

# Use of Fractional Flow Reserve Versus Stress Perfusion Scintigraphy After Unstable Angina

## Effect on Duration of Hospitalization, Cost, Procedural Characteristics, and Clinical Outcome

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<b>OBJECTIVES</b>	The present study sought to determine the value of fractional flow reserve (FFR) compared with stress perfusion scintigraphy (SPS) in patients with recent unstable angina/non-ST-segment elevation myocardial infarction (UA/NSTEMI).
<b>BACKGROUND</b>	Fractional flow reserve, an invasive index of stenosis severity, is a reliable surrogate for SPS in patients with normal left ventricular function. An FFR $\geq 0.75$ can distinguish patients after myocardial infarction (MI) with a positive SPS from those with a negative SPS. However, the use of FFR has not been investigated after UA/NSTEMI.
<b>METHODS</b>	Seventy patients who had recent UA/NSTEMI and an intermediate single-vessel stenosis were randomized to either SPS (n = 35) or FFR (n = 35). Patients in the SPS group were discharged if the SPS revealed no ischemia, whereas those in the FFR group were discharged if the FFR was $\geq 0.75$ . Patients with a positive SPS and those with an FFR $< 0.75$ underwent percutaneous transluminal coronary angioplasty.
<b>RESULTS</b>	The use of FFR markedly reduced the duration and cost of hospitalization compared with SPS ( $11 \pm 2$ h vs. $49 \pm 5$ h [ $-77\%$ ], $p < 0.001$ ; and $\$1,329 \pm \$44$ vs. $\$2,113 \pm \$120$ , respectively, $p < 0.05$ ). There were no significant differences in procedure time, radiation exposure time, or event rates during follow-up, including death, MI, or revascularization.
<b>CONCLUSIONS</b>	These data indicate that: 1) the use of FFR in patients with recent UA/NSTEMI markedly reduces the duration and cost of hospitalization compared with SPS; and 2) these benefits are not associated with an increase in procedure time, radiation exposure time, or clinical event rates. (J Am Coll Cardiol 2003;41:1115-21) © 2003 by the American College of Cardiology Foundation

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It is well-documented that the angiographic assessment of an epicardial coronary lesion correlates poorly with its physiologic significance (1). Angiography, with its inherent limitations, may not reliably predict whether a stenosis induces ischemia (2,3). The angiographic assessment of lesions of intermediate severity, defined as a percent diameter stenosis between 40% and 70%, is particularly challenging. Even quantitative coronary angiography, which is

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designed to minimize variability in the interpretation of lesions, cannot reliably predict the physiologic impact of stenoses of intermediate severity (4). Consequently, physicians frequently use angiography in conjunction with stress perfusion scintigraphy (SPS) to facilitate clinical decision.

Fractional flow reserve (FFR) is defined as the ratio of the maximal blood flow achievable in a stenotic vessel to the normal maximal flow in the same vessel. The characteristics of FFR have been described and validated extensively (5,6).

An accurate estimate of FFR can be derived from the ratio of mean distal coronary artery pressure to aortic pressure during maximal coronary hyperemia (7). The normal value of FFR is 1.0; a value of  $< 0.75$  reliably identifies stenoses associated with inducible ischemia (8). A number of studies (7,9) have shown that in patients with normal left ventricular systolic function, the information obtained with FFR was equivalent to that obtained from stress perfusion scintigraphy (SPS). The measurement of FFR is highly reproducible and is independent of changes in hemodynamics or left ventricular contractility (5).

Performing SPS after angiography to determine whether a lesion should be dilated delays the hospital discharge and, therefore, can potentially increase the cost of hospitalization. Because the physiologic assessment of stenosis severity by FFR is now possible in the catheterization laboratory, the use of this index may obviate the need for performing SPS. On the other hand, several studies (10-12) have demonstrated derangements of coronary flow in the infarct and noninfarct zones early after MI, which could confound measurements for days or weeks following the event. Although FFR has been reported to be a valid surrogate for noninvasive testing in patients within six days of myocardial infarction (MI) (13), its utility in patients with unstable angina/non-ST-segment elevation myocardial infarction (UA/NSTEMI) within 48 h of admission is unknown.

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**Abbreviations and Acronyms**

CABG	= coronary artery bypass grafting
FFR	= fractional flow reserve
MI	= myocardial infarction
PCI	= percutaneous coronary intervention
RN	= registered nurse
RT	= radiologic technologist
SPECT	= single-photon emission computed tomography
SPS	= stress perfusion scintigraphy
TCU	= transitional care unit
Tl-201	= thallium
UA/NSTEMI	= unstable angina/non-ST-segment elevation myocardial infarction

Therefore, the present study was undertaken to examine the value of FFR in patients with recent UA/NSTEMI who had a coronary stenosis of intermediate severity (40 to 70%) by visual assessment. The primary objective was to determine whether, in these patients, the use of FFR reduces the duration and cost of hospitalization compared with SPS, without prolonging the procedure time or radiation exposure time. In addition, we sought to determine whether clinical event rates at follow-up were affected by the use of FFR versus SPS.

**METHODS**

**Study population and medical management.** From August 1999 to March 2001, a total of 312 patients were screened with a diagnosis of UA/NSTEMI. Of these, 70 patients (46 men, 24 women) with a mean age of  $57 \pm 4$  years (range 37 to 77 years) who met the inclusion criteria were enrolled. All patients underwent coronary angiography. Patients were enrolled into this study if they had had an episode of angina lasting >20 min or recurrent episodes of angina at rest and had at least one of the following criteria: a new finding of ST-segment depression; transient (<20 min) ST-segment elevation; a new finding of T-wave inversion in at least two leads; elevated levels of cardiac markers; history of MI, including a Q-wave on the electrocardiogram or previous admission with a diagnosis of MI; and evidence of prior coronary artery disease or history of percutaneous coronary intervention (PCI). Patients received 325 mg of aspirin daily, a bolus and continuous intravenous infusion of unfractionated heparin and a glycoprotein IIb/IIIa inhibitor (eptifibatide), or subcutaneous low-molecular-weight heparin for 48 h or until revascularization; glycoprotein IIb/IIIa inhibitor infusion was continued for 12 h after PCI. We enrolled patients in the study who met these criteria, were stabilized on medical therapy  $\geq 48$  h after admission, and were found to have a single coronary lesion of intermediate severity on coronary angiogram. The following were reasons for exclusion from the study: 1) incessant chest pain not responding to medical therapy; 2) left main or multivessel coronary artery disease; 3) prior coronary artery bypass grafting (CABG); and 4) vessels that

**Table 1.** Clinical Features and Lesion Characteristics

	<b>Group 1 (SPS) (n = 35)</b>	<b>Group 2 (FFR) (n = 35)</b>
Age	55 $\pm$ 4	59 $\pm$ 6
Gender M/F	22/13	24/11
EF	53 $\pm$ 4	50 $\pm$ 4
MI without ST-segment elevation (n)	24	20
ST-segment changes (n)	16	14
ST-segment changes or T-wave changes (n)	20	18
Prior coronary artery disease	14	9
Hypertension (n)	26	25
Diabetes mellitus (n)	11	13
Hyperlipidemia (n)	22	19
Tobacco abuse (n)	15	20
Lesion		
Left anterior descending (n)	13	15
Circumflex (n)	10	9
Right coronary artery (n)	12	11
Minimal lumen diameter (mm)	1.51 $\pm$ 0.1	1.43 $\pm$ 0.1
Reference lumen diameter (mm)	3.1 $\pm$ 0.2	2.88 $\pm$ 0.2
% Diameter stenosis	49 $\pm$ 2	48 $\pm$ 2

FFR = fractional flow reserve; EF = ejection fraction; MI = myocardial infarction; SPS = stress perfusion scintigraphy.

were totally occluded or supplying an akinetic territory by visual assessment of the left ventricular angiogram. The protocol was approved by the Institutional Review Board and all patients gave written informed consent.

**Experimental protocol.** All patients underwent coronary angiography from the femoral approach by the use of standard catheters and conventional views. After the coronary angiograms were reviewed, eligible patients who were found to have coronary stenoses of intermediate severity and none of the aftermentioned exclusion criteria were randomly allocated to an SPS or an FFR group. The SPS group consisted of 35 patients (22 men and 13 women, ranging in age from 43 to 73 years; mean age,  $55 \pm 4$  years). The FFR group consisted of 35 patients (24 men and 11 women, ranging in age from 37 to 77 years, mean age  $59 \pm 6$  years) (Table 1). Patients in the SPS group were transferred back to a monitored bed and underwent SPS on the next day. Patients in the FFR group underwent FFR measurement following cardiac catheterization.

**Pressure measurements and calculation of FFR.** In the FFR group, at the conclusion of coronary angiography, the coronary artery was selectively engaged with a 7F guiding catheter and 100  $\mu$ g of nitroglycerin was given intracoronary. A 0.014-inch pressure guide wire (WaveWire, Jomed, Rancho Cordova, California) was set at zero, advanced into the coronary artery, normalized, and then positioned distal to the stenosis to be measured. The aortic pressure and the distal coronary pressure were measured continuously by the guiding catheter and the pressure guide wire, respectively. Fractional flow reserve was calculated as:  $FFR = Pd/Pa$ , where Pd (distal coronary pressure) and Pa (aortic pressure) were recorded simultaneously during maximal coronary hyperemia induced by intracoronary infusion of adenosine

(36 to 42  $\mu\text{g}$  in the left coronary artery and 18 to 24  $\mu\text{g}$  in the right coronary artery), as described previously (14).

Patients in whom FFR was  $\geq 0.75$  did not undergo PCI and were discharged on the same or the next day; if the FFR was  $< 0.75$ , PCI was performed during the same session using the pressure guide wire and FFR was measured again at the completion of the procedure. The selection of 0.75 as the cutoff value of FFR in deciding whether to perform PCI was based on the results of previous studies (9,13).

**Stress testing and thallium (Tl-201) or Tc-99m sestamibi scintigraphy.** One day following cardiac catheterization, patients in the SPS group underwent either adenosine ( $n = 21$ ) or treadmill ( $n = 14$ ) stress testing. Patients who were unable to exercise on a treadmill were tested using intravenous adenosine, which was infused at a rate of 0.14 mg/kg/min for a total duration of 6 min. Tc-99m sestamibi (Cardiolite, Bristol-Myers Inc., New York, New York) was injected at 3 min into the adenosine infusion. Treadmill stress testing was performed by using the Bruce protocol and patients were required to reach 85% of their target heart rate; if they were not able to exercise to the target heart rate, adenosine stress testing was performed. Tc-99m sestamibi was injected at least 30 to 60 s before the end of the exercise.

Resting imaging was performed with either Tl-201 or Tc-99m sestamibi. Patients who weighed  $< 200$  lbs received a 4-mCi dose of intravenous Tl-201 and underwent stress testing, whereas those who weighed  $> 200$  lbs received a 30-mCi dose of intravenous Tc-99m sestamibi and underwent stress testing the next morning. The rest and stress Tc-99m sestamibi single-photon emission computed tomography (SPECT) images and Tl-201 SPECT images were acquired 6 to 90 min and 30 to 40 min, respectively, after the administration of the radiopharmaceutical. The images were analyzed qualitatively by two reviewers who were blind to the study data.

**Cost analysis.** The total cost of the procedure related to cardiac catheterization and FFR measurement consisted of the cost incurred in the catheterization laboratory and that incurred with postprocedural care (TCU [transitional care unit]) until discharge from the hospital as reported previously (15). In the cath lab, the cost categories, which were analyzed by accounting for resources utilized, included equipment (pressure guide wire, guiding catheter, and Tuohy steering kit), supply (contrast media), registered nurse (RN), and radiologic technologist (RT) (total time spent per patient multiplied by the hourly wages and fringe benefits). The cost of each item was determined by using actual manufacturer's charge to the hospital during the financial year 2000. Costs in the TCU included the cost of RN, pertinent laboratory tests, SPS, and room (calculated on hourly basis until the time of hospital discharge).

**Quantitative coronary angiography.** Quantitative coronary angiography was performed using the contrast-filled distal guiding catheter for calibration. The angiographic projection with the most severe diameter narrowing without foreshortening was used for analysis of stenosis severity.

**Table 2.** Procedural and Postprocedural Characteristics

	Group 1 (SPS) (n = 35)	Group 2 (FFR) (n = 35)	p Value
Procedure time (min)	36 $\pm$ 2	47 $\pm$ 3	NS
Radiation exposure time (min)	7 $\pm$ 1	9 $\pm$ 1	NS
Amount of contrast media used (ml)	167 $\pm$ 8	182 $\pm$ 12	NS
Duration of hospitalization (h)	49 $\pm$ 5	11 $\pm$ 2	$< 0.001$
Post-procedural time in the cath lab (min)	75 $\pm$ 7	162 $\pm$ 25	$< 0.01$

Abbreviations as in Table 1.

Minimal lumen diameter, reference lumen diameter, and percent diameter stenosis were determined using validated, commercially available edge detection software (QCA-CMS 3.0 system, CMS-MEDIS, Nuenen, the Netherlands) (16).

**Follow-up and clinical events.** Investigators contacted patients and examined the medical records of those having events. Clinical events were defined as death, MI, CABG, PCI, and readmission because of UA. Myocardial infarction was diagnosed when two of these three criteria were met: prolonged ( $> 30$  min) chest pain, creatine kinase-MB fraction and troponin I elevation above the normal limit, or development of new Q waves.

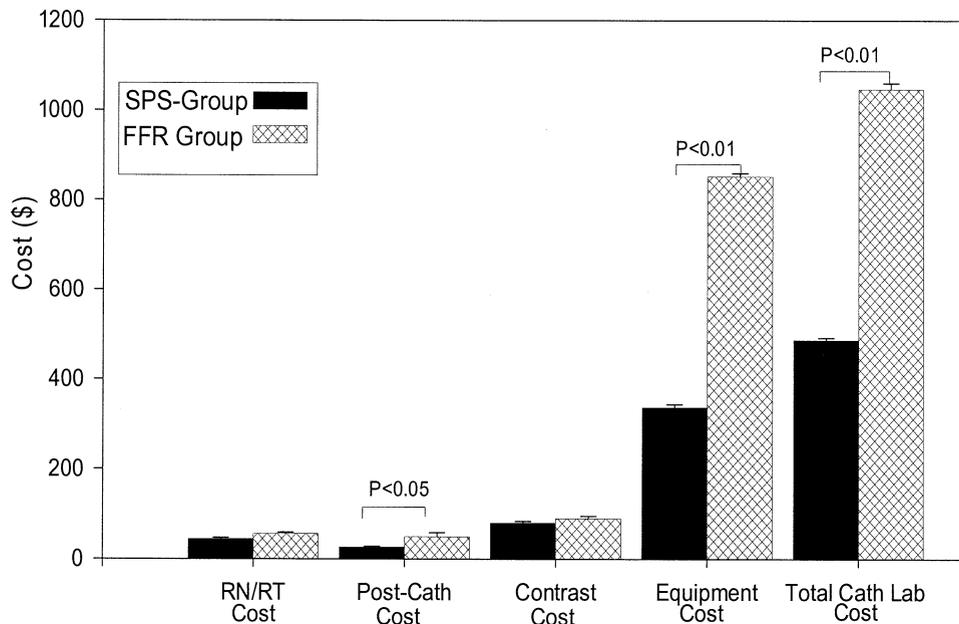
**Statistical analysis.** Continuous variables are reported as mean  $\pm$  SEM. All continuous variables were compared by unpaired Student *t* tests and categorical variables by chi-square tests. Probability values  $< 0.05$  were considered significant.

## RESULTS

**Clinical characteristics.** A total of 35 patients in the SPS group and 35 in the FFR group met the criteria detailed under Methods. Fractional flow reserve was successfully performed in all 35 patients. The clinical features and angiographic characteristics of the SPS and FFR groups are outlined in Table 1. There were no differences between the groups with regard to age, gender, incidence of MI, incidence of ST-segment changes or T-wave changes, evidence of prior coronary artery disease, and major risk factors for cardiovascular disease. Likewise, there were no differences between the groups with respect to the vessel involved, ejection fraction, and the angiographic severity of stenosis.

**Procedural characteristics.** In the SPS group, 14 patients had reversible ischemia on Tl-201 or Tc-99m sestamibi imaging; of these 14 patients, 10 underwent PCI whereas four patients were continued on medical treatment and discharged at the discretion of the attending cardiologist. In the FFR group, 13 patients had an FFR  $< 0.75$  and underwent PCI in the same setting.

The procedure time, radiation exposure time, and amount of contrast media used were not statistically different between the two groups (Table 2). The duration of hospitalization, however, was markedly shorter in the FFR group than in the SPS group (11  $\pm$  2 h vs. 49  $\pm$  5 h,  $-77\%$ ,



**Figure 1.** Costs incurred in the cath lab in patients who were randomized to stress perfusion scintigraphy (SPS) vs. fractional flow reserve (FFR). The itemized costs include: registered nurse (RN)/radiologic technologist (RT) cost, post-cath cost (the time that RN and RT spent per patient during and after cardiac catheterization multiplied by the hourly wages), contrast cost (the cost of contrast media used during the catheterization), and equipment cost (the costs of the WaveWire, guiding catheter, and Tuohy steering kit). Values are means  $\pm$  SEM.

respectively;  $p < 0.001$ ). In the FFR group, nine patients in whom FFR was  $>0.75$  and in whom MI was ruled out were directly discharged home from the recovery room after a period of observation; consequently, the post-catheterization recovery time increased from  $75 \pm 7$  min in the SPS group to  $162 \pm 25$  min in the FFR group ( $p < 0.01$ ).

**Cost of the procedure.** In the FFR group, the use of pressure guide wire and other equipment in the cath lab increased the cost of equipment from  $\$337 \pm \$7$  in the SPS group to  $\$852 \pm \$7$  ( $p < 0.01$ ) (Fig. 1). In addition, prolongation of post-catheterization recovery time in this group increased the cost of RN from  $\$34 \pm \$3$  in the SPS group to  $\$56 \pm \$3$  in the FFR group ( $p < 0.05$ ) (Fig. 1). Because the procedure time and amount of contrast media used during cardiac catheterization did not differ significantly between the two groups, the cost of RN/RT and contrast media also did not differ between the groups (Fig. 1).

In the SPS group, performing SPS prolonged the duration of hospitalization and increased the cost of occupying a TCU bed from  $\$202 \pm \$36$  in the FFR group to  $\$941 \pm \$92$  ( $p < 0.01$ ) (Fig. 2). In line with this, the costs of the RN in the TCU ( $\$235 \pm \$22$  vs.  $\$52 \pm \$9$ ) and of diagnostic laboratory tests including SPS ( $\$450 \pm \$9$  vs.  $\$28 \pm \$7$ ) were significantly greater in the SPS group than in the FFR group (Fig. 2).

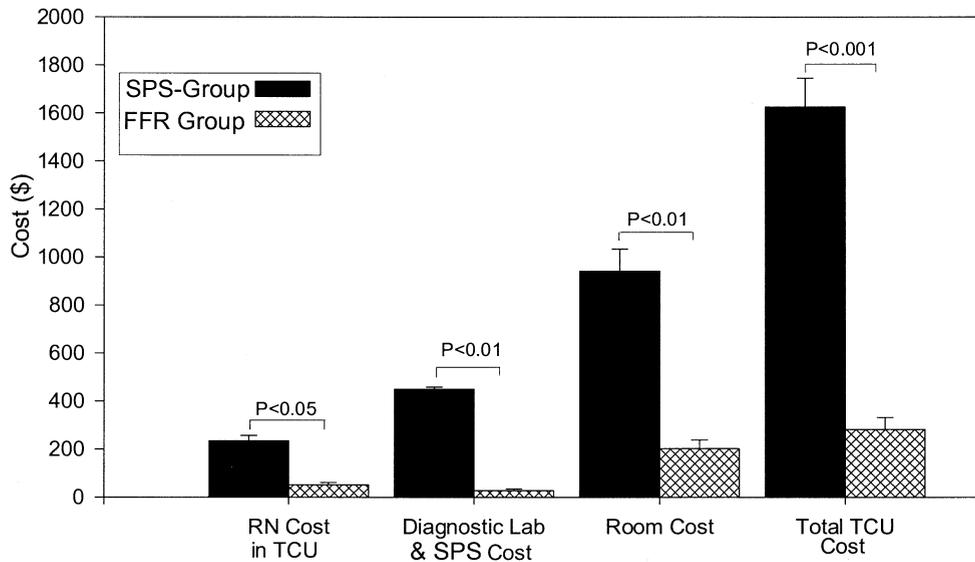
The costs incurred in the cath lab were significantly greater in the FFR group than in the SPS group ( $\$1,047 \pm \$13$  vs.  $\$487 \pm \$5$ , respectively;  $p < 0.01$ ) (Fig. 3). In contrast, the costs incurred in the TCU were significantly greater in the SPS group than in the FFR group ( $\$1,626 \pm$

$\$120$  vs.  $\$282 \pm \$50$ , respectively;  $p < 0.001$ ) (Fig. 3). The total cost (costs of cath lab plus TCU) was significantly increased from  $\$1,329 \pm \$44$  in the FFR group to  $\$2,113 \pm \$120$  in the SPS group ( $p < 0.05$ ) (Fig. 3).

**Procedural safety and follow-up.** There were no complications related to cardiac catheterization or FFR measurement. Complete follow-up was available in 34 patients in the SPS group and 34 patients in the FFR group (Table 3). The average follow-up was  $12.0 \pm 0.8$  months in the SPS group and  $14.0 \pm 1.0$  months in the FFR group. During the follow-up period, no death occurred in either group and there were no differences between the SPS and FFR groups with respect to the angina class (Canadian Cardiovascular Society classification [17]), MI, or CABG (Table 3). Six patients in the SPS group and five patients in the FFR group were admitted to the hospital with a diagnosis of unstable angina and ruled out for MI; the characteristics of these patients are shown in Table 3. In addition, two patients (one from each group) were admitted with a diagnosis of acute non-Q-wave MI; cardiac catheterization revealed disease progression in the other coronaries and they underwent CABG.

## DISCUSSION

The present study demonstrates that in a subset of patients with recent UA/NSTEMI who have an intermediate coronary stenosis and single-vessel disease, measurements of FFR can be safely performed in the same setting as coronary angiography and that this approach shortens the duration of hospitalization significantly (by 77%) compared with SPS, resulting in a decrease in the costs of hospital admission.

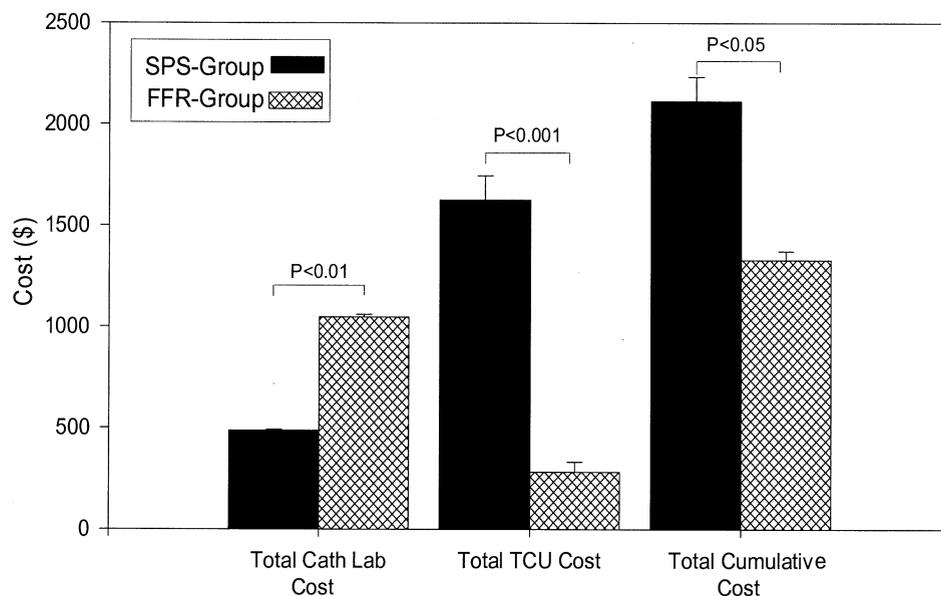


**Figure 2.** Costs incurred in the transitional care unit (TCU) in patients who were randomized to stress perfusion scintigraphy (SPS) vs. fractional flow reserve (FFR). The itemized costs include registered nurse (RN) cost in the TCU (the time that RN spent per patient multiplied by the hourly wages), diagnostic lab and SPS costs (the costs of laboratory tests and stress perfusion scintigraphy), and room cost (the cost of dwelling in the monitored bed). Values are means  $\pm$  SEM.

Measuring FFR was not associated with a significant increase in procedure time, radiation exposure time, or amount of contrast media used during the procedure. Furthermore, there were no differences with respect to event rates in patients in whom PCI was deferred, because the FFR was  $\geq 0.75$  compared with those in whom it was deferred because the SPS was negative for ischemia. Although the use of the pressure guide wire increased the costs incurred in the cath lab in the FFR group compared with the SPS group, a significant reduction in the duration of hospitalization in the FFR group offset the cost of the pressure guide wire and thereby reduced the total cost.

Taken together, the present data suggest that in a select population of patients with UA/NSTEMI who have an intermediate coronary artery stenosis and single-vessel disease, the FFR can be used as a surrogate for noninvasive testing, resulting in shorter duration of hospitalization and reduced total cost. Previous studies have examined the validity of an FFR  $\geq 0.75$  measured  $>6$  days after an MI (13) or stable angina (6); however, to our knowledge, this is the first report to document the usefulness of FFR measured within 48 h after a UA/NSTEMI.

Validation studies of FFR measurements have demonstrated a good agreement with the results of SPS, both in



**Figure 3.** Total cost incurred in the cath lab, total cost incurred in the transitional care unit (TCU), and total cumulative cost from the time of cardiac catheterization to discharge in patients who were randomized to stress perfusion scintigraphy (SPS) vs. fractional flow reserve (FFR). Values are means  $\pm$  SEM.

**Table 3.** Follow-Up and Clinical Events

	Group 1 (SPS) (n = 34)	Group 2 (FFR) (n = 34)
Average follow-up (months)	12.0 ± 0.8	14.0 ± 1.0
Death	0	0
Angina		
No angina (n)	17	24
CCS classification of angina (n)		
1-2	17	10
3-4 (admitted to the hospital)	6	5
Stress perfusion scintigraphy	4	4
Negative (n)	4	4
Cardiac catheterization	2	3
Results (no change)	2	2
Disease progression	0	1
MI	1	1
CABG including target vessel	1	2
PCI	0	0

CABG = coronary artery bypass graft; CCS = Canadian Cardiovascular Society; PCI = percutaneous coronary intervention. Other abbreviations as in Table 1.

intermediately or severely stenosed coronary arteries (7). In partially infarcted regions, de Bruyne et al. (13) have reported that a threshold value of FFR  $\geq 0.75$  measured >6 days after MI can still distinguish patients with a positive from those with a negative SPS, and that FFR does not underestimate the severity of the stenosis. Likewise, Takeuchi et al. (18) reported that after PCI, the FFR improved to the same extent in vessels supplying the infarcted territories compared with those supplying noninfarcted regions. In the present study, 57% of patients had a non-Q-wave MI, and on the basis of these observations (13,18) were not excluded from the study.

Bech et al. (19) demonstrated that deferral of PCI in patients with a coronary lesion that was angiographically intermediate but functionally nonsignificant, as assessed by FFR, was associated with a much lower clinical event rate than if the patients had undergone PCI as initially planned. This group (20) also reported that in patients with stable angina who had a coronary stenosis and an FFR  $>0.75$ , event-free survival and freedom from angina at 24 months follow-up were similar irrespective of the performance or deferral of PCI. These data are conceptually congruent with the present study, in which we found that the deferral of PCI in patients with recent UA/NSTEMI and an FFR  $\geq 0.75$  was associated with outcomes similar to those observed in patients that underwent SPS and in whom PCI was deferred.

**Study limitations.** The present study was performed in a select subset of patients (22% of patients admitted with UA/NSTEMI) who were medically stabilized, had single-vessel disease, and had an intermediate coronary stenosis. Our findings cannot be extrapolated to the patients with UA/NSTEMI who have multivessel disease. These stringent inclusion criteria enhanced the power of this study, which was conducted in a relatively small group of patients. It could be argued that the study design introduced an

intrinsic bias by stipulating that the SPS be performed the day after catheterization, thereby increasing the duration of hospitalization and the attendant costs. However, in most cases it would be impossible to perform coronary angiography and SPS on the same day. As described in the Methods section, intravenous infusion of unfractionated heparin and glycoprotein IIb/IIIa inhibitors was continued during cardiac catheterization. Subcutaneous low-molecular-weight heparin was also administered on the day of cardiac catheterization. All antithrombin and antiplatelet agents were discontinued after catheterization in patients randomized to SPS. In patients who were receiving intravenous infusion of unfractionated heparin and glycoprotein IIb/IIIa inhibitors, an interval of 3 to 4 h was typically necessary for the activated clotting time levels to return to  $<170$  s and to remove the introducer sheath. In patients who were receiving low-molecular-weight heparin, the introducer sheath was removed 4 to 6 h after cardiac catheterization. Following sheath removal, the patients were kept at bed rest for 4 to 6 h to assure complete hemostasis; shortening this time in order to perform a stress test would have been unsafe. Furthermore, an exercise stress test could not have been performed on the same day as the cardiac catheterization. These considerations, coupled with the fact that approximately 3 h were required to complete both the rest and the stress images during adenosine stressing, indicate that in most patients the invasive and noninvasive studies could not be performed on the same day.

It could be argued that in the SPS group, if the patients had been discharged a day after catheterization and undergone outpatient SPS, the total cost would not have been significantly different from that of the FFR group. However, the discharge of such patients without SPS and revascularization could have imposed a safety concern because, thus far, no study supports the safety of discharging patients with UA/NSTEMI who meet the intermediate or high-risk criteria without SPS or revascularization.

The use of a single stress modality would have been more consistent. We used two different stress modalities (exercise or adenosine) in order to accommodate all patients. That is, we scheduled exercise stress to test the functional capacity of the patients and adenosine stress to evaluate those patients who were unable to exercise to 85% of their target heart rate. Adenosine stress does not produce true "ischemia." Nevertheless, the usefulness of adenosine in predicting early and late cardiac events is supported by published studies, such as that by Brown et al. (21), who used dipyridamole two to four days after uncomplicated MI. Our adenosine myocardial perfusion imaging was comparable to their study.

**Clinical implications and conclusions.** Until recently, there was continued controversy as to whether a routine, early invasive strategy was superior to a conservative strategy for the management of UA/NSTEMI. Two recent large trials (22,23) reported that among patients with UA/NSTEMI treated with glycoprotein IIb/IIIa inhibitors or low-molecular-weight heparin, an early invasive strategy

was superior to a conservative strategy in reducing the incidence of major cardiac event rates. In addition, the 2000 guidelines of the American College of Cardiology/American Heart Association (24) recommend that patients >65 years old or patients with ST-segment depression or elevated cardiac markers undergo an early invasive strategy. Performing PCI in a lesion of intermediate severity without evidence of inducible ischemia not only exposes the patient to the risk of the procedure and to restenosis, but also increases the cost of hospitalization dramatically. On the other hand, if a decision is made to perform SPS to determine the physiologic significance of a lesion, prolongation of hospitalization to perform the test increases the duration of hospital stay and thus the total cost of the admission.

The optimal timing for measuring FFR after an acute ischemic event is unknown. In addition, the presence of an intermediate lesion on the coronary angiogram represents a challenge regarding a decision for revascularization. In a recent study (13) a good correlation was found between an FFR  $\geq 0.75$  and SPS performed >6 days after an episode of MI; however, assessing the functional significance of a lesion by FFR >6 days of an MI is not cost-effective. In the present study, FFR was measured within 48 h after admission with UA/NSTEMI when most patients undergo catheterization and PCI was performed at the same setting.

In conclusion, our data demonstrate that in patients with recent UA, single vessel disease and intermediate coronary stenosis, a decision-making strategy predicated upon the use of FFR appears to be superior to one based on SPS. Consequently, we suggest that the most logical approach for managing lesions of intermediate severity in patients with recent UA is to measure FFR in the same session where coronary angiography is performed and proceed with PCI if FFR is  $< 0.75$ , which markedly reduces the duration and cost of hospitalization with no increase in procedure time, radiation exposure time, or amount of contrast media used. The validity of this paradigm needs to be corroborated in a larger, multicenter, prospective, randomized trial.

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