Cost-effectiveness of measuring fractional flow reserve to guide coronary interventions

William F. Fearon, MD,[a] Alan C. Yeung, MD,[a] David P. Lee, MD,[a] Paul G. Yock, MD,[a] and Paul A. Heidenreich, MD, MS[b] ***Stanford and Palo Alto, Calif***

Background Most patients come to the catheterization laboratory without prior functional tests, which makes the cost-effective treatment of patients with intermediate coronary lesions a practical challenge.

Methods We developed a decision model to compare the long-term costs and benefits of 3 strategies for treating patients with an intermediate coronary lesion and no prior functional study: 1) deferring the decision for percutaneous coronary intervention (PCI) to obtain a nuclear stress imaging study (NUC strategy); 2) measuring fractional flow reserve (FFR) at the time of angiography to help guide the decision for PCI (FFR strategy); and 3) stenting all intermediate lesions (STENT strategy). On the basis of the literature, we estimated that 40% of intermediate lesions would produce ischemia, 70% of patients treated with PCI and 30% of patients treated medically would be free of angina after 4 years, and the quality-of-life adjustment for living with angina was 0.9 (1.0 = perfect health). We estimated the cost of FFR to be $761, the cost of nuclear stress imaging to be $1093, and the cost of medical treatment for angina to be $1775 per year. The extra cost of splitting the angiogram and PCI as dictated by the NUC strategy was $3886 by use of hospital cost-accounting data. Sensitivity and threshold analyses were performed to determine which variables affected our results.

Results The FFR strategy saved $1795 per patient compared with the NUC strategy and $3830 compared with the STENT strategy. Quality-adjusted life expectancy was similar among the 3 strategies (NUC-FFR = 0.8 quality-adjusted days, FFR-STENT = 6 quality-adjusted life days). Compared with the FFR strategy, the NUC strategy was expensive (>$800,000 per quality-adjusted life year gained). Both screening strategies were superior to (less cost, better outcomes) the STENT strategy. Sensitivity analysis indicated that the NUC strategy would only become attractive (<$50,000/quality-adjusted life years compared with FFR) if the specificity of nuclear stress imaging was >25% better than FFR. Our results were not altered significantly by changing the other assumptions.

Conclusion In patients with an intermediate coronary lesion and no prior functional study, measuring FFR to guide the decision to perform PCI may lead to significant cost savings compared with performing nuclear stress imaging or with simply stenting lesions in all patients. (Am Heart J 2003;145:882-7.)

In the United States, despite the recommendations of clinical practice guidelines, most patients with chest pain who are at intermediate risk for coronary artery disease undergo coronary angiography before a noninvasive assessment for ischemic heart disease.[1,2] Management of an angiographic intermediate coronary lesion in these patients remains a practical challenge. Definitive therapy is often delayed while a noninvasive test is performed to determine the functional significance of the intermediate lesion. Recently, the miniaturization of accurate pressure-sensing guide wires and the development of the myocardial fractional flow reserve (FFR) index have offered a new and convenient method for measuring the physiologic impact of intermediate coronary lesions immediately, while patients are in the catheterization laboratory.[3] FFR is defined as the maximum blood flow to the myocardium achieved in the presence of a narrowing compared with the theoretical maximum blood flow possible in the absence of the narrowing.[4] It is calculated by dividing the mean coronary pressure distal to a stenosis, as measured with a coronary pressure wire, by the mean proximal coronary pressure, as measured with a guiding catheter, at maximal hyperemia.[5] Studies have demonstrated that an FFR <0.75 accurately predicts the presence of ischemia as determined by a variety of noninvasive stress testing modalities.[6-8] Furthermore, deferral of a percutaneous coronary intervention (PCI) when the FFR of an intermediate lesion is ≥0.75 is

From the [a]Stanford University Medical Center, Stanford, Calif, and [b]VA Palo Alto Health Care Systems, Palo Alto, Calif.
Reprint requests: William F. Fearon, MD, Falk Cardiovascular Research Center, Division of Cardiovascular Medicine, Stanford University Medical Center, 300 Pasteur Dr, Stanford, CA 94305-5406.
E-mail: wfearon@stanford.edu

0002-8703/2003/$30.00 + 0
doi:10.1016/S0002-8703(03)00072-3

predictive of low event rates during the ensuing 2 years.[9] In evaluating the usefulness of a new test, a formal assessment of its cost-effectiveness is critical because health care resources are limited. To our knowledge, such an assessment has not been performed for the use of the coronary pressure wire in evaluating intermediate coronary lesions. In this study, we evaluate the cost implications of deferring the decision for PCI to obtain a nuclear stress imaging study (NUC strategy) versus measuring FFR at the time of angiography to help guide the decision for PCI (FFR strategy) versus stenting intermediate lesions in all patients (STENT strategy).

Methods

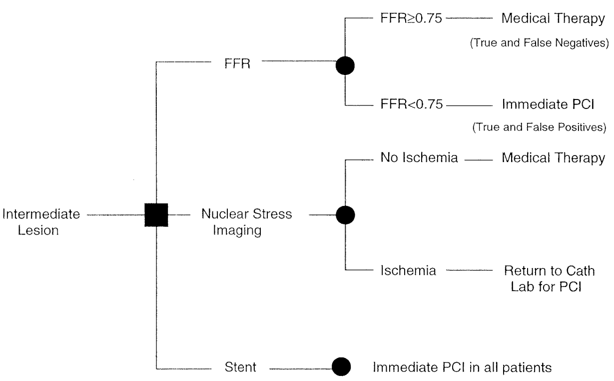
Decision model

We developed a decision model from the health care system perspective (defined as the societal perspective without indirect costs) to compare the long-term (the life of the patient) costs and benefits of 3 treatment strategies for patients with chest pain who undergo coronary angiography before stress perfusion imaging and have an intermediate coronary lesion of unclear physiologic significance (Figure 1). We have limited this analysis to patients with single-vessel disease because of the increased number of approaches to managing multivessel disease. Figure 1 describes the events leading up to the decision to stent or ignore the lesion. In the NUC strategy, the current standard method for examining these patients, PCI is deferred to allow for outpatient nuclear stress imaging assessment of the intermediate lesion. When an ischemia-producing lesion is demonstrated by the nuclear stress imaging study, then the patient is admitted to the hospital for PCI. When the lesion is not deemed physiologically important on the basis of the nuclear stress imaging study, PCI is deferred and the patient is treated medically. The FFR strategy dictates measuring the FFR of the culprit vessel at the time of initial angiography. When the FFR is <0.75, PCI is performed. When the FFR is ≥0.75, PCI is deferred and the patient is treated medically. Patients with false-negative results do not undergo stenting but continue to have angina, leading to an increased cost of antianginal and PCI treatment and to a decreased quality of life. The STENT strategy bypasses a functional assessment of the intermediate lesion, and PCI is performed in all patients.

In developing the decision model, we based our assumptions on prominent studies when available. When there were no published data, we used local expert opinion to make an estimate.

On the basis of recent literature, we assumed that 40% of the intermediate coronary lesions would be ischemia-producing (Table I).[7] The test characteristics of nuclear stress imaging for detecting ischemia (as opposed to coronary stenosis) are not clear. In our base case, we assumed that these lesions would be detected with equal accuracy with FFR and nuclear stress imaging and assigned them a sensitivity rate of 88% and a specificity rate of 96%.[10] These values were the midpoint between 2 estimates: 1) a sensitivity rate (75%) and specificity rate (93%) from a study that evaluated nuclear imaging before and after coronary stenting and assumed that all

Figure 1



Decision tree outlining the short-term decision model for the cost-effectiveness analysis. Patients with abnormal FFR results (true- and false-positive undergoing stenting) or ischemia with nuclear stress imaging undergo stenting.

prestented lesions produced ischemia and that all dilated lesions were no longer ischemia-producing; and 2) a sensitivity rate and specificity rate of 100%, which assumed that nuclear imaging is the gold standard.[10] Several studies have found that FFR is similar to, if not more accurate than, nuclear stress imaging in the detection of ischemia.[7,10] We estimated that 30% of patients would have angina relief with medical therapy and 70% of patients would have angina relief with PCI.[11,12] The duration of angina relief was estimated to be 4 years, and the quality-of-life adjustment for living with angina was 0.9 (1.0 = perfect health).[13–15]

There was a 0.3% risk of death from PCI, with no difference whether PCI was performed at the time of initial angiography or at a later date.[16] We assumed that measuring FFR increased the risk of death 0.015%, whereas nuclear stress imaging did not increase this risk.

Costs

We chose to use marginal costs for both inhospital and outpatient services because they provide the best estimate of the cost of doing additional procedures. Measuring FFR cost $761, consisting of $550 for the wire (Radi Medical Systems, Uppsala, Sweden); $36 for intracoronary adenosine (Fujisawa Healthcare, Deerfield, Ill); and $175 for professional fees (Current Procedural Terminology code 93571). Nuclear stress imaging was estimated to cost $1093 (technical and professional fees, on the basis of hospital cost accounting data). By use of published data, adjusted to year-2000 dollars, the medical cost of treating angina was $1775 per year.[17] We also accounted for differences among the strategies in follow-up costs for developing angina and for repeat PCI.[18] We estimated repeat PCI rates after stenting of 11% at 1 year and 2.5% per year for the next 4 years.[18] All costs were discounted at a rate of 3% per year.[19]

To determine the extra cost of splitting the angiogram and the PCI, as dictated by the NUC strategy, we obtained hospital cost accounting data from an academic university hospital

Table I. Model assumptions and references

Variable	Estimate	Range*	Reference
Percent of lesions producing ischemia	47%	± 15%	Pijls[7]
Relief of angina with medical therapy	29%	± 20%	Bucher[11]
Relief of angina with PCI	70%	40-90%	Bucher,[11] Versaci[12]
Duration of angina relief	4 years	2-6 years	RITA-2,[13] Hartigan[14]
Utility for living with angina	0.9	0.75-0.95	Nease[15]
Sensitivity of nuclear imaging†	0.88	± 0.10	De Bruyne,[10] Estimate
Specificity of nuclear imaging†	0.96	± 0.05	De Bruyne,[10] Estimate
Sensitivity of FFR†	0.88	± 0.12	Pijls,[7] Estimate
Specificity of FFR†	0.96	± 0.09	Pijls,[7] Estimate
Risk of death from PCI	0.3%	± 0.9%	Kimmel[16]
Cost of FFR	$761	$400-$1000	
Wire	$550		Radi Medical Systems
Adenosine	$36		Fujisawa Healthcare
Professional fee	$175		CPT Code 93571
Cost of nuclear stress imaging	$1093	$700-$1300	Transition Systems Inc
Cost of treating angina per year	$1775	$1400-$2100	Cohen[17]
Years of survival with angina	20	10-30	Garber[20]

*Range tested with sensitivity analysis (± 95% CI when available). Discount rate of 3%.
†For predicting ischemia, see text for details of derivation.

(Transition Systems Incorporated, Boston, Mass). Each resource or unit of care was assigned a cost at the departmental level. These cost multiplied by the number of resources for each resource used are summed across departments to determine the total cost. Hospital costs of 10 consecutive cases in which patients underwent PCI at the same time as the initial angiogram were tabulated and averaged. Hospital costs of 11 consecutive cases in which patients underwent an initial outpatient angiogram and then returned for PCI on a separate date were also tabulated and averaged. The first angiogram was an outpatient procedure in all cases. Only patients who were discharged within 23 hours of their PCI were included.

The average cost of performing angiography followed by PCI at a later date was $16,588 ± $3761 (angiography alone was $4126 ± $762 and PCI alone was $12,463 ± $3886). The average cost of performing angiography and PCI at the same time was $12,703 ± $4963. The increased cost of performing angiography and PCI separately was $3886.

Survival

The median survival period for a 55-year-old patient with angina was assumed to be 20 years.[7,20] After adjustment for the decreased quality of life for living with angina (utility = 0.9), the survival was 18 quality-adjusted life years (QALYs). Discounting at 3% per year yields 14 QALY.

Analyses

The difference in life-time costs and survival (life-years) among the NUC strategy, the FFR strategy, and the STENT strategy was calculated by use of the decision model. The incremental cost-effectiveness of the FFR strategy compared with the other strategies was calculated by dividing the difference in life-time costs by the difference in survival. By use of 95% CIs when available or a reasonable range when not, a 1-way sensitivity analysis was performed for each of the major variables in the model to determine the impact each variable had on the cost-savings or the cost-effectiveness of the 3 strategies (Table I). A threshold analysis was performed to determine what relative sensitivity or specificity of FFR for nuclear stress imaging was necessary for the NUC strategy to become financially attractive (<$50,000/QALY) in relation to other commonly accepted medical interventions. Although no absolute threshold for cost-effectiveness exists, we chose $50,000/QALY on the basis of recent literature.[19,21]

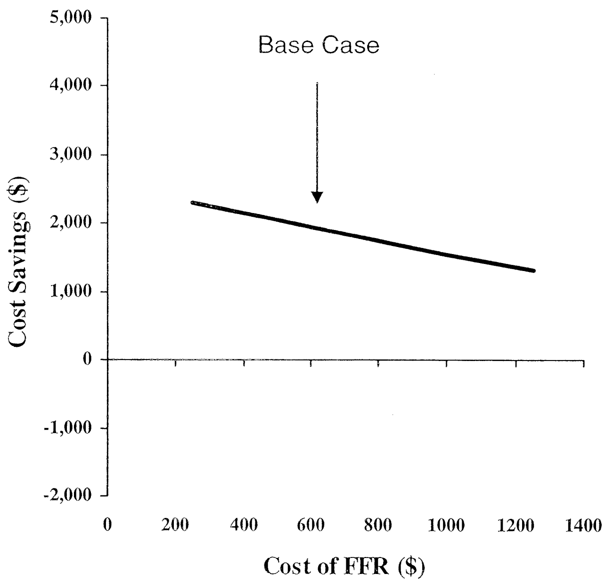
Results

When all costs and potential complications were accounted for, the FFR strategy saved $1795 per patient compared with the NUC strategy and $3830 per patient compared with the STENT strategy (Table II). Quality-adjusted survival was similar for the 3 strategies, but the cost per QALY gained for the NUC strategy (>$800,000/QALY) was substantial (Table II). The STENT strategy was dominated by the FFR strategy and the NUC strategy, because it was more costly and provided fewer benefits.

Sensitivity analysis

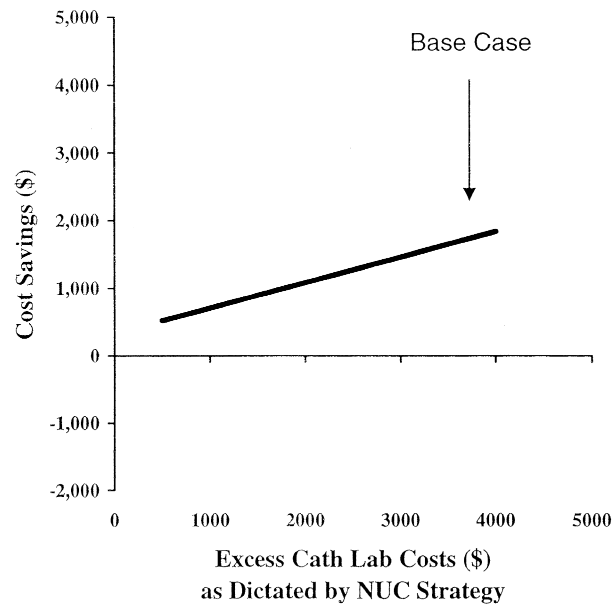
Altering the cost of FFR, the cost of nuclear stress imaging, or the cost of splitting the angiogram and the PCI within a reasonable range did not significantly change the amount saved with the FFR strategy (Figures 2 and 3). Even when the extra cost of splitting the angiogram and PCI was eliminated, the FFR strategy still saved $331 per patient. The NUC strategy remained financially unattractive (>$50,000/QALY) in all cases with this model. Using 2000 Medicare reimbursement data in place of the hospital costs for performing

Figure 2



Plot of the relation between cost of the FFR strategy and cost-savings compared with the NUC strategy.

Figure 3



Plot of the relation between excess catheterization laboratory costs as dictated by the NUC strategy and cost-savings with the FFR strategy.

Table II. Costs and outcomes of the NUC, FFR and Stent Strategies

	Total cost	QALYs*	Cost/QALY gained
NUC Strategy	$13,190	14.7962	
FFR Strategy	$11,395	14.7940	
Difference	$1795	0.0022	$808,000
STENT Strategy	$15,225	14.7761	
FFR Strategy	$11,395	14.7940	
Difference	$3830	–0.0179	FFR dominates†

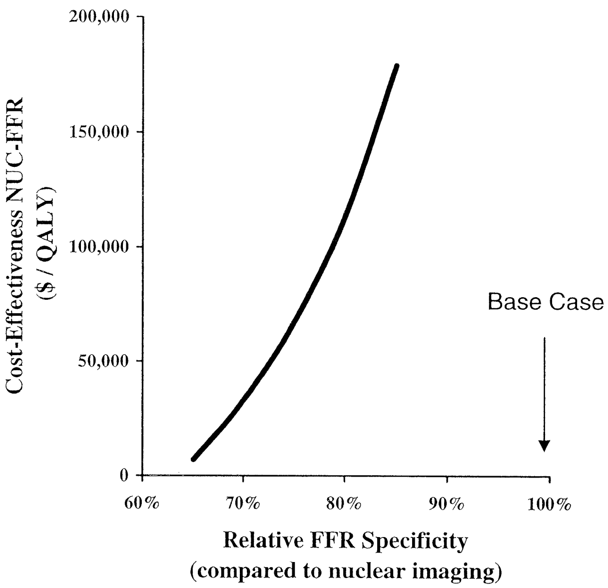
*Discounted.
†FFR is less expensive and provides more QALYs.

FFR and nuclear stress imaging ($283.11 and $553.21, respectively) also did not significantly affect the results. Eliminating any increase in mortality from stenting did not significantly change the results. The NUC strategy became even more expensive (>$1,000,000/QALY), compared with the FFR strategy; the Stent strategy was no longer dominated (more expensive, less effective) by the FFR strategy, but it remained very expensive ($500,000/QALY).

To assess when the NUC strategy would become financially attractive compared with the FFR strategy, we altered the sensitivity or specificity of FFR for nuclear stress imaging for detecting ischemia-producing lesions. Altering the sensitivity of FFR had no impact on the cost-effectiveness of either strategy. The NUC strategy became financially attractive (<$50,000/QALY) compared with the FFR strategy only after the specificity of FFR was decreased to <74% (Figure 4).

Sensitivity analysis of the other variables included in the decision analysis did not significantly impact these findings. For example, varying the percentage of lesions that were estimated to be ischemia-producing, the percentage of patients who would have angina relieved with medical therapy or PCI, the duration of angina relief, the quality-of-life adjustment for living with angina, or the risks associated with performance of FFR within a reasonable range did not significantly alter the results. Even when the increased death rate

Figure 4



Plot of the relation between the relative specificity of FFR for detecting ischemia and the cost-effectiveness of the NUC strategy versus the FFR strategy. The nuclear strategy is expensive (>$50,000/QALY) unless the specificity rate of FFR is <74% of that of nuclear stress imaging.

was 0% and angina relief was lifelong with stenting all patients, the FFR strategy remained cost-saving and cost-effective compared with the STENT strategy.

Discussion

Performing a noninvasive assessment for ischemia before coronary angiography is the recommended approach for treating patients with chest pain who are at intermediate risk for coronary artery disease. Most patients, however, undergo catheterization before a noninvasive evaluation.[2] In this setting, determining the appropriate management of an intermediate coronary lesion can be challenging. The main finding of this study is that measuring FFR at the time of initial angiography to evaluate the functional significance of an intermediate coronary lesion (FFR strategy) saves costs compared with performing a nuclear stress imaging study to guide the decision for PCI (NUC strategy) and compared with simply implanting stents in all patients (STENT strategy).

Measuring FFR has been shown by recent studies to be an accurate method for determining the physiologic significance of an intermediate coronary lesion.[6-8] Pijls et al evaluated 45 patients with chest pain and intermediate coronary lesions, all of whom underwent exercise testing, nuclear stress imaging, and dobutamine echocardiography.[7] In all 21 patients in whom the FFR was <0.75, at least 1 of the 3 stress tests had abnormal results. After performing revascularization in these patients, all the abnormal stress test results reverted to normal and all FFR values were ≥0.75. Of the 24 patients who had no evidence of ischemia on all 3 stress tests, 21 had an FFR ≥0.75. Overall, the sensitivity rate of FFR in identifying ischemia with stress testing was 88%, the specificity rate was 100%, and the predictive accuracy rate was 93%.

More recently, Bech et al have evaluated the clinical outcomes in a group of patients with chest pain, no prior stress test, intermediate coronary lesions, and an FFR ≥0.75.[9] This group was randomized to undergo either PCI or deferral of PCI. At 2 years follow-up, the rate of clinical events was similar in both groups, with a trend toward a better outcome in the group in which PCI was deferred. These data suggest an important role for measuring FFR as a means of guiding treatment of patients who have not had prior stress testing and are found to have intermediate coronary lesions. To date, however, the cost-effectiveness of this approach has not been formally evaluated.

In this study, we found that the FFR strategy saved $1795 per patient compared with the traditional approach of deferring PCI to assess the functional significance of the intermediate lesion noninvasively and saved $3830 per patient compared with simply stenting all intermediate lesions. Because outcomes were similar in the 3 strategies, the FFR strategy was also the most cost-effective. Compared with the FFR strategy, the STENT strategy cost more and was associated with a worse outcome, and the NUC strategy cost >$800,000/QALY. These data were generated by assuming that FFR was equally sensitive and specific for detecting reversible myocardial ischemia compared with nuclear stress imaging. However, altering the sensitivity of FFR did not have any important impact on these data. Only when the specificity of FFR was assumed to be ≤73% did the NUC strategy become financially attractive (<$50,000/QALY) (Figure 4). Studies suggest, however, that FFR is highly specific for detecting reversible myocardial ischemia and comparable with nuclear stress imaging.[6-8]

We chose to perform this analysis from a societal perspective (without indirect costs). From a hospital perspective, either measuring FFR or performing nuclear stress imaging and either implanting stents in all patients or treating all patients medically might be most attractive, depending on the reimbursement system.

We made a number of other estimations that could potentially impact our results. Modifying the cost of performing FFR or nuclear stress imaging within a plausible range did not change the results (Figure 2), including substituting Medicare reimbursement data in place of cost for FFR and nuclear stress imaging. The start-up costs for performing FFR and nuclear stress imaging were not incorporated into the model; however, start-up costs for nuclear stress imaging are likely to be much higher. The difference in costs ($3900) associated with the second visit to the catheterization laboratory, as dictated by the NUC strategy, was the most important factor in determining the cost savings associated with the FFR strategy. However, altering this additional cost within the plausible range did not lead to a significant change in our results (Figure 3). Even after eliminating this additional cost, the FFR strategy remained cost-saving. We modeled only costs of angina treatment, including repeat PCI. Other health care costs are unlikely to be significantly different in the diagnostic strategies and should not affect the decision to choose one strategy over another.

We made the assumption that perfusion imaging and FFR are similar for determining whether a lesion is flow-limiting and the cause for angina. It is possible that FFR is better than perfusion imaging in determining lesion significance, which would make FFR more financially attractive than suggested with our results.

Conclusion

Because patients with chest pain who are at an intermediate risk for coronary disease are commonly referred for angiography before the performance of noninvasive stress testing, the interventional cardiologist is faced with the practical dilemma of determining the functional significance of intermediate coronary lesions. With the increased use of electron beam computed tomography scanning, the number of patients undergoing angiography without a noninvasive investigation for ischemia will likely continue to grow.[22]

Our data suggest that measuring fractional flow reserve with a coronary pressure wire and using the result to guide the decision for intervention leads to significant cost savings compared with the traditional strategy of performing a nuclear stress imaging study and returning to the catheterization laboratory for intervention when the nuclear imaging study results are abnormal, and compared with simply implanting stents in all patients.

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