Clinical Investigation

Current Use of Fractional Flow Reserve:

A Nationwide Survey

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*Major medical society guidelines recommend the measurement of fractional flow reserve (FFR) as an aid in choosing percutaneous coronary intervention in patients with stable coronary artery disease. We investigated the measurement of FFR among interventionalists, analyzing operators' attributes and decision-making processes to reveal differences in their applications of FFR and the reasons for those differences. An electronic survey study of 1,089 interventionalists was performed from 2 February through 6 March 2012, yielding 255 responses. Most respondents were >45 years old (58%), worked primarily in a community hospital (59%), and performed 10 to 30 cases per month (52%). More than half (145/253, 57%) used FFR measurement in less than one third of cases, and 39 of 253 (15%) never used it. There were no differences in use of FFR by age, practice location, or angiogram volume (*P *>0.05 for all). Respondents used FFR measurement more frequently than intravascular ultrasonography (73% vs 60%) to help guide the decision to stent (*P *<0.01). Operators reported that their primary reasons for not using FFR were lack of availability (47%) and problems with reimbursement (39%). There was no difference in FFR use by operator age, practice setting, or case volume.* ***(Tex Heart Inst J 2014;41(6):579-84)***

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Coronary angiography has been well established as the initial invasive technique for evaluating coronary stenoses in patients with stable coronary artery disease (CAD), but its ability to determine the functional significance of an angiographically intermediate lesion is quite limited. Indeed, flow through a stenotic vessel is affected by multiple factors that cannot be measured by visual evaluation alone, such as flow entrance and exit angle, orifice shape, and degree of turbulence. Guidelines have recommended noninvasive functional tests before angiography.[1] Nevertheless, only 44.5% of patients undergo stress testing in the 90 days before their elective percutaneous coronary intervention (PCI).[2] Therefore, in many elective cases, the decision to stent is guided mainly by standard coronary angiographic findings. Indeed, 60.6% of PCIs in the American College of Cardiology National Cardiovascular Data Registry are performed ad hoc.[3]

Fractional flow reserve (FFR), defined as the pressure distal to a stenosis relative to the pressure proximal to that stenosis, enables the determination of flow impediment during maximal hyperemia and incorporates many lesion-specific variables, such as anatomic variability and the contribution of collateral vessels. The relative ease and safety of the test, as well as its documented sensitivity and specificity[4] (88% and 100%, respectively), make it ideal as objective documentation of the appropriateness of ad hoc PCI.

The frequency of FFR use in daily practice is unknown. A recent study by Orvin and colleagues[5] showed that the operator's decision to stent was in discordance with FFR measurements in nearly 20% of cases. It is important to note that 83% of patients in Orvin's study had acute coronary syndrome (ACS), in which the clinical usefulness of FFR is less well established than in patients with stable CAD; in addition, interventionalists are generally more willing to perform PCI on ACS patients than on patients with stable CAD, even if their lesions are angiographically comparable. We performed a nationwide survey to determine how FFR is being applied by interventionalists in the United States to patients with stable CAD.

Materials and Methods

We developed a brief online survey that was approved by our center's institutional review board. We administered our survey through the Society of Cardiovascular

Angiography and Interventions (SCAI). The survey was sent to members of the SCAI, who by definition have completed at least one full year (or its equivalent) of training exclusively in cardiac catheterization and angiographic techniques and who, after training, have spent a significant percentage of their practice time performing and interpreting cardiac catheterization and angiographic studies. The survey was sent only to American members of the SCAI through only 2 methods: a direct e-mail invitation sent on behalf of one of the authors (GY), and an advertisement in the weekly newsletter of the SCAI. The survey was available from 2 February through 6 March 2012 and comprised questions regarding the operator's use of FFR in the catherization laboratory. Only respondents who used FFR were directed to more detailed questions; those who did not use FFR (n=39) were directed away from questions 5 through 12 and were counted as having skipped these questions.

The survey was created by using SurveyMonkey® (Palo Alto, Calif). Comparative statistics (via the χ^2 test) was used to examine differences in respondents' ages, practice types, and operator volumes, and descriptive statistics was used to summarize survey responses. For statistical analysis, we used Statistical Analysis System version 9.3 for Windows (SAS Institute; Cary, NC). A *P* value of less than 0.05 was considered statistically significant.

Results

The survey (see Appendix) was sent by direct e-mail invitation to 3,474 SCAI members; 1,089 (31.3%) opened the e-mail, and 245 of this group (22.5%) took and completed the survey. The survey was also sent through the weekly newsletter of the SCAI, which collected 10 additional responses.

Most respondents were older than 45 years (58.3%), worked primarily in a community hospital (59.1%), and performed 10 to 30 angiograms per month (51.9%; 17.8% performed <10, and 30.1% performed >30). More than half (145/253, 57.3%) measured FFR in less than one third of their angiograms, and 39 of 253 (15.4%) never measured FFR. There were no significant differences in the use of FFR by age (*P*=0.3481), practice location (*P*=0.739), or angiogram volume (*P*=0.2378). Intermediate stenoses were studied equally (91.7% vs 92.8%, *P*=0.7946) by infrequent FFR users (who used FFR <1/3 of the time) and frequent FFR users (who used FFR >1/3 of the time).

With 72% of operators using an FFR cutoff of 0.80 and 28% using 0.75, revascularization was deferred more than half the time by 40% of operators. The patient's disease burden was downgraded from multivessel disease more than half the time by 19% of operators.

Respondents chose to measure FFR most often in intermediate stenoses (197/212, 92.9%) and when noninvasive test results were equivocal or absent (155/212, 73.1%). Other instances in which the 212 respondents used FFR measurement included multivessel disease (104, 49.1%), sequential stenoses in a single vessel (101, 47.6%), left main coronary artery disease (92, 43.4%), single stenosis (76, 35.8%), ostial lesions (76, 35.8%), bifurcation lesions (57, 26.9%), and bypass grafts (21, 9.9%).

Although FFR is more frequently measured in intermediate lesions, it was also used in angiographically severe (>70%) lesions when the results of noninvasive functional testing were absent or equivocal (43.1%), were positive but not correlated with angiographic findings (64.7%), or were negative (51.9%). Suspected severe lesions were not commonly studied with FFR when there was appropriate correlation between noninvasive and angiographic findings (4.4%).

Among our respondents, the Fractional Flow Reserve versus Angiography for Multivessel Evaluation trial (FAME)[6] led to more widespread use of FFR to analyze intermediate lesions (135/243, 55.6%). In contrast, fewer interventionalists credited this study for their increased use of FFR in severe lesions (19/243, 7.8%), or for their decision to try FFR for the first time (10/243, 4.1%).

The survey also revealed that the most common application of FFR outside the coronary vasculature was in the renal arteries, by 59 operators (29%). In addition, respondents used FFR more frequently than intravascular ultrasonography (73% vs 60%) to help guide the decision to place coronary stents (*P*=0.006). Finally, the primary reasons operators reported not using FFR were lack of availability (47%) and problems with reimbursement (39%).

Discussion

Fractional flow reserve is determined through a 0.014-in guidewire-based procedure that provides accurate information about flow through a vascular stenosis. The determination of fractional flow reserve has received a class IA recommendation from the European Society of Cardiology and a class IIA recommendation from the American College of Cardiology as an adjunct to help guide coronary revascularization decisions.[7] Although the use of FFR has become increasingly widespread only since the DEFER trial in 2007,[8] our study shows that interventionalists' use of FFR does not differ with their age, practice setting (university vs community-based), or workload (angiograms performed per month).

To guide the decision on whether to treat a given lesion, FFR cutoff values of 0.75 or 0.80 have been used. We found that most interventionalists use a cutoff of 0.80 to minimize the number of ischemic lesions left

untreated. When these 2 cutoff values were applied, intervention was deferred in nearly 40% of the cases in which FFR was used, which is comparable to what has been previously reported.[6]

As might be expected, FFR was used more often for intermediate than for severe stenoses, regardless of the results of noninvasive testing. However, a subgroup analysis of the FAME trial[9] showed that 20% of stenoses that had been visually estimated to be 71% to 90% occlusive were not functionally significant when evaluated by FFR results, indicating that this modality can indeed be useful in further study of lesions thought to be angiographically severe. In the present survey, we found that 43% of operators would pursue FFR when evaluating angiographically severe (>70%) stenoses if noninvasive functional studies were equivocal or absent, and that 65% would pursue FFR if those noninvasive studies did not correlate anatomically with angiographic findings.

Intravascular ultrasonography gives information that is fundamentally different from FFR information: it is strictly anatomic, rather than physiologic, and therefore is not suitable for determining functional significance. The Fractional Flow Reserve and Intravascular Ultrasound Relationship (FIRST) trial[10] showed some correlation between FFR values and intravascular ultrasonography data, but intravascular ultrasonography had little accuracy in helping to guide intervention decisions in cases of intermediate stenosis. It should be used with caution in such circumstances.

Fractional flow reserve might have applications in areas other than the coronary arteries. In our study, 28.8% of operators reported using FFR guidance in the renal arteries. An FFR-guided intervention might help identify patients for whom renal artery stenting would be beneficial, although this approach is supported by only a few small studies, and criteria to guide this type of decision are lacking.[11]

Because up to 56.5% of patients do not undergo stress testing within the 90 days before an elective PCI,[2] the functional significance of an indeterminate stenosis is frequently determined at the time of angiography. In a study that compared the costs associated with an FFR-based approach, with a nuclear stress imaging (NUC) approach (deferring the decision for PCI until a NUC could be obtained), and with a stent approach (stenting all intermediate lesions), FFR saved $1,795 compared with the NUC approach and $3,830 compared with the stent approach, while producing similar quality-adjusted life expectancy.[12,13]

Despite such data associating FFR with significant cost reductions, 39.1% of our respondents cited unspecified reimbursement issues as an impediment to FFR use. A larger issue, however, was lack of access to the technology: 46.9% noted that problems with FFR availability prevented wider use.

Limitations

Our study is limited by the low overall response rate, which might restrict its external validity. However, this response rate is comparable to those of previously published surveys conducted through SCAI.[14,15]

Other limitations include the survey's distribution via e-mail, which might have created a bias toward more technologically inclined physicians, or those with smaller clinical workloads. Nonetheless, we think that the data accurately reflect clinical practice, given that of the 22.5% of invited physicians who responded, 82% were experienced interventionalists who perform more than 10 angiograms per month.

Conclusions

It is our hope that this pilot study of the application of FFR in daily practice to patients with stable CAD reveals patterns of FFR usage and increases awareness of this useful test. Our data showed no significant difference in FFR use by the operator's age, practice setting, or case volume. As expected, FFR was most often used in the evaluation of intermediate lesions, in the absence of functional data, or in cases of discrepancy between functional data. Even so, problems with availability of the test and reimbursement for its cost were the most common barriers to the wider application of FFR in appropriate patients.

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See Appendix on next page.

Appendix

SURVEY RESPONSES (N=255)

Item and Answer Choices	No. Responses (%)
What is your age?	
<45 years	*105 (41.7)*
≥45 years	*147 (58.3)*
Skipped question	*3*
In what type of facility do you perform the majority of your PCI?	
University-based academic medical center	*103 (40.9)*
Community hospital	*149 (59.1)*
Skipped question	*3*
Approximately how many coronary angiograms do you perform for stable angina, chest pain or non-ACS indications in a typical month?	
Less than 10	*45 (17.9)*
10–30	*131 (52)*
More than 30	*76 (30.1)*
Skipped question	*3*
When performing coronary angiography in a non-ACS setting, approximately how often might you use FFR?	
<1/3 of the cases	*145 (57.3)*
1/3–2/3 of the cases	*55 (21.7)*
>2/3 of the cases	*10 (4)*
Always	*4 (1.6)*
Never	*39 (15.4)*
Skipped question	*2*
In which of these settings do you use FFR to guide decision-making? (Please check all applied choices)	
Single stenosis	*76 (35.8)*
Intermediate stenosis	*197 (92.9)*
Multivessel disease	*104 (49.1*
Sequential stenoses in a single vessel	*101 (47.6)*
Left main disease	*92 (43.4)*
Ostial lesions	*76 (35.8)*
Bifurcation lesions	*57 (26.9)*
Bypass grafts	*21 (9.9)*
As an alternative to noninvasive functional testing when their results are equivocal or absent	*155 (73.1)*
Skipped question	*4*
What is your FFR cutoff to treat the lesion?	
0.8	*152 (72)*
0.75	*59 (28)*
Skipped question	*5*
In each of the following scenarios with an angiographically indeterminate (30%–70%) lesion, would you perform FFR? Assume the patient's anatomy is otherwise, in your estimation, appropriate for PCI (calcification, tortuosity, etc.).	
—The results of the noninvasive functional study are absent or equivocal.	
Yes	*195 (92.9)*
No	*9 (4.3)*
I am not sure	*6 (2.8)*
Skipped question	*6*
—The results of the noninvasive functional study are positive and correlate with the stenosis discovered on angiography.	
Yes	*34 (16.2)*
No	*166 (79)*
I am not sure	*10 (4.8)*
Skipped question	*6*
—The results of noninvasive functional study are positive but do NOT correlate with the stenosis discovered on angiography.	
Yes	*186 (88.6)*
No	*12 (5.7)*
I am not sure	*12 (5.7)*
Skipped question	*6*
—The patient has typical angina with a negative noninvasive functional study.	
Yes	*179 (84.9)*
No	*22 (10.4)*
I am not sure	*10 (4.7)*
Skipped question	*5*
In each of the following scenarios with an angiographically severe (>70%) lesion, would you perform FFR? Assume the patient's anatomy is otherwise, in your estimation, appropriate for PCI (calcification, tortuosity, etc.).	
—The results of the noninvasive functional study are absent or equivocal.	
Yes	*90 (43.1)*
No	*96 (45.9)*
I am not sure	*23 (11)*
Skipped question	*7*

Continued on next page

—The results of the noninvasive functional study are positive and correlate with the stenosis discovered on angiography.	
Yes	*9 (4.4)*
No	*194 (94.2)*
I am not sure	*3 (1.4)*
Skipped question	*10*
—The results of noninvasive functional study are positive but do NOT correlate with the stenosis discovered on angiography.	
Yes	*134 (64.7)*
No	*54 (26.1)*
I am not sure	*19 (9.2)*
Skipped question	*9*
—The patient has typical angina with a negative noninvasive functional study.	
Yes	*108 (51.9)*
No	*82 (39.4)*
I am not sure	*18 (8.7)*
Skipped question	*8*
If a nuclear stress test is negative but the patient clinically exhibits angina, and catheterization reveals intermediate disease in 3 vessels and the possibility of balanced ischemia, would you pursue multivessel FFR to help clarify functional significance of the stenoses?	
Yes	*173 (83.6)*
No	*20 (9.6)*
I am not sure	*14 (6.8)*
Skipped question	*9*
How often does FFR assessment lead you to defer revascularization?	
Less than 25% of the time	*28 (13.5)*
25%–50% of the time	*98 (47.1)*
50%–75% of the time	*69 (33.2)*
More than 75% of the time	*13 (6.2)*
Skipped question	*8*
When performing FFR to assess the significance of multivessel disease, how frequently have you reclassified the anatomy as single-vessel disease or no functionally significant stenosis at all?	
Less than 25% of the time	*79 (38.5)*
25%–50% of the time	*87 (42.4)*
50%–75% of the time	*34 (16.6)*
More than 75% of the time	*5 (2.4)*
Skipped question	*11*
Have you performed FFR on stenoses outside the coronary vasculature?	
Renal arteries	*59 (28.8)*
Mesenteric arteries	*2 (1)*
Carotid arteries	*1 (0.5)*
Upper or lower extremities	*16 (7.8)*
Never	*142 (69.3)*
Other, please specify (aortic valve)	*4 (2)*
Skipped question	*11*
How did the results of the FAME trial alter your approach?	
I started relying on FFR measurement for the first time	*10 (4.1)*
I started using FFR much more frequently for intermediate lesions	*135 (55.6)*
I started to utilize FFR to confirm functional significance [of] lesions that appeared >70% angiographically	*19 (7.8)*
It did not affect my approach: I always relied on it, regardless of the degree of angiographic stenosis	*47 (19.3)*
It did not affect my approach: I still don't use it	*32 (13.2)*
Skipped question	*12*
Other than the clinical presentation and degree of angiographic stenosis, what tests do you use to help guide your decision to stent?	
Syntax score	*95 (39.3)*
FFR	*177 (73.1)*
IVUS	*147 (60.7)*
OCT	*5 (2)*
None	*24 (9.9)*
Skipped question	*13*
If you do not use FFR, why not?	
Not available at our institution	*30 (46.9)*
Not ACC/AHA class I recommended	*2 (3.1)*
More risk to patient than reward	*3 (4.7)*
Takes too much time to set up and perform the test	*16 (25)*
Reimbursement issues	*25 (39.1)*
I do not understand enough about FFR	*1 (1.6)*
I do not trust FFR	*3 (4.7)*
Skipped question	*191*

ACC = American College of Cardiology; ACS = acute coronary syndrome; AHA = American Heart Association; FAME = Fractional Flow Reserve versus Angiography for Multivessel Evaluation; FFR = fractional flow reserve; IVUS = intravascular ultrasonography; OCT = optical coherence tomography; PCI = percutaneous coronary intervention

All response frequencies are reported as number and percentage. Percentages do not include respondents who skipped the question.