

Fractional Flow Reserve and the Appropriate Use Criteria

Determining best practices in coronary revascularization.

BY MANESH R. PATEL, MD

The central goal of invasive care of patients in the cardiac catheterization laboratory is that patients with life-limiting symptoms believed to be related to coronary atherosclerosis are identified to have significant stenosis and receive targeted revascularization, often with percutaneous coronary intervention, to alleviate symptoms and improve quality of life. For patients with acute coronary syndromes, intervention is believed to reduce the risk for cardiovascular events. It is within this context that the use of fractional flow reserve (FFR) and the Appropriate Use Criteria (AUC) are reviewed.

AUC

The AUC, written by the American College of Cardiology in conjunction with the American Heart Association and several professional societies, provide guidance on when it is reasonable to perform a cardiovascular procedure. The AUC were established as a result of increasing health care costs, documented variability with procedural use, and concerns from patients, payers, and clinicians about overuse, misuse, and underuse.

The criteria were developed using the RAND methodology with the modified Delphi process¹ to allow for review of the available evidence for several clinical scenarios followed by a face-to-face meeting. Although originally aimed at noninvasive technologies, the AUC for coronary revascularization were developed in 2009 and updated in 2012.²

The writing group for the AUC for coronary revascularization stated that “coronary revascularization is

appropriate when the expected benefits, in terms of survival or health outcomes (symptoms, functional status, and/or quality of life) exceed the expected negative consequences of the procedure.”² In order to quantify and categorize as many percutaneous coronary interventions (PCIs) as possible, the AUC group identified several variables as key to determining whether revascularization is appropriate. These include the syndrome or symptoms leading to the presentation, the degree of ischemia on noninvasive testing, the degree of anti-anginal medical therapy, and the coronary anatomy. Within this framework, more than 180 clinical scenarios were developed that have been used to categorize and evaluate coronary revascularization. These scenarios were not anticipated to cover all the coronary scenarios that exist in clinical practice, but rather were designed to provide a framework and structure for considering revascularization procedures.

FFR

In 2012, the AUC for diagnostic invasive angiography and catheterization were published.² In an effort to capture the reasons for diagnostic invasive procedures, the focus of this document is on preprocedure risk and testing in order to understand the benefit of the diagnostic test. Within this document, there is a table that provides the value of fractional flow reserve in patients without previous noninvasive imaging, or patients in whom the prior testing is not in concordance with the symptoms or angiographic findings (Table 1). This table demonstrates that for coronary stenosis with lesions

TABLE 1. USE OF FFR AND IVUS IN THE DIAGNOSTIC APPROPRIATE USE CRITERIA

Indication		Appropriate Use Score (1-9)		
		Unexpected Angiographic Finding or No Prior Noninvasive Testing	Prior Testing = No Ischemic Findings	Prior Testing = Concordant Ischemic Findings
FFR for Lesion Severity				
40.	Angiographically indeterminate severity left main stenosis (defined as two or more orthogonal views contradictory whether stenosis > 50%)	A (7)	A (7)	A (7)
41.	Nonobstructive disease by angiography (non-left main) < 50%	I (3)	I (2)	U (5)
42.	Angiographically intermediate disease (non-left main) 50% to 69%	A (7)	U (6)	A (7)
43.	Angiographically obstructive significant disease (non-left main) ≥ 70% stenosis	A (7)	A (7)	I (3)
IVUS for Lesion Severity				
44.	Angiographically indeterminate left main stenosis (defined as two or more orthogonal views contradictory whether stenosis > 50%)	A (7)	A (7)	A (7)
45.	Nonobstructive disease by angiography (non-left main) < 50%	I (3)	I (3)	U (6)
46.	Angiographically intermediate disease (non-left main) 50% to 69%	U (5)	U (5)	U (6)
47.	Angiographically obstructive significant disease (non-left main) ≥ 70% stenosis	U (4)	U (5)	I (3)
IVUS—Examination of Lesion or Artery Morphology				
48.	Coronary lesions or structures difficult to characterize angiographically (eg, aneurysm, extent of calcification, stent fracture, stent apposition, stent expansion, dissections) or for sizing of vessel before stent placement			A (8)
Abbreviations: A, appropriate; I, inappropriate; U, uncertain. Reprinted with permission from Catheterization and Cardiovascular Interventions. ²				

between 50% to 69%, invasive FFR is the test preferred for diagnostic purposes.

The FFR is the ratio of mean coronary artery pressure distal to an obstructive coronary lesion to the mean aortic pressure during maximal coronary blood flow, usually induced by adenosine infusion. This represents a physiologic measure of coronary stenosis. Originally described with correlation to noninvasive myocardial

perfusion imaging, the FFR level of 0.75 was used to differentiate between lesions that were treated with percutaneous intervention.³ Subsequently, patients with multivessel disease as determined by angiographic analysis were studied in a cohort analysis in which PCI was performed only on lesions with abnormal FFR levels, and angiographic stenoses without evidence of hemodynamic stenosis by FFR were medically treated

TABLE 2. UNADJUSTED RATES AND ADJUSTED HAZARDS OF DEATH OR RECURRENT ACUTE CORONARY SYNDROME AT 3 YEARS, ACCORDING TO APPROPRIATENESS CATEGORIES AND CORONARY REVASCULARIZATION

Appropriateness Category	n	Crude Rate %		HR (95% CI)	Adjusted P Value
		No Revascularization	Revascularization		
Inappropriate ^a	311	16 (9.4%)	20 (14.2%)	0.99 (0.48—2.02)	.97
Uncertain ^a	326	23 (15.3%)	14 (8.0%)	0.57 (0.28—1.16)	.12
Appropriate ^b	991	50 (16.1%)	80 (11.8%)	0.61 (0.42—0.88)	.0087

^aHazard ratio (HR) to compare outcomes in the inappropriate and uncertain patients adjusted for age, sex, clinical characteristics (hypertension, diabetes, chronic kidney disease, prior myocardial infarction, heart failure, peripheral vascular disease), physician characteristics, and hospital characteristics.

^bHazard ratio comparing outcomes in the appropriate patients adjusted for age, sex, clinical characteristics (Canadian Cardiovascular Society angina classification, extent of coronary artery disease, hypertension, diabetes, chronic kidney disease, COPD, prior myocardial infarction, heart failure, peripheral vascular disease), left ventricular ejection fraction, physician characteristics, and hospital characteristics.

Abbreviations: CI, confidence interval.

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without intervention.⁴ The 5-year clinical outcomes from this study demonstrated that angiographic stenosis without hemodynamic significance can be safely deferred and not treated percutaneously.

These initial pilot studies formed the basis for two informative randomized trials with FFR that provide clinical evidence for FFR-guided revascularization. The FAME study randomized patients with multivessel disease to FFR-guided revascularization versus angiographically guided revascularization and found a statistically significant reduction in the rate of death, myocardial infarction, and repeat revascularization at 1 year.⁵ Additionally, patients treated with the FFR-guided strategy had similar rates of being free from angina compared to the angiographically treated patients. Hence, for patients with multivessel disease, FFR guidance provides specific lesion assessment for future cardiovascular risk, a risk that may be attenuated by PCI compared to traditional revascularization based on angiographic findings alone.

Recently, FAME-2 studied randomized stable angina patients to FFR-guided PCI with optimal medical therapy compared to optimal medical therapy alone. The trial was halted early due to a statistically significant reduction in the composite primary endpoint of death, myocardial infarction, and urgent revascularization.⁶ This benefit was driven primarily by the reduction in urgent revascularization, but all of the components of the endpoints trended in favor of FFR, especially when

viewed in context of events occurring in the immediate periprocedural areas. Taken in total, these trial findings provide a robust evidence base for invasive FFR as a specific tool for lesion assessment that helps guide PCI with improved outcomes.

FURTHER APPLICATIONS

In principle, these findings are in keeping with the goal of ischemia-driven revascularization outlined by the AUC for coronary revascularization. In fact, the idea of functional assessment of patients prior to revascularization is central to the existing criteria. However, the rapidly evolving evidence base for FFR does highlight the need for more possible clinical scenarios in which FFR would be used. Additionally, when angiographic stenoses do not fit with the clinical symptoms or prior noninvasive testing, the FFR findings should be utilized as tie-breakers for clinical decision making.²

Studies have also evaluated the existing AUC for coronary revascularization in both the National Cardiovascular Data Registry and in cohort analysis from Canada. The National Cardiovascular Data Registry analysis demonstrated that the majority of PCIs in the United States are appropriate, and a small number (approximately 4%) are categorized as inappropriate. The analysis also showed that when only elective PCIs are reviewed, again a minority (approximately 12%) are categorized as inappropriate.

(Continued on page 74)

(Continued from page 66)

Ko et al reviewed more than 1,600 PCIs performed between 2006 and 2007 using the AUC.⁷ They found that only 69% of patients with appropriate designations for coronary revascularization actually received a PCI or coronary artery bypass grafting. The rates of death and recurrent acute coronary syndrome were significantly less in the patients with scenarios rated as appropriate who underwent coronary revascularization compared to medical therapy. In contrast, patients who underwent revascularization for uncertain or inappropriate indications did not have a difference in the rate of death or recurrent acute coronary syndrome at 3 years (Table 2). These findings highlight the importance of underutilization of revascularization in patients at risk for adverse cardiovascular events. Again, real-time hemodynamic- and ischemia-driven revascularization would alleviate concerns of underuse.

Therefore, the field of coronary disease management is moving closer to the identification of the best way to apply coronary revascularization. The available evidence would suggest that several factors affecting patient risk should be considered. Additionally, the evolving evidence for the use of FFR to determine the hemodynamic significance of coronary lesions and to help direct ischemia-driven revascularization provide strong support for the expansion of its use in clinical practice and in the scenarios categorized by the AUC. ■

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