

The Economic Consequences of Available Diagnostic and Prognostic Strategies for The Evaluation of Stable Angina Patients: An Observational Assessment of the Value of Precatheterization Ischemia

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- OBJECTIVES** The study aim was to determine observational differences in costs of care by the coronary disease diagnostic test modality.
- BACKGROUND** A number of diagnostic strategies are available with few data to compare the cost implications of the initial test choice.
- METHODS** We prospectively enrolled 11,372 consecutive stable angina patients who were referred for stress myocardial perfusion tomography or cardiac catheterization. Stress imaging patients were matched by their pretest clinical risk of coronary disease to a series of patients referred to cardiac catheterization. Composite 3-year costs of care were compared for two patients management strategies: 1) direct cardiac catheterization (aggressive) and 2) initial stress myocardial perfusion tomography and selective catheterization of high risk patients (conservative). Analysis of variance techniques were used to compare costs, adjusting for treatment propensity and pretest risk.
- RESULTS** Observational comparisons of aggressive as compared with conservative testing strategies reveal that costs of care were higher for direct cardiac catheterization in all clinical risk subsets (range: \$2,878 to \$4,579), as compared with stress myocardial perfusion imaging plus selective catheterization (range: \$2,387 to \$3,010, $p < 0.0001$). Coronary revascularization rates were higher for low, intermediate and high risk direct catheterization patients as compared with the initial stress perfusion imaging cohort (13% to 50%, $p < 0.0001$); cardiac death or myocardial infarction rates were similar ($p > 0.20$).
- CONCLUSIONS** Observational assessments reveal that stable chest pain patients who undergo a more aggressive diagnostic strategy have higher diagnostic costs and greater rates of intervention and follow-up costs. Cost differences may reflect a diminished necessity for resource consumption for patients with normal test results. (J Am Coll Cardiol 1999;33:661-9) © 1999 by the American College of Cardiology

Medicine has long been afforded the luxury of developing basic and applied research techniques in the hope of identifying and providing treatment for all afflicted patients.

A balance between cost and increased efficacy has only recently been considered. Cost-efficiency techniques have been proposed as a method for integrating the economic and efficacy measures into one ratio that may be used by society as a standard for use of any given therapy or technology. The importance of cost-efficiency in diagnosis stems not only from the initial diagnostic cost but also in the extent to which the initial choice of testing drives subsequent resource use. Cost-efficiency of screening is related to subsequent treatment efficacy (1). Efficiency also depends upon the test's ability to classify those with and without the disease, and the initial cost of the test, as well as the direct health benefits and resource use resulting from the testing procedure (1).

For patients undergoing cardiac catheterization, important diagnostic and prognostic information is in part a result

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Manuscript received October 14, 1997; revised manuscript received September 28, 1998, accepted November 5, 1998.

of information obtained at the time of angiography. However, a major benefit of stress tomographic myocardial perfusion imaging, in terms of cost-efficient resource use, is derived from a selective use of subsequent cardiac catheterization. The cost of selecting a direct catheterization approach, as compared to a selective catheterization approach, in patients with evidence of provocative ischemia or those at high pretest risk is unknown. It is the purpose of this report to compare two observational series of patients who underwent varying initial diagnostic testing strategies and to compare resource use consumption between these two cohorts of symptomatic patients. The goal of this strategy is to develop insight into actual practice patterns and derive insight into the development of a prospective diagnostic management algorithm for similarly at-risk patients.

METHODS

Patient selection. Two patient cohorts were enrolled into a registry of stable angina pectoris patients including 1) 5,423 patients undergoing initial direct diagnostic cardiac catheterization and 2) 5,826 patients undergoing stress myocardial perfusion imaging. The patient cohort undergoing stress perfusion imaging was matched to an initial diagnostic catheterization cohort by their pretest risk of coronary artery disease (2-4). The pretest probability of coronary disease was defined using the probability of disease from 12 variables (2-4). The resulting diagnostic catheterization cohort is a lower clinical risk cohort than previously reported in the literature, representing a subset of all catheterized patients (5). The methods for patient matching has been previously described in prior series (5). Registry enrollment was limited to patients with typical cardiac symptoms referred for initial noninvasive or invasive diagnostic evaluation enrolled from seven hospitals (Cedars-Sinai Medical Center, Cleveland Clinic Foundation, Duke University Medical Center, Hartford Hospital, Roger Williams Medical Center, St. Louis VA Medical Center and St. Louis University Health Sciences Center). Patients undergoing a pre-discharge evaluation or those recently hospitalized for unstable angina, myocardial infarction or coronary revascularization were excluded.

Stress testing protocol. For the stress perfusion imaging cohort, patients underwent symptom-limited exercise testing using the standard Bruce protocol. Resting heart rate, blood pressure and 12-lead electrocardiograms were recorded during preexercise, exercise and recovery time periods. Exercise testing was discontinued if exertional hypotension, life-threatening ventricular arrhythmias, marked ST depression (≥ 3 mm) or limiting chest pain was reported. An abnormal exercise ST response was defined as ≥ 1 mm of horizontal or downsloping ST depression (at 80 ms).

Myocardial perfusion tomography. Single-photon emission computed tomographic imaging was performed using previously described protocols (6-8). All patients gave

informed consent. Tomographic perfusion scans were performed using a same-day or two-day imaging protocol. For technetium-99m sestamibi imaging (83% of patients), on average 8 mCi was injected at rest, and 22 mCi was injected at near peak exercise. For thallium-201 imaging, on average 3 mCi was injected. Single-photon emission computed tomography acquisition was performed at rest and after peak exercise using a gamma camera with a computer interface. Imaging was performed over a 180° semicircular orbit. Data were acquired in a 64 × 64 matrix for 64 projections for Tc-99m sestamibi and 32 projections for Tl-201 in a step and shoot format. Image processing was done using a ramp back-projection filter. All image sets (horizontal and vertical long-axis and short-axis planes) were normalized to the maximal myocardial activity in that set.

Standard procedures for image interpretation included review of all scans by ≥ 2 experienced observers who were blinded to clinical history and physical examination data. Final segmental image interpretation was achieved by consensus. Stress images were compared with the rest images. Defects that were present at rest and remained unchanged during stress were considered as fixed defects. The appearance of new or worsening defects after stress were considered to be defect reversibility. The segmental scoring system used for this analysis included documentation of infarct (i.e., fixed defects) or ischemia (i.e., reversible defects) in the left anterior descending, right coronary artery and circumflex vascular territories. Perfusion defect extent was coded as none, and one, two and three vascular territory involvement.

Follow-up. All patients were prospectively followed for an average of 2.5 ± 1.5 years for the date and occurrence of cardiac death as a primary end point. Secondary events including the occurrence of coronary revascularization procedures and cardiac hospitalizations (e.g., myocardial infarction) were also recorded. Follow-up information was obtained by clinic visit or telephone interview yearly. The cause of death was classified as cardiac versus noncardiac by an independent reviewer who was unaware of the patient's clinical history, stress imaging or cardiac catheterization result.

End points. Prognostic outcomes included cardiac survival, myocardial infarction and admission for unstable angina. The economic outcomes included total cost = diagnostic cost (including all noninvasive and invasive testing) + follow-up cost (including cardiac hospitalizations through three years). The economic perspective used in this analysis acquired "big ticket" cost items and compared diagnostic and 3-year costs of care by patient management strategy (9-12). We included a second model that provided insight into estimated costs for annual medical therapy.

Statistical analyses. Methods used for this analysis have been described previously (9,10). Descriptive statistics were generated using percentages for discrete variables and means and standard deviations for continuous variables. All con-

tinuous variables were compared by outcome rates by analysis of variance techniques. Categorical variables were compared by chi-square analyses. A Cox proportional hazard regression analysis was used for comparison of the prognostic outcomes. To control for selection bias in the referral process, a propensity score was developed that includes independent predictors of cardiac catheterization (5). The independent predictors of cardiac catheterization were defined by developing a multivariable logistic regression model estimating the use of angiography as a dichotomous outcome. Independent predictors included the presence of anginal symptoms, gender, and prior myocardial infarction. The Cox proportional hazard model included the assessment of clinical history and demonstrable evidence of ischemic heart disease (as determined by the varying testing strategies) in standard, risk-adjusted methodologies. Clinical risk-adjusted models were completed using the clinical index as developed by Pryor and colleagues, as listed below (2). Diagnostic and follow-up costs of care through 3 years of follow-up were compared by means of analysis of variance techniques. A general linear model, simple factorial analysis of variance with adjustment of covariates was used that included the pretest clinical risk probability value and the propensity score. Post hoc comparisons were made, with a Bonferroni procedure, for variables with more than two levels. We also compared the percentage of high and low cost patients by testing strategies using Kaplan–Meier curve comparisons.

Pretest clinical risk estimates. The clinical index, derived from clinical history and physical examination data, was previously described by Pryor et al. (2). To derive an estimate of pretest risk, the estimated risk from a Cox proportional hazards model was calculated to predict cardiac death using the 12 clinical history and physical examination parameters (2).

$$\begin{aligned} \text{Clinical Index} &= 0.4506 \cdot (\text{Congestive Heart Failure}) \\ &+ 0.08975 \cdot (\text{Electrocardiographic Conduction Abnormalities}) \\ &+ 0.0226 \cdot (\text{Age in Years}) - 0.6732 \cdot (\text{Gender: Male} \\ &= 0, \text{Female} = 1) + 0.2952 \cdot (\text{Typical Angina}) - 1.833. \end{aligned}$$

The model development process included the development of several predictive models estimating a patient's likelihood of coronary disease. A number of validation sets in diverse community-based samples have tested and extended the use of these models to a more generalizable cohort of patients with symptoms suggestive of coronary disease (including typical, atypical and nonanginal chest pain). For our analysis, the pretest risk index was calculated based upon the cardiac survival model of Pryor et al. (2). The original weights from the Pryor model were tested to assess their fit in the current series. This assessment included consideration of reweighting the index to our patient population. This was done for the entire patient series as well as individually for the perfusion imaging and catheterization patient series. Several results from this process

included: a) weights for the regression equation derived from the Pryor model were similar to the current patient series; b) calculated risk by the clinical index was linearly related to the rate of cardiac death (similar results as in the developmental set), and c) we compared the original clinical risk to several possible revised scores for the index by the concordance index for a Cox model estimating cardiac death (Cox indices similarly ranged from 0.71 to 0.76). We finally added a dummy variable of the type of initial test entered as an interaction with the clinical risk index to a univariable Cox model with the result being a nonsignificant interaction effect estimating cardiac mortality. From these analyses, the clinical risk index developed by Pryor et al. was a significant estimator of cardiac mortality whose risk estimation appeared similar by patient management strategy.

Patient management strategies. Based upon the matched pretest probability estimates, patients were categorized into low (pretest probability of $\leq 15\%$), intermediate (pretest probability 16% to 59%) and high (pretest probability $\geq 60\%$) risk. Other pretest risk strata were considered (i.e., high risk $\geq 75\%$), however, the above-listed groupings afforded a larger proportion of high risk subsets for comparison. A comparison of the results of varying pretest risk threshold produced similar outcome results.

We compared cost between two strategies: 1) use of direct catheterization to 2) initial stress myocardial perfusion imaging followed by selective catheterization in patients who were clinically high risk and those with evidence of ischemia on initial noninvasive imaging techniques. Non-random assignment to treatment after diagnostic testing was adjusted for by using the previously reported propensity score (5). The propensity score attempts to control for the effects of baseline imbalances that may account for differential treatment selection. This model will allow for varying underlying hazard functions. Subsequent Cox proportional hazards models included stratification by treatment. The propensity score, included in the Cox model, was developed from a logistic regression model that calculates a linear score from estimators of and comparisons of varying treatments. The developmental reports by Mark et al. (5) compared outcome of patients receiving angioplasty as compared with coronary bypass surgery with diverse underlying risk patterns and outcomes. During the analytical phase of our analysis, risk profiles between the two patient management strategies were statistically similar.

Cost analysis. The methods for obtaining cost data have been those developed by Mark and colleagues (9–12) and revised for use in noninvasive testing populations (9,10). Several sources were used for cost estimates: 1) direct cost estimates from a microcost accounting system and 2) Medicare hospital charge (adjusted by cost–charge ratio) including physician billing data (9–12). Cost data from both the top-down and bottom-up microcost accounting systems were averaged for use in all clinical decision making models. Hospital charges were obtained from the

hospital-specific Medicare cost report and per diems from each participating hospital. For physician service costs, we used the Medicare Fee Schedule that provides a standardized resource-based approach for cost of these services (9-12). All costs were expressed in 1995 U.S. dollars. Total costs were calculated by summing the costs of all noninvasive tests, catheterization and cardiac hospitalizations. The cost of outpatient medical therapy was not available for this analysis. There was a standard discount rate of 3% for this analysis.

The primary analysis was that of cost minimization due to the similar risk profiles between the two patient management strategies. We compared observational resource use and cost between two strategies: 1) use of direct catheterization to 2) initial stress myocardial perfusion imaging followed by selective catheterization in patients who were clinically high risk and those with evidence of ischemia on initial noninvasive imaging techniques.

Sensitivity analysis. Sensitivity analyses were performed to assess uncertainties and bias that may have arisen within the modeling assumptions. This involved varying assumptions, based upon expert judgment, and then repeating calculations over a range of values. The results of the sensitivity analyses allowed us to determine to what degree the final results were dependent upon a given assumption. We varied the diagnostic and in-hospital costs by 50% to examine how varying costs may change the results of our analysis. The results of the sensitivity analysis were similar to those presented here, and are not detailed in the Results section. Several additional analyses were included that evaluated estimated medical therapy costs as well as varying costs by the extent of perfusion abnormalities.

To more clearly define expected cost savings in the nuclear imaging patients, a multivariate linear regression model was used to estimate costs including pretest clinical risk as well as cardiac outcomes. Predicted costs were derived from this risk-adjusted cost model and then compared with observed costs in the study. Differences between the observed and predicted costs were considered significant based upon a comparison using a paired *t* statistic.

RESULTS

Clinical and noninvasive testing characteristics. Due to the fact that the two patient cohorts were matched by pretest clinical risk, most of the clinical characteristics were similar (Table 1). However, the stress perfusion imaging patients were older (*p* < 0.05).

The stress tomographic imaging results are summarized in Table 2. Most patients underwent exercise testing with an average exercise duration of 6 min. Nearly one quarter of patients had exertional chest pain or electrocardiographic ST segment depression ≥1.0 mm. A lower frequency of patients undergoing pharmacologic stress imaging had stress-induced chest pain or ST segment depression

Table 1. Clinical Characteristics of the Two Study Cohorts Undergoing Initial Direct Cardiac Catheterization and Stress Perfusion Imaging Plus Selective Catheterization

	Stress Perfusion Imaging (n = 5,826)	Cardiac Catheterization (n = 5,423)
Age (yr)	64 ± 12	62 ± 12*
Female gender	36%	38%
Diabetes	19%	20%
Hypertension	52%	52%
Congestive heart failure symptoms	6%	7%
Pretest clinical risk		
Low risk	14%	15%
Intermediate risk	58%	54%
High risk	28%	31%
Outcome status		
Cardiac death	2.8%	3.3%
Myocardial infarction	2.8%	3.0%

**p* < 0.05.

≥1.0 mm. The presence of three or more fixed perfusion defects occurred in only 7% of patients, and the presence of three or more reversible defects occurred in 19% of patients.

Outcome status and resource use. The cardiac death and myocardial infarction rates at 3 years were similar for initial stress perfusion imaging and direct cardiac catheterization patients (*p* > 0.20) (Table 1 and Fig. 1). The rate of cardiac death or myocardial infarction was 2.5, 5 and 9% for clinically low, intermediate and high risk catheterization patients; similar outcome rates were reported for those patients undergoing initial stress perfusion imaging between risk groups (*p* < 0.00001). Figure 1 depicts the rate of coronary revascularization and adverse outcomes for the two patient management strategies subclassified by initial pretest clinical risk strata. The rate of reversible perfusion defects is

Table 2. Stress Myocardial Perfusion Tomography Results

	Stress Myocardial Perfusion Imaging (n = 5,826)
Exercising patients (n = 4,901)	
Exercise duration (min)	6 ± 4
Exertional chest pain	23%
ST depression ≥1.0 mm	23%
Pharmacologic stress imaging (n = 925)	
Stress-induced chest pain	20%
ST depression ≥1.0 mm	12%
Tomographic results	
≥1 fixed defect	44%
≥3 fixed defect	7%
≥1 reversible defect	35%
≥3 reversible defect	19%

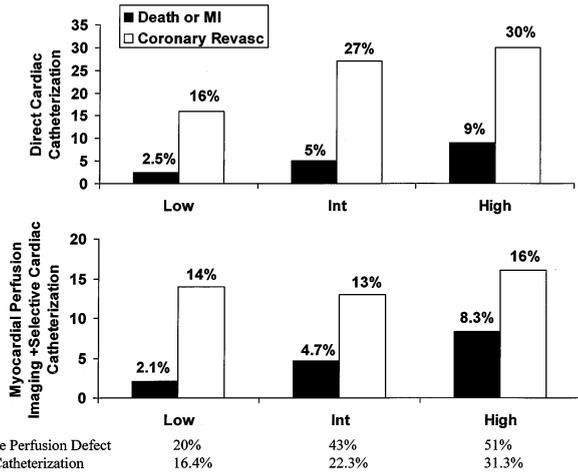


Figure 1. Rates of cardiac death or myocardial infarction (MI) and coronary revascularization (Revasc) by pretest clinical risk subsets of low, intermediate (Int) and high risk patients. The rates of ≥ 1 reversible perfusion defect and cardiac catheterization rates for patients undergoing a noninvasive diagnostic strategy are presented for low, Int, and high risk patients.

also reported and ranged from 20% to 51% for clinically low to high risk patients ($p < 0.0001$).

For patients undergoing initial diagnostic catheterization, the rate of subsequent coronary revascularization was 16% for clinically low risk patients, 27% for intermediate risk patients and 30% for high risk patients. The cardiac catheterization rate for patients who initially underwent stress perfusion imaging was 34% of the 5,826. Of the stress perfusion imaging cohort, 90.4% were referred to subsequent cardiac catheterization as a result of demonstrable perfusion abnormalities, whereas the remaining 9.6% were referred on the basis of high pretest risk. Of the patients who initially underwent stress myocardial perfusion imaging and selective cardiac catheterization, the rate of coronary

revascularization was 14%, 13% and 16% for clinically low, intermediate and high risk patients (compared to catheterization cohort $p = 0.0001$). Of this group of patients who underwent cardiac catheterization after stress perfusion imaging, the rate of coronary revascularization was 86%, 58% and 51% for low, intermediate and high risk patients ($p < 0.00001$).

Comparative diagnostic yield. For patients proceeding directly to catheterization, the rate of patients without a significant coronary artery disease ($\geq 70\%$ stenosis) was 43% as compared to 33% for the 1,981 patients with imaging evidence of inducible myocardial ischemia or high pretest risk ($p < 0.00001$) (Fig. 2). By comparison, the rate of multivessel coronary disease was 34% for those undergoing direct cardiac catheterization and 42% for those undergoing initial stress perfusion imaging ($p < 0.0001$).

Comparative diagnostic and follow-up costs. Figure 3 depicts the varying 2-year cost distribution for medical care among the 5,826 patients undergoing initial stress myocardial perfusion imaging. The majority of costs for 2.5-year care ranged from 2 to 10 thousand dollars. However, overall costs of care were substantially higher for patients with evidence of myocardial perfusion defect reversibility as compared with patients without inducible ischemia.

When compared between the two patient cohorts (Fig. 4), composite costs were substantially higher in the 5,423 patients undergoing direct cardiac catheterization, as compared with those undergoing initial noninvasive stress myocardial perfusion imaging with selective invasive resource use. The average total costs for 2.5 years of care ranged between 4 and 15 thousand dollars. Overall, the costs of care increased with greater pretest risk in both patient management strategies, but were elevated by 30% to 41% for patients undergoing direct catheterization (Fig. 5, $p < 0.00001$).

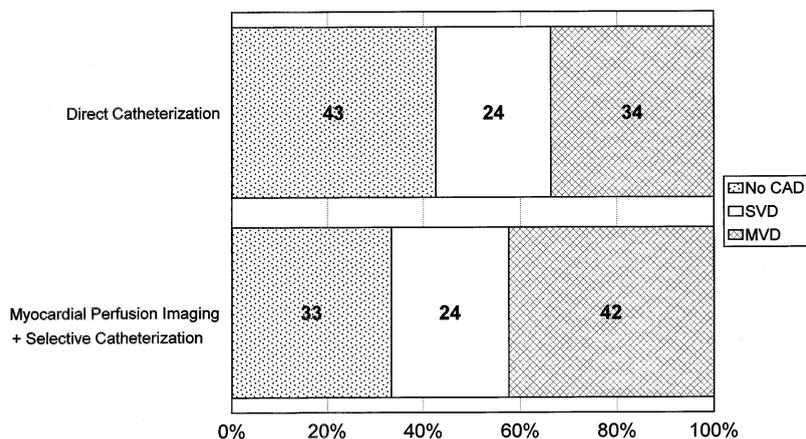


Figure 2. The extent of coronary artery disease for matched cohorts of coronary disease pretest risk subsets. The rate of no coronary disease (No CAD) is lower for patients undergoing direct cardiac catheterization. The rate of single vessel coronary disease (SVD) is comparable between the two diagnostic strategies. The rate of multivessel coronary disease (MVD) is higher in patients with evidence of ischemia on their initial stress perfusion scan and in those with a high pretest risk of coronary disease.

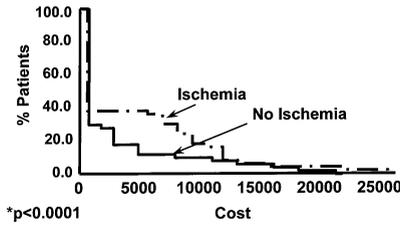


Figure 3. The percentage of low and high cost patients for patients with no reversible defect and reversible defects for the 5,826 stable chest pain patients undergoing stress perfusion imaging. On average, patients with a reversible perfusion defect were higher cost than those without a perfusion defect.

The diagnostic costs were \$1,320, \$1,275 and \$1,229 greater for low, intermediate and high risk patients undergoing initial cardiac catheterization, as compared to those who had initial stress myocardial perfusion imaging ($p < 0.0001$). Follow-up costs were higher for low risk patients undergoing initial stress myocardial perfusion imaging (on average \$383 dollars higher). However, the follow-up costs of care were \$517 and \$704 dollars higher for clinically intermediate and high pretest risk patients undergoing initial cardiac catheterization as compared to the costs for those undergoing initial stress myocardial perfusion imaging ($p < 0.00001$).

Predicted, risk-adjusted cost versus observed cost in the nuclear imaging cohort. Further refinement of cost and outcome management in the nuclear imaging cohort revealed that the largest cost savings would be expected for patients with none to one vascular territory with ischemia (Fig. 6). In a risk-adjusted multivariate linear regression model, predicted costs were significantly less than observed costs for patients with no (\$749 dollars less) to one vessel ischemia (\$917 dollars less) on their nuclear scan ($p < 0.0001$), after controlling for pretest clinical risk and follow-up cardiac outcomes (including death or myocardial infarction). By comparison, the predicted rates that included

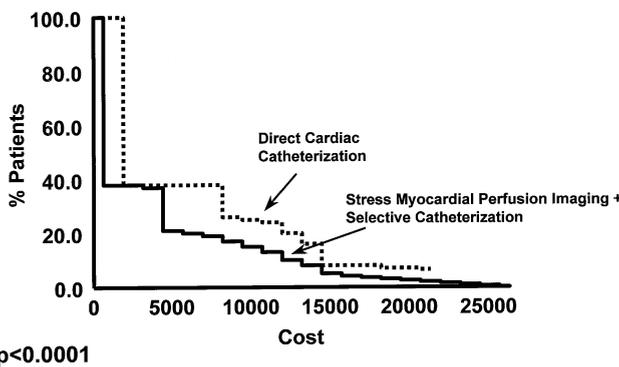


Figure 4. The percentage of low and high cost patients for patients undergoing direct catheterization and initial stress perfusion imaging. On average, patients proceeding directly to cardiac catheterization were higher cost than those having an initial stress perfusion scan.

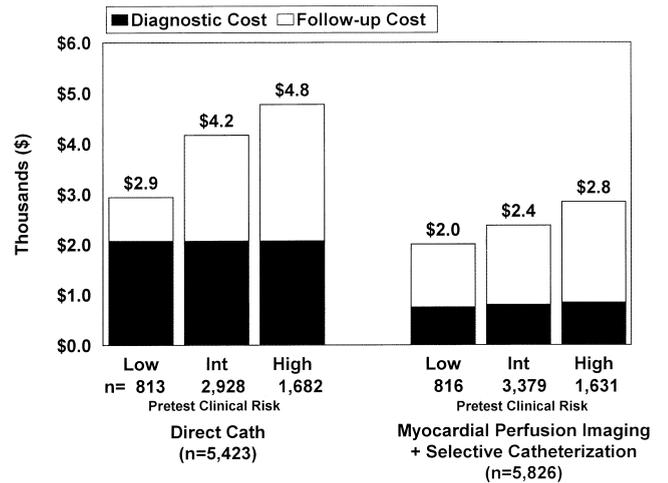


Figure 5. Overall diagnostic and follow-up costs of care for direct catheterization and initial stress perfusion imaging are presented. Diagnostic and follow-up costs of care were 30% to 41% higher for patients undergoing direct cardiac catheterization. **Solid bars** = diagnostic cost; **open bars** = follow-up cost.

adjustment for pretest risk and major cardiac outcomes remained similar to observed cost for patients with two or three vascular territories with ischemia.

DISCUSSION

The United States has witnessed a dramatic and progressive increase in the use of diagnostic and therapeutic technologies. Rates of cardiac catheterization and coronary revascularization among Medicare acute myocardial infarction patients have increased by 45% and 70% between 1987 and 1992 (13). These rates of cardiac catheterization are approximately two times higher than what would have been estimated by classifying patients according to their risk of

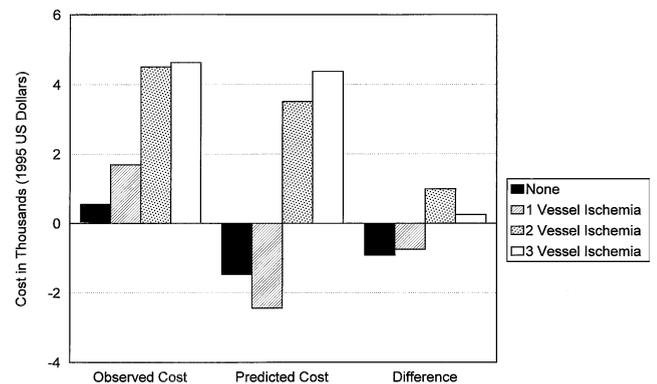


Figure 6. Risk-adjusted predicted three-year costs as compared with observed three-year costs of care for patients undergoing nuclear imaging by the extent of myocardial ischemia. After controlling for pretest clinical risk and cardiac outcomes, significant ($p < 0.0001$) cost savings could be realized by decreasing resource use in patients with none to minimal ischemia on their nuclear scan.

death or left ventricular dysfunction (13). Regardless of the health care reimbursement system, providers are placing a greater emphasis on decreasing length of stay and limiting resource use. To continue to provide high quality care while controlling medical costs in today's health care environment, providers must employ a risk- and quality-based strategy that quantifies overall short- and long-term patient risk, while integrating the economic implications of varying patient management strategies.

To date, there are few economic data available to guide medical decision making regarding the use of interventions for stable coronary disease patients. The current study provides an observational comparison of diagnostic and follow-up costs for two widely utilized diagnostic strategies, one invasive and one noninvasive, for the evaluation of patients with stable angina. The current report revealed by examining practice patterns in seven hospitals that the initial use of noninvasive stress cardiac imaging decreases the overall costs of patient care during an observational period of nearly 3 years. Composite cost of care was 30% to 40% less when cardiac catheterization was employed selectively in the diagnostic evaluation of stable angina patients. Further refinement of the estimated cost savings revealed that a conservative management approach may be employed in patients with minimal to no provocative ischemia. These multicenter data provide insight into the advantage of a selective use of cardiac catheterization for patients with inducible myocardial ischemia on noninvasive testing. The results of this study should be useful to assist health care providers and payers alike in defining a broadly applicable clinical pathway for the evaluation of stable angina patients, a large cohort of patients in this country. Furthermore, these results may be used to provide a more efficient method for resource use on noninvasive and invasive diagnostic techniques.

Minimizing cost without a health detriment. This analysis attempts to identify the value of a diagnostic efficacy model. Such a model attempts to evaluate the diagnostic yield of a given test, in this case, tomographic myocardial perfusion imaging, in influencing diagnostic management decisions. The resultant degree to which nuclear imaging may influence management is manifest in the improvement in cost-efficient outcomes management of this symptomatic patient cohort. This analysis attempts to identify a low cost, resource efficient strategy for the evaluation of stable angina patients. In a cost minimization analysis, an underlying assumption for this analysis is that outcomes are equal between the two comparative patient cohorts. Thus, the only difference between the two cohorts is that of differences in the cost of care. Similar low rates of subsequent myocardial infarction and cardiac death were observed in the two patient cohorts.

Within the context of noninvasive cardiac testing, patients are often referred for stress testing in an attempt to define subsequent diagnostic and therapeutic strategies of

care as well as to provide insight into the patient's short-term risk of cardiac events. However, noninvasive testing also has the potential to accrue cost savings by excluding patients at low risk from further intervention who have minimal disease and few cardiac events. In many cases, exercise testing is considered the gatekeeper study for additional noninvasive imaging or more invasive cardiac evaluations (14). Of the 5,826 patients undergoing initial stress myocardial perfusion imaging, only one third of patients underwent selective cardiac catheterization. This included a majority (>90%) of patients with abnormal noninvasive testing results, with an additional 9% who could be categorized before testing as clinically high risk. In this cohort, a substantial cost savings was accrued by using a noninvasive testing strategy, thus excluding approximately two thirds of patients with normal test results from additional expensive diagnostic evaluation. Furthermore, the risk of cardiac death, given a normal perfusion test, was exceedingly low over three years of follow-up.

Limitations on resource use could be realized by restricting additional procedure use to patients with multivessel ischemia. In 1993, guidelines for the use of percutaneous interventions recommend that a moderate to large amount of demonstrable ischemia be present for patients with stable chest pain symptoms (15). The results of the current series support this recommendation. In the nuclear imaging cohort with multivessel ischemia, cardiac outcomes were high, warranting an aggressive management approach to care. Thus, a diagnostic outcomes-based cost-efficient management strategy could be developed that would recommend referral to cardiac catheterization for patients with multivessel ischemia and stable chest pain symptoms. This diagnostic pathway would result in selective resource use (subsequent referral of only high risk patients) and cost savings (by excluding low risk patients who warrant a watchful waiting approach to care).

The results of the report are divergent from a recent analysis of Medicare beneficiaries from northern New England (16). In this report, using an administrative database, the rates of stress testing were correlated with rates of coronary angiography. The authors concluded that limiting noninvasive testing would thereby limit more invasive, costly interventions. In addition to the limited risk-adjusted techniques that may be applied to an administrative database, this analysis appears to consider only a portion of the clinical decision making and subsequent medical care that may be implemented for patients undergoing noninvasive testing. In fact, in any stress testing population, the majority of patients will have a normal test result, with clinical follow-up limited to those patients with recurrent symptoms or worsening clinical status. When the northern New England results were examined nationally, the rates of cardiac catheterization were actually less than that for patients undergoing initial stress testing (17).

In the current analysis, the rate of resource use and costs of care increased with the pretest probability of coronary

disease (for clinically low, intermediate and high risk patients, Fig. 5). In a similar comparison on the use of invasive and noninvasive diagnostic imaging procedures in hospitalized acute myocardial infarction patients, the use of noninvasive techniques was not associated with age-related differences in use (18-20). However, older patients, regardless of disease severity, underwent significantly fewer cardiac catheterization procedures than younger patients (18-20). Further, in a recent analysis, diagnostic follow-up and total cost of care from the initial evaluation through 2 years of follow-up were higher for men than women, with older women having the lowest rate of subsequent diagnostic and interventional follow-up (21).

Enhancing the diagnostic yield with provocative ischemia. There have been numerous reports regarding the apparent "overuse" of cardiac catheterization. In a recent analysis of 305 metropolitan statistical areas, the rate of coronary bypass surgery and percutaneous transluminal coronary angioplasty was correlated with the rate of cardiac catheterization (22). This study concluded that use of cardiac catheterization had a direct influence on the rate of coronary revascularization that was unrelated to the rate of coronary disease in the population but was more strongly related to an increasingly aggressive approach to coronary disease treatment. In a recent analysis of 499 patients who underwent coronary angiography in Israel, 58% of the procedures were considered inappropriate (23). In a recent analysis of elderly acute myocardial infarction patients, the survival benefits resulting from a higher rate of cardiac catheterization were minimal (18-20). Guadagnoli and colleagues, in a recent analysis of administrative data, reported on the use of cardiac catheterization in 478 elderly patients (24). They reported a higher rate of elective cardiac catheterization in Texas that was unrelated to mortality risk or health-related quality of life. Thus, it appears that aggressive treatment may not always be considered appropriate, or result in improved cardiac outcomes.

In our patients referred for direct cardiac catheterization, the rate of coronary revascularization was almost twofold higher in the clinically intermediate and high risk patients undergoing direct catheterization, with the majority of this increased use being percutaneous transluminal coronary angioplasty. In a recent report by Topol et al. (25), evidence of ischemia before percutaneous transluminal coronary angioplasty provided additional prognostic information, thus enhancing the clinical efficacy of this treatment strategy.

Laupacis and colleagues (26) have proposed guidelines for integrating clinical and economic outcome analyses. Using this approach, technology that is found to be highly effective is often similarly economically useful. In areas where the use of a technology is less efficacious or inappropriate, the cost-effectiveness ratios are exceedingly high. For example (27-29), cost per gain in quality-adjusted life year for coronary bypass surgery ranged from \$7,000 to \$14,000 for three vessel or left main disease, from \$55,000 for one vessel

disease with severe angina and \$850,000 for one vessel disease with mild angina, and was not cost-effective for one vessel disease with mild angina. Using this approach, establishing guidelines for care based upon precatheterization evidence of provocative ischemia would be helpful in enriching the population with a greater frequency of diseased patients. Although these guidelines require prospective evaluation, patients without evidence of provokable ischemia, due to their low rate of cardiac death (1% over 3 years) could be safely managed medically, thus limiting subsequent resource use.

Study limitations. We have attempted through rigorous risk-adjustment techniques to "level the playing field" between the two comparative patient cohorts; there are, however, limitations and bias that may exist in the use of nonrandomized comparisons that must be considered in this analysis. Second, quality of life comparisons between these stable angina patients were not available and could have contributed to our analysis of outcomes in these two patient cohorts.

Conclusions. In an observational series, a more aggressive intervention strategy that includes direct cardiac catheterization in stable angina patients not only leads to higher diagnostic costs but also contributes to greater rates of coronary intervention and composite costs of care. At all levels of pretest clinical risk, the costs of initial and subsequent follow-up care are substantially less when a selective, provocative ischemia-driven catheterization strategy is employed using nuclear imaging. The observed lower cost of care with noninvasive stress imaging was due to a reduction in resource use for patients with a normal test result. The diagnostic yield for cardiac catheterization was enriched for populations with stress-induced myocardial ischemia, reflecting a higher pretest and posttest probability of significant coronary heart disease.

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