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Cost-Effectiveness of Diagnostic Strategies for Patients with Chest Pain

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Background: Many noninvasive tests exist to determine whether patients should undergo coronary angiography. The routine use of coronary angiography without previous noninvasive testing is typically not advocated.

Objective: To determine the cost-effectiveness of diagnostic strategies for patients with chest pain.

Design: Cost-effectiveness analysis.

Data Sources: Published data.

Target Population: Patients who present with chest pain, have no history of myocardial infarction, and are able to perform an exercise stress test.

Time Horizon: Lifetime.

Perspective: Societal.

Interventions: No testing, exercise electrocardiography, exercise echocardiography, exercise single-photon emission computed tomography (SPECT), and coronary angiography alone.

Outcome Measures: Quality-adjusted life expectancy, lifetime cost, and incremental cost-effectiveness.

Results of Base-Case Analysis: The incremental cost-effectiveness ratio of routine coronary angiography compared with exercise echocardiography was $36 400 per quality-adjusted life-year (QALY) saved for 55-year-old men with typical angina. For 55-year-old men with atypical angina, exercise echocardiography compared with exercise electrocardiography cost $41 900 per QALY saved. If adequate exercise echocardiography was not available, exercise SPECT cost $54 800 per QALY saved compared with exercise electrocardiography for these patients. For 55-year-old men with nonspecific chest pain, the incremental cost-effectiveness ratio of exercise electrocardiography compared with no testing was $57 700 per QALY saved.

Results of Sensitivity Analysis: On the basis of a probabilistic sensitivity analysis, there is a 75% chance that exercise echocardiography costs less than $50 900 per QALY saved for 55-year-old men with atypical angina.

Conclusions: Exercise electrocardiography or exercise echocardiography resulted in reasonable cost-effectiveness ratios for patients at mild to moderate risk for coronary artery disease in terms of age, sex, and type of chest pain. Coronary angiography without previous noninvasive testing resulted in reasonable cost-effectiveness ratios for patients with a high pretest probability of coronary artery disease.

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Coronary artery disease continues to be the leading cause of death in the United States. Approximately 500 000 patients receive a new diagnosis of coronary artery disease each year, 47% of whom will have angina as their initial event (1). The prevalence of coronary artery disease in patients who present with typical angina is 93% for men and 72% for women; approximately 48% of these patients have triple-vessel or left main coronary artery disease (2). Even for patients who present with nonspecific chest pain, the prevalence of coronary artery disease can be as high as 27% (for example, among 65-year-old men) (2). Selective use of revascularization with coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA) can improve both the prognosis and the health-related quality of life of many patients.

For patients who present with chest pain, many noninvasive tests can be used to determine whether they should undergo coronary angiography. Exercise electrocardiography is widely used and has a demonstrated sensitivity and specificity of 68% and 77%, respectively (3). Adjunctive imaging techniques, such as echocardiography or single-photon emission computed tomography (SPECT), improve the overall diagnostic performance of the exercise test, although at higher cost. The routine use of coronary angiography without previous noninvasive testing is typically not advocated because of the associated risk for morbidity and death and its relatively high cost.

From a health care policy perspective, the value of diagnostic test strategies for patients with chest pain should reflect not only the diagnostic accuracy, risk, and cost of the test but also the probability that the patient has significant coronary artery disease, the costs of further testing or treatments that may be induced by the test result, the costs of events that may be averted by subsequent treatment, and the health-related quality of life associated with various degrees of chest pain. We constructed a decision-analytic model to evaluate the cost-effectiveness of various diagnostic strategies for patients with chest pain from a health care policy perspective (4). We extend the work of a previous cost-effectiveness analysis of exercise electrocardiography in patients with chest pain (5) by including two widely used noninvasive tests that are often the initial test selected in current clinical practice: exercise echocardiography and exercise SPECT.

Methods

We evaluated cohorts of patients stratified by decade of age (40 to 49 years, 50 to 59 years, or 60 to 69 years), sex, and characteristics and severity of chest pain. Three types of chest pain were consid-

Figure 1. Decision tree. Patients who do not undergo diagnostic testing are stratified by extent of underlying coronary artery disease and receive medical treatment. Patients who undergo noninvasive exercise testing undergo coronary angiography if the test result is positive. The postcatheterization management strategy depends on the result of angiography; the standard approach is shown. At the end of each branch, if patients are still alive, they enter a Markov cycle tree (*M*) that models their lifetime prognosis. CABG = coronary artery bypass grafting; CAD = coronary artery disease; LMD = left main disease; MEDS = medical therapy; PTCA = percutaneous transluminal coronary angioplasty.

Table 1. Selected Model Variables*

Variable	Base-Case Value (Range)	Reference Source
Diagnostic performance of noninvasive tests†		
Exercise electrocardiography		
Sensitivity	0.68 (0.67–0.69)	3
Specificity	0.77 (0.76–0.78)	3
Exercise echocardiography		
Sensitivity	0.85 (0.83–0.87)	8
Specificity	0.77 (0.74–0.80)	8
Exercise SPECT		
Sensitivity	0.87 (0.86–0.88)	8
Specificity	0.64 (0.60–0.68)	8
Mortality risk ratio for extent of coronary artery disease†‡		
Single- or double-vessel disease	2.3 (1.9–2.8)	9
Triple-vessel disease	3.6 (3.1–4.1)	9
Left main coronary artery disease	9.6 (6.1–14.3)	9
Mortality risk reductions by CABG, %†		
Single- or double-vessel disease§	15 (0–49)	9
Triple-vessel disease	48 (32–64)	9
Left main coronary artery disease	67 (43–87)	9
Annual risk for nonfatal myocardial infarction‖		
Single- or double-vessel disease	0.022 (0.016–0.029)	10
Triple-vessel or left main coronary artery disease	0.028 (0.021–0.035)	10
Risk reduction in late myocardial infarction with revascularization, %¶		
PTCA	17 (12–22)	11
CABG	42 (29–55)	11, 12
Annual risk for revascularization by initial treatment and extent of disease¶**		
Medical therapy (single-vessel disease)	0.010 (0.001–0.022)	13, 14
Medical therapy (double-vessel disease)	0.042 (0.028–0.056)	13, 14
Medical therapy (triple-vessel disease)	0.075 (0.061–0.089)	13, 14
PTCA††	0.036 (0.026–0.046)	15, 16
CABG	0.018 (0.011–0.025)	14, 15

* CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty; SPECT = single-photon emission computed tomography.
† Ranges based on 95% CIs from meta-analyses.
‡ Compared with no significant coronary artery disease.
§ Range bounded by no effect (0).
‖ Ranges based on reported standard errors.
¶ Ranges based on ±30% (best guess) of base-case estimates.
** The percentage of revascularizations that were CABG were as follows: 16% (single-vessel disease and initial medical therapy), 58% (double-vessel disease and initial medical therapy), 87% (triple-vessel disease and initial medical therapy), 22% (initial PTCA), 7% (initial CABG).
†† The rate was 0.34 in the first year after PTCA.

ered: typical angina (substernal chest pain that is exertional in nature and is relieved promptly by nitroglycerin therapy), atypical angina (pain with two of the three characteristics of typical angina), and nonspecific chest pain (pain with no more than one of the three characteristics of typical angina). We assumed that the severity of chest pain was either mild or severe. Because most of the available data applied to men 50 to 59 years of age, this demographic population was used in the base-case analyses.

Decision-Analytic Model

We constructed a decision-analytic model to evaluate various diagnostic work-up scenarios for patients who present with chest pain, have no history of myocardial infarction, and are able to perform an exercise stress test. We used Markov models (6) to estimate lifetime costs and quality-adjusted life expectancy because patients with chest pain often experience important events after their initial presentation and evaluation. The strategies considered were 1) no testing and medical therapy as appropriate, 2) exercise electrocardiography with coronary angiography if test results are positive, 3) exercise echocardiography with coronary angiography if test results are positive, 4) exercise SPECT with coronary angiography if test results are positive, and 5) routine coronary angiography without previous noninvasive testing.

Several possible courses of action can follow once the initial test is performed. We considered two diagnostic thresholds for each exercise test: pos-

Figure 2. Prevalence of coronary artery disease. The prevalence of any coronary artery disease is shown, based on age range, sex, and type of chest pain. Bars represent 95% CIs. Diamonds represent patients with typical angina; circles represent those with atypical angina; and Xs represent those with nonspecific chest pain.

Table 2. Cost and Quality-of-Life Estimates*

Variable	Estimate (Range)†
Costs, $	
Exercise electrocardiography	110 (77–143)
Exercise echocardiography	262 (183–341)
Exercise SPECT	574 (402–746)
Coronary angiography	4741 (3319–6163)
Percutaneous transluminal coronary angioplasty	12 476 (8733–16 219)
Coronary artery bypass grafting	33 088 (23 162–43 014)
Myocardial infarction	14 168 (9918–12 893)
Annual cost (no event)	
No angina	160 (112–208)
Mild angina	1600 (1120–2080)
Severe angina	3500 (2450–4550)
Health-related quality-of-life weight	
No chest pain symptoms	0.87 (0.77–1.0)
Mild chest pain symptoms	0.81 (0.68–1.0)
Severe chest pain symptoms	0.67 (0.40–0.98)

* SPECT = single-photon emission computed tomography.
† Ranges for cost estimates represent ±30% of baseline estimate. Ranges for utilities represent the 25th and 75th percentiles of the data (Nease RF, 10 August 1998. Personal communication).

itive (indicative of any coronary artery disease) and strongly positive (indicative of triple-vessel or left main coronary artery disease). We also considered two possible postcatheterization strategies: standard (CABG for triple-vessel or left main coronary artery disease, PTCA for single- or double-vessel coronary artery disease if the patient is eligible; otherwise, medical therapy as appropriate) and conservative (CABG for triple-vessel or left main coronary artery disease; otherwise, medical therapy as appropriate). We based the standard postcatheterization strategy primarily on the appropriateness guidelines developed by RAND Corp. (7).

The model outputs were quality-adjusted life expectancy and expected lifetime cost. Incremental analyses were performed by rank ordering all 15 competing strategies by increasing effectiveness after eliminating strategies that were more costly and less effective than another strategy (that is, they were ruled out by simple dominance). We then calculated the incremental cost-effectiveness ratio for each strategy (additional cost divided by additional benefit) compared with the next least expensive strategy. If a strategy was less effective and had a higher incremental cost-effectiveness ratio than another strategy, it was ruled out by weak dominance. A weakly dominated strategy was eliminated from the rank-ordered list, and the incremental cost-effectiveness ratios were recalculated. This process of eliminating weakly dominated strategies and recalculating cost-effectiveness ratios continued until no more weakly dominated strategies were left. Costs and life years were discounted at an annual rate of 3%. All analyses were performed by using SMLTREE software, version 2.99 (James Hollenberg, MD, Roslyn, New York). A schematic representation of the decision tree is shown in **Figure 1**.

Data Sources

Number of Diseased Coronary Arteries

The result of coronary angiography was quantified as the number of diseased vessels (zero to three) with a separate category for left main coronary artery disease. Underlying coronary artery disease status, stratified by age, sex, and type of chest pain, was based on the prevalence reported by the Coronary Artery Surgery Study (CASS) registry (2) for patients with no history of myocardial infarction. Among patients with typical, atypical, and nonspecific chest pain, the prevalence of any coronary artery disease was 95%, 71%, or 18% in men 50 to 59 years of age and 68%, 30%, or 6% in women in this age range (**Figure 2**).

Noninvasive Test Characteristics

The sensitivity and specificity of exercise electrocardiography for the detection of any coronary artery disease were obtained from a meta-analysis of 150 studies (3) (**Table 1**). The sensitivity and specificity of exercise echocardiography and exercise SPECT for the detection of any coronary artery disease were obtained from a recent meta-analysis (8), which yielded similar sensitivities but statistically different specificities (**Table 1**). The sensitivity for multivessel (double-vessel, triple-vessel, or left main coronary artery) disease was calculated by using the ratio of the sensitivity among patients with multivessel disease relative to that among patients with any coronary artery disease, estimated from studies in which details on the extent of coronary artery disease were reported (17–21). The sensitivities for severe (triple-vessel or left main coronary artery) disease and for left main coronary artery disease were also calculated on the basis of similar ratios. The probability of strongly positive test results by coronary disease category were calculated by using the estimated ratio of the probability of a strongly positive result to the probability of any positive result among each of the coronary artery disease categories (17–20). Some patients undergoing an exercise test were assumed to have an indeterminate result (30% of those undergoing exercise electrocardiography, 10% of those undergoing exercise echocardiography, and 2% of those undergoing exercise SPECT); another noninvasive test was done in these patients. Because data are inadequate on the sensitivity and specificity of each exercise test among a group of patients with indeterminate test results on their first test, we assumed that the overall sensitivity and specificity of the test remained unchanged if it was preceded by another test with indeterminate results and that only the cost of the additional test was incurred.

Short-Term Risks

Coronary angiography was associated with an overall 0.1% probability of death and 0.06% probability of nonfatal myocardial infarction. These rates varied depending on extent of coronary anatomy involved (22, 23). In single- and double-vessel coronary artery disease, PTCA was associated with mortality rates of 0.2% and 0.9% and nonfatal myocardial infarction rates of 3.5% and 5.2%, respectively (24). The overall probability of death associated with CABG was 3.2%, and the probability of nonfatal myocardial infarction was 7.0% (25–27). The risk for death of CABG was adjusted to be higher for women and for patients in older age ranges (27). We assumed that 5% of patients treated with PTCA undergo emergent CABG for immediate occlusions (15, 28–30).

Long-Term Prognosis

Long-term survival was modeled on an intention-to-treat basis in that prognosis was determined only by the initial patient variables (age, sex, extent of coronary artery disease, and treatment) (16, 31–37). Mortality risk ratios for extent of coronary artery disease and mortality risk reductions by CABG (that is, the percentage of coronary artery disease–related mortality reduced by surgery) were derived to match the mean survival times at 10 years reported in a systematic overview of seven CABG clinical trials (9) (**Table 1**). We assumed that these risk reductions persisted for 10 years (and were 0% thereafter) and that the survival efficacy of PTCA for patients with single- or double-vessel disease equalled that of CABG (13, 16). All-cause mortality was adjusted for age and sex and was obtained from U.S. life tables (38).

Nonfatal myocardial infarction and revascularization procedures occurring after the initial treatment decision were modeled to capture their effects on cost and quality of life (10, 13–16). The risk for late nonfatal myocardial infarction, PTCA, or CABG depended on the extent of coronary artery disease and type of initial treatment (**Table 1**). We allowed differences in revascularization probabilities among initial treatments to persist for 10 years.

Health-Related Quality of Life

We estimated the immediate change in severity of chest pain due to CABG and the subsequent annual probabilities of changing from one severity level of chest pain (none, mild or severe) to another level by using the CASS quality-of-life study (39). This study reported the proportion of patients in each severity group after treatment and periodically over time, stratified by coronary artery disease extent and initial treatment. On the basis of an over-

Table 3. Quality-Adjusted Life Expectancy, Cost, and Cost-Effectiveness Ratios for Men 50 to 59 Years of Age with Mild Chest Pain

Strategy*			Quality-Adjusted Life Expectancy†	Cost†	Incremental Cost-Effectiveness Ratio‡
Type of Chest Pain and Initial Test	Criterion for Further Work-up	Type of Revascularization Strategy	*y*	*$*	*$/y*
Typical angina					
No testing	–	–	10.4267	32 117	–
Exercise electrocardiography	Strongly positive result	Conservative§	10.7124	39 589	26 200
Exercise echocardiography	Strongly positive result	Conservative	10.7457	40 657	32 000
	Positive result	Conservative	10.8089	42 845	34 700
Angiography	–	Conservative	10.8373	43 883	36 400
	–	Standard‖	10.9528	51 143	62 900
Atypical angina					
No testing	–	–	11.8937	28 666	–
Exercise electrocardiography	Strongly positive result	Conservative	12.0359	32 964	30 200
Exercise echocardiography	Strongly positive result	Conservative	12.0524	33 656	41 900
	Positive result	Conservative	12.0833	35 398	56 500
	Strongly positive result	Standard	12.1092	37 042	63 300
	Positive result	Standard	12.1781	41 677	67 300
Angiography	–	Standard	12.2087	44 404	89 000
Nonspecific chest pain					
No testing	–	–	14.2269	24 304	–
Exercise electrocardiography	Strongly positive result	Conservative	14.2442	25 304	57 700
	Strongly positive result	Standard	14.2555	26 076	68 400
Exercise echocardiography	Strongly positive result	Standard	14.2608	26 540	88 000
	Positive result	Standard	14.2779	28 806	132 200
Angiography	–	Standard	14.2836	32 132	584 500

* Strategies not shown are ruled out by either simple or weak dominance.
† Costs and quality-adjusted life expectancy are discounted at an annual rate of 3%.
‡ Incremental cost-effectiveness ratios for each strategy are calculated compared with the next most effective strategy shown in the table, and are rounded to the nearest $100. (Note: Cost-effectiveness ratios calculated directly by quality-adjusted life expectancies and costs from the table may be off because of rounding.)
§ Conservative postcatheterization strategy is coronary artery bypass grafting for triple-vessel or left main coronary artery disease and medical therapy otherwise.
‖ Standard postcatheterization strategy is coronary artery bypass grafting for triple-vessel or left main coronary artery disease, coronary angioplasty for single- or double-vessel coronary artery disease, and medical therapy otherwise.

Table 4. Pairwise Cost-Effectiveness Ratios for Men 50 to 59 Years of Age with Mild Chest Pain*

Base Comparison	Incremental Cost-Effectiveness Ratio for Alternative Strategy			
	Exercise Electrocardiography	Exercise Echocardiography	Exercise SPECT	Angiography
	←——— $/QALY ———→			
Typical angina				
No testing	26 200	26 800	27 600	28 700
Exercise electrocardiography	–	32 000	38 000	34 400
Exercise echocardiography	–	–	62 800	35 200
Exercise SPECT	–	–	–	32 600
Atypical angina				
No testing	30 200	31 400	33 300	40 600
Exercise electrocardiography	–	41 900	54 900	65 000
Exercise echocardiography	–	–	108 900	73 600
Exercise SPECT	–	–	–	70 200

* Cost-effectiveness ratios are calculated for each alternative strategy relative to a base comparison, and are rounded to the nearest $100. Criterion for further work-up was a strongly positive test result, followed by coronary artery bypass grafting for triple-vessel or left main coronary artery disease and medical therapy otherwise (based on results shown in **Table 3**). QALY = quality-adjusted life-year; SPECT = single-photon emission computed tomography.

view of trials comparing PTCA with CABG, we assumed that PTCA was 85% as effective as CABG for immediate change in chest pain severity and that these two procedures had similar effects on symptoms thereafter (16). The differences among the three treatment groups were allowed to persist for 10 years. We assigned utilities (health values) of 0.87 for no symptoms, 0.81 for mild symptoms, and 0.67 for severe symptoms on the basis of a survey of 211 patients with chronic stable angina by using the standard gamble method (40), where 0 represents death and 1 represents perfect health (**Table 2**).

Costs

All cost estimates are shown in **Table 2**. For the exercise tests, we used Medicare-allowed charges, which include both technical and professional fees, to approximate the cost to society (41). Hospital costs for coronary angiography, revascularizations, and myocardial infarction were estimated from Medicare administrative data, the details of which have been described elsewhere (41, 42). Professional costs associated with myocardial infarction and cardiac interventions were estimated from the Medicare fee schedule. We assigned an annual cost associated with medications, subsequent tests, and outpatient follow-up visits for various levels of pain severity (11, 42). We assumed that the differences in annual costs between the revascularization and medical therapy groups held for 10 years, after which those two costs were equivalent. All costs were adjusted to 1996 U.S. dollars by using the medical care component of the Consumer Price Index.

Sensitivity Analysis

We performed one-way and two-way sensitivity analyses on all of the variables in our model to assess the effect of varying baseline estimates within clinically plausible ranges on our results. We also performed a Monte Carlo simulation (43) in which we simultaneously varied all of the values for the variables listed in **Tables 1** and **2** (except the risk for revascularization variables). Each variable was entered as a probability distribution based on reported 95% CIs when available or as a reasonable range. New values from within each of the probability distributions were randomly selected during each of 1000 iterations, and the quality-adjusted life expectancy and lifetime cost for each of the five basic strategies were calculated.

Results

Base-Case Analysis

The preferred strategy depends on various factors, including the nature and severity of chest pain and the dollar amount that society is willing to spend to gain an additional QALY (cost-effectiveness threshold). **Table 3** shows the quality-adjusted life expectancy, lifetime cost, and incremental cost-effectiveness ratios by type of chest pain in men 50 to 59 years of age who present with mild chest pain. The incremental cost-effectiveness ratio of routine coronary angiography compared with exercise echocardiography ranged from $36 400 to $62 900 per QALY gained (depending on the revascularization strategy) for patients with typical angina. The incremental cost-effectiveness ratio of exercise echocardiography compared with exercise electrocardiography ranged from $41 900 to $67 300 per QALY gained (depending on the post-test strategy) for patients with atypical angina. For patients with nonspecific chest pain, exercise electrocardiography cost from $57 700 to $68 400 per QALY gained (depending on the post-test strategy).

The analysis in **Table 3** assumes that all diagnostic techniques are available with adequate diagnostic performance. Because this may not be the case at all centers, we also present a pairwise comparison of the five basic strategies (**Table 4**). For example, for 55-year-old men with atypical angina, exercise SPECT cost $54 900 per QALY saved compared with exercise electrocardiography and $33 300 per QALY gained compared with no testing.

Alternative Patient Cohorts

The incremental cost-effectiveness ratios varied with age, sex, and the type and severity of chest pain. **Figure 3** shows the incremental cost-effectiveness ratios for exercise electrocardiography compared with no testing, exercise echocardiography compared with exercise electrocardiography, and coronary angiography compared with exercise echocardiography for three demographic subgroups with similar outcomes: 1) women 40 to 59 years of age, 2) women 60 to 69 years of age and men 40 to 49 years of age, and 3) men 50 to 69 years of age. The cost-effectiveness ratios were high for all testing strategies for women and younger men with nonspecific chest pain, which represents patients with a very low probability of coronary artery disease. Noninvasive testing, particularly exercise echocardiography, showed reasonable cost-effectiveness ratios for patients who had a low to moderate probability of coronary artery disease. Coronary angiography without previous noninvasive testing had reasonable cost-effectiveness ratios for patients who had a high probability of coronary artery disease, such as older men with typical angina.

Sensitivity Analysis

Coronary Artery Disease Prevalence

Although the CIs of the probabilities of coronary artery disease were relatively small (**Figure 2**), we decreased the probability of coronary artery disease to be 20% that of the baseline estimates to evaluate the effect of coronary artery disease prevalence on the cost-effectiveness ratios. The cost-effectiveness ratios of the exercise tests were not very sensitive to this variable, but the ratios for routine coronary angiography were. If the prevalence of coronary artery disease were as low as 76% (the baseline prevalence was 95%), the cost-effectiveness ratio of routine coronary angiography compared with exercise echocardiography would increase to more than $66 800 per QALY gained for 55-year-old men with typical angina and mild symptoms.

Diagnostic Performance of Noninvasive Testing

Although the specificity of exercise echocardiography was statistically better than that of exercise SPECT (8), center-dependent variability exists for the diagnostic performance of exercise SPECT compared with exercise echocardiography. **Figure 4** shows the effects of varying the sensitivity and specificity of exercise SPECT over wide ranges for 55-year-old men with atypical angina and mild symptoms. This figure should be interpreted in the context of the baseline estimates of sensitivity and specificity of exercise echocardiography (0.85 and 0.77, respec-

Figure 3. Cost-effectiveness ratios for alternative patient cohorts. **Top.** Women 40 to 59 years of age. **Middle.** Women 60 to 69 years of age and men 40 to 49 years of age. **Bottom.** Men 50 to 69 years of age. Diamonds represent exercise electrocardiography compared with no testing; circles represent exercise echocardiography compared with exercise electrocardiography; and plus signs represent coronary angiography compared with exercise echocardiography. Comparisons not shown represent cases in which the incremental cost-effectiveness ratio is greater than $200 000 per quality-adjusted life-year (*QALY*) gained or dominated strategies.

Figure 4. Sensitivity analysis of the diagnostic performance of exercise single-photon emission computed tomography (*SPECT*). Results of three-way sensitivity analysis of the sensitivity and specificity of exercise SPECT and the acceptable cost-effectiveness threshold for 55-year-old men with atypical angina and mild symptoms are shown. Lines indicate four possible thresholds for allocating health-care resources. For a particular cost-effectiveness threshold, points to the top right of the line indicate that exercise SPECT compared with exercise echocardiography has a lower cost-effectiveness ratio than that depicted by the line. The *X* indicates an example in which the sensitivity and specificity of exercise SPECT are both 0.88. QALY = quality-adjusted life-year.

tively). For example, if the sensitivity and specificity of exercise SPECT were both 0.88 (**Figure 4**), the incremental cost-effectiveness ratio of exercise SPECT compared with exercise echocardiography is \$55 000 to \$60 000 per QALY gained.

Monte Carlo Analysis

We performed a probabilistic sensitivity analysis for men 50 to 59 years of age with atypical chest pain and mild symptoms. For this analysis, we used a strongly positive criterion for further work-up followed by CABG if the patient had triple-vessel or left main coronary artery disease or medical therapy otherwise. The 25th, 50th, and 75th percentiles were \$27 000, \$31 500, and \$36 100 per QALY saved for exercise electrocardiography compared with no testing and \$37 100, \$44 200, and \$50 900 per QALY saved for exercise echocardiography compared with exercise electrocardiography. Exercise SPECT was not ruled out by simple or weak dominance in only 4.5% of the simulations. When exercise SPECT was not dominated, the median for exercise SPECT compared with exercise echocardiography was \$71 800 per QALY saved. The 25th, 50th, and 75th percentiles for coronary angiography were \$64 000, \$77 700, and \$90 900 per QALY saved.

Discussion

We used well-established methods of cost-effectiveness analysis to integrate the available data on the potential benefits of exercise testing and treatment guided by its results in patients with chest pain. Exercise echocardiography and exercise SPECT have been shown to be superior to exercise electrocardiography in diagnostic performance. Because the costs of these newer testing techniques are greater than those of exercise electrocardiography alone, it is important to understand the trade-offs between improved diagnostic capabilities and the increased burden on the U.S. health care budget. In patient subgroups with a high probability of coronary artery disease (such as 55-year-old men with typical angina), we found that performing coronary angiography without previous noninvasive testing was associated with a reasonable cost-effectiveness ratio. Alternatively, for patients who have a very low probability of coronary artery disease (such as 55-year-old women with nonspecific chest pain), the cost-effectiveness ratios of all testing strategies were higher than those of most well-accepted medical interventions. The use of noninvasive diagnostic testing, particularly with exercise echocardiography, was associated with reasonable cost-effectiveness ratios for patients at moderate risk for coronary artery disease.

No prospective studies have compared the long-term costs and prognosis of different diagnostic strategies among patients with chest pain. To address this important question, we included data from several sources in a decision-analytic computer model to simulate hypothetical cohorts of patients under various alternative scenarios. We used certain assumptions to make a complex decision more tractable. Thus, the results of our analysis are affected by the inherent limitations of using heterogeneous data sources and making simplifying assumptions. For example, we assumed that all patients with atypical angina (pain with any two of the three characteristics of typical angina) were comparable. Although sensitivity analysis can be a useful tool to explore the impact of these assumptions, we emphasize that such an analysis always has to be informed by clinical acumen and judgment and is not meant as a substitute.

We only evaluated strategies that used a single noninvasive test. We did not consider strategies of sequential exercise tests, except in patients with indeterminate initial test results. To evaluate appropriately sequential test strategies, one must estimate the probability that the result of the second test is positive given that the result of the first test is positive (among patients with and without coronary artery disease). These relations are uncertain based on data from the literature alone, and estimating them would require a large sample size. A strategy of exercise electrocardiography followed by exercise echocardiography for positive test results is likely to have a low overall sensitivity (59% under the assumption of conditional independence given presence of coronary artery disease), although specificity will be better.

The pretest probability of coronary artery disease depended on certain patient characteristics in our model: age, sex, and type of chest pain, based on data from the CASS registry. In practice, however, other patient characteristics may also determine the chance of underlying disease (44). Our analysis does not explicitly address other factors. Thus, if a patient has other risk factors, such as a strong family history of coronary artery disease, a more aggressive approach may be warranted. In addition, the prevalence estimates may be overestimated because of selection bias in the CASS registry. However, the coronary anatomy distributions reported by the registry are similar to those reported by Diamond and Forrester (45) on the basis of autopsy data. The cost-effectiveness ratios of exercise electrocardiography or exercise echocardiography were only modestly affected by changes in prevalence. However, favorable cost-effectiveness ratios for routine coronary angiography required the prevalence to be close to that used in our base-case analysis.

We assumed that a positive result on the exercise test was useful only in predicting the presence and extent of coronary artery disease and that it did not add independent prognostic information. This simplifying assumption was necessary because the sensitivities and specificities that we used were based on predicting the presence and extent of coronary artery disease. Some studies have shown this to be a reasonable assumption (33, 35), but others have not (46). However, if a positive result on an exercise test had a prognostic effect independent of predicting coronary artery disease (for example, triple-vessel disease with a positive exercise test result carries a higher mortality risk ratio than triple-vessel disease with a negative exercise test result), the cost-effectiveness ratios would be lower for exercise testing than the ratios that we found in our analysis and higher for routine coronary angiography.

Our analysis extended the work of Doubilet and colleagues (5) to reflect choices in current clinical practice by the inclusion of two widely used noninvasive tests: exercise echocardiography and exercise SPECT. This previous cost-effectiveness analysis compared strategies of exercise electrocardiography, no testing, and routine coronary angiography among middle-aged men with chest pain. Our conclusions corroborate theirs for patients who present with typical angina or nonspecific chest pain. However, for some patients who present with atypical angina, we found that exercise echocardiography had a reasonable cost-effectiveness ratio and that routine coronary angiography was too expensive, whereas they found coronary angiography to be a reasonable strategy.

Our results may not be generalizable to all settings given that substantial center-specific variability exists for the relative diagnostic performances of each of the exercise tests. Although our analysis suggests that exercise echocardiography is a reasonable testing strategy for patients who are at moderate risk for coronary artery disease, we found that if exercise SPECT is substantially better than exercise echocardiography within a particular center, exercise SPECT may be a reasonable strategy (**Figure 4**). Thus, the choice of a noninvasive test will depend on center-specific estimates of sensitivity and specificity for all available tests (exercise electrocardiography, exercise echocardiography, and exercise SPECT). This will ultimately depend on local experience and expertise.

Interpretation of our results should be placed in the context of other generally accepted medical interventions. For example, coronary artery bypass grafting for patients with triple-vessel coronary artery disease and severe left ventricular function costs $40 700 per QALY gained (11), surgery to repair a 4-cm abdominal aortic aneurysm costs $21 200 per QALY gained (47), and therapy with cholesterol-lowering agents for 60-year-old men with cholesterol levels greater than 300 mg/dL (7.758 mmol/L) costs $22 900 to $87 300 per year of life saved (all values updated to 1996 U.S. dollars) (48). Thus, exercise echocardiography in patients who are at moderate risk for coronary artery disease seems to be a cost-effective use of resources compared with other generally accepted medical procedures.

In summary, for most patients who present with typical or atypical angina, performing a noninvasive diagnostic test is a reasonable use of health care resources. A more accurate but more costly noninvasive testing strategy is appropriate for patients who are at high risk for coronary artery disease on the basis of age, sex, and type and severity of chest pain. Coronary angiography without previous noninvasive testing should be reserved for patients who have a very high probability of coronary artery disease and present with severe symptoms or typical angina.

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