory" (as determined by the operator) post-PCI FFR, a "subsequent intervention" was performed in many cases which may have included additional post dilation, further stenting, intravascular ultrasound (IVUS), optical coherence tomography (OCT), or a combination depending on the operator's discretion. Following the subsequent intervention, FFR was repeated (final FFR). All the pre- and post-PCI angiograms were evaluated by the operator to estimate percent diameter stenosis.

CLINICAL ENDPOINTS. Primary endpoint was major adverse cardiac events (MACE) defined as a composite of death, myocardial infarction (MI) (not related to intervention) and target vessel revascularization (TVR). MI after index hospitalization was defined as a clinical syndrome of ischemic symptoms and a rise in serum troponin a >99th percentile of reference lab value with or without or new ischemic ST-segment and T-wave changes (18). TVR was defined as subsequent revascularization of the index vessel by either

ABBREVIATIONS AND ACRONYMS

BMS = bare-metal stent(s)
CI = confidence interval
DES = drug-eluting stent(s)
FFR = fractional flow reserve
HR = hazard ratio
IVUS = intravascular ultrasound
MACE = major adverse cardiovascular event(s)
MI = myocardial infarction
OCT = optical coherence tomography
PCI = percutaneous coronary intervention
ROC = receiver-operating characteristic
TVR = target vessel revascularization

TABLE 1 Clinical Characteristics of Study Population

	Overall (N = 574)	MACE Group (n = 109) (19%)	No MACE Group (n = 465) (81%)	p Value
Age, yrs	64 ± 9	66.9 ± 10.1	63.2 ± 8.6	<0.001
Males	560 (98)	105 (96)	455 (98)	0.6
Diabetes	267 (45)	54 (50)	213 (46)	0.6
Hypertension	536 (93)	105 (96)	431 (93)	0.2
Hyperlipidemia	488 (85)	92 (84)	396 (85)	0.9
Prior MI	147 (26)	30 (28)	117 (25)	0.7
CABG	116 (20)	29 (27)	87 (19)	0.08
CKD	102 (18)	31 (28)	71 (15)	<0.01
Smoker	193 (34)	36 (33)	157 (34)	0.9
Beta-blocker	427 (74)	88 (81)	339 (73)	0.1
ACS	184 (32)	47 (43)	137 (29)	<0.01

Values are mean ± SD or n (%).

ACS = acute coronary syndrome(s); CABG = coronary artery bypass grafts; CKD = chronic kidney disease; MACE = major adverse cardiac event(s); MI = myocardial infarction.