Nuclear Exercise Testing and the Management of Coronary Artery Disease

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Three hundred seventy-eight patients referred for nuclear exercise testing were classified using demographics and symptoms into low, intermediate, and high coronary disease likelihood categories. These likelihood groups constituted 15%, 41%, and 15% of referrals, respectively. Patients with prior infarction or disease at angiography (proven disease) made up the remaining 29% of patients. Only 2% of low likelihood patients had typical angina, but physicians diagnosed coronary disease in 64%, prescribed antianginal therapy in 50%, and were considering catheterization in 28% of these patients, all as frequently as for patients with intermediate or high likelihoods for disease. Patients with proven disease were treated differently in that 79% were receiving antianginal therapy and 56% were considered for catheterization ($p < 0.001$). Nuclear exercise test results reduced the perceived need for catheterization in all groups, on average by 49%. Nuclear exercise tests are a standard by which patients are managed, sometimes substituting for the traditional role of the history in physician decision making.

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Probability analysis has proven to be a useful tool not only for statisticians but also for practicing clinicians involved in patient management (*1,2*). For probability analysis to work effectively in the management of a given patient, the clinician must commit to an initial estimate of that patient's likelihood of having coronary disease (pretest likelihood) from patient age, gender, and the history for chest pain. If this estimate of coronary disease likelihood is sufficiently low, the patient can be reassured without going through further testing. If further testing is deemed necessary, Bayes' theorem is used to generate a post-test likelihood for coronary disease based on the interaction of pretest likelihood and test results. Exercise thallium scintigraphy and radionuclide ventriculography have maximal utility for establishing the presence or absence of disease in patients with a moderate initial probability of having coronary disease (*1,3*). Nuclear exercise tests are also useful in identifying the risk for a significant coronary event among patients with a moderate or high probability for disease or proven coronary disease (*4,5*). However, in a previous study, we documented the application of nuclear exercise tests to the entire spectrum of possible clinical presentations of ischemic heart disease, ranging from low probability groups to those with proven disease (*3*).

The current investigation was undertaken to characterize more fully physician management decisions for patients referred for nuclear exercise tests. During a prospective study of the efficacy of nuclear exercise tests (*6*), an extensive data base was generated containing detailed clinical information on all patients referred, along with their physicians' opinion as to whether they had coronary artery disease, and how referring physicians were managing their problems. The results suggest that clinical distinctions which form the basis for the initial estimates of disease likelihood in probability analysis are being devalued, while nuclear exercise tests take on greater importance in clinical decision making.

METHODS

The methods of this investigation have been published in detail elsewhere (*6*). Briefly, full-time and voluntary attending physicians, as well as house staff (in consultation with attending physicians), refer patients for nuclear exercise tests. Any one physician contributed less than 5% of the referrals. Several months prior to the start of this study, a new exercise test request form was distributed to the inpatient services and to the offices of referring physicians (Appendix). The request form contained questions about the patient's suspected heart disease(s), the severity of the suspect disease(s), the issues to be addressed by testing, and the physician's assessment of the patient's treatment and condition. If a physician checked "ischemic" in the category of suspected heart diseases, that patient was eligible for analysis.

On the day of the exercise procedure, after giving written informed consent for participation in this study, the patients were interviewed and examined by a trained project cardiologist. The history for angina was obtained according to the method of Diamond and Forrester and, along with patient age and gender,

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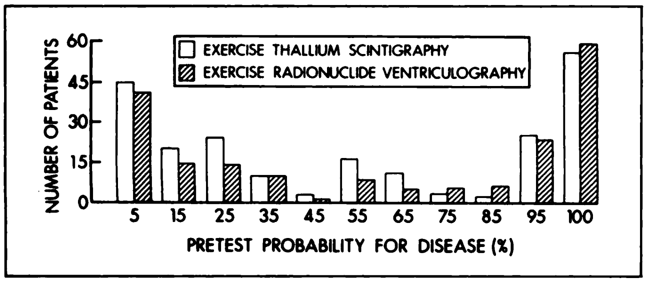

FIGURE 1. Frequency distribution of patients referred for exercise thallium scintigraphy and radionuclide ventriculography as a function of pretest probability for coronary disease. Both tests were employed over the entire spectrum of disease likelihoods and in patients with known disease (100% probability).

was used to arrive at the pre-test likelihood for coronary disease (*2,3,7–9*). Cardiac risk factors and prior electrocardiographic exercise test results were not used in the probability calculations. Resting electrocardiograms and comparative tracings were reviewed. Pertinent past medical history and laboratory results also were reviewed from the medical record. Data on prior exercise testing, cardiac catheterization, surgery, and hospitalizations also were gathered. Consecutive patients sent for nuclear exercise tests over a 1-yr period who had a complete pre-test cardiologic evaluation were included in this analysis.

Nuclear exercise tests then were performed using standard procedures (*3,10*) and the results were mailed to the referring physicians. A return postcard asking whether they planned to perform catheterization as a result of the nuclear exercise test findings was included with the test results.

Statistical Analyses (Reference 11)

Patients were prospectively divided into four likelihood groups: patients with documented prior infarction or disease at coronary angiography were considered to have known disease, or a 100% likelihood for disease. The remaining patients were categorized by age, gender, and anginal symptoms into low (<11%); intermediate (11–90%); or high (>90%<100%) likelihoods for disease. These groupings define important clinical subgroups: asymptomatic and nonanginal chest pain for the low probability group; atypical chest pain for the intermediate probability group; typical angina for the high probability group. Comparisons among the four disease-likelihood categories were done using the chi-square statistic for discrete variables.

RESULTS

Patient Demographics

Pre-test data were available for 378 of 391 patients (mean age 54 yr, 65% male). Ninety-four percent were outpatients. One hundred ninety-nine patients underwent exercise thallium scintigraphy while 179 underwent exercise radionuclide ventriculography. Figure 1 shows that the pre-test probability distribution of patient referrals for these two procedures was virtually identical. The distribution of referrals by pre-test likelihood of disease for both tests was U-shaped, with a concentration of patients in the low and high likelihood categories (i.e., asymptomatic or nonanginal chest pain and typical angina or known disease). Since there were no significant differences in patient clinical characteristics or referring physician management objectives by test type (*12*), the two nuclear exercise tests were combined in subsequent analyses.

Referring physicians responded that 25% of their patients had no symptoms suggestive of coronary disease, and 75% had chest discomfort (Fig. 2). Only 14% of symptomatic patients were believed to have typical angina, while two-thirds of the patients complaining of chest discomfort were deemed to have atypical chest pain by referring physicians. Seventy-one percent of responding physicians stated that they were treating their patients with standard antianginal medications and 77% were using the test to confirm the clinical diagnosis of coronary disease or determine its severity under the assumption that disease was present.

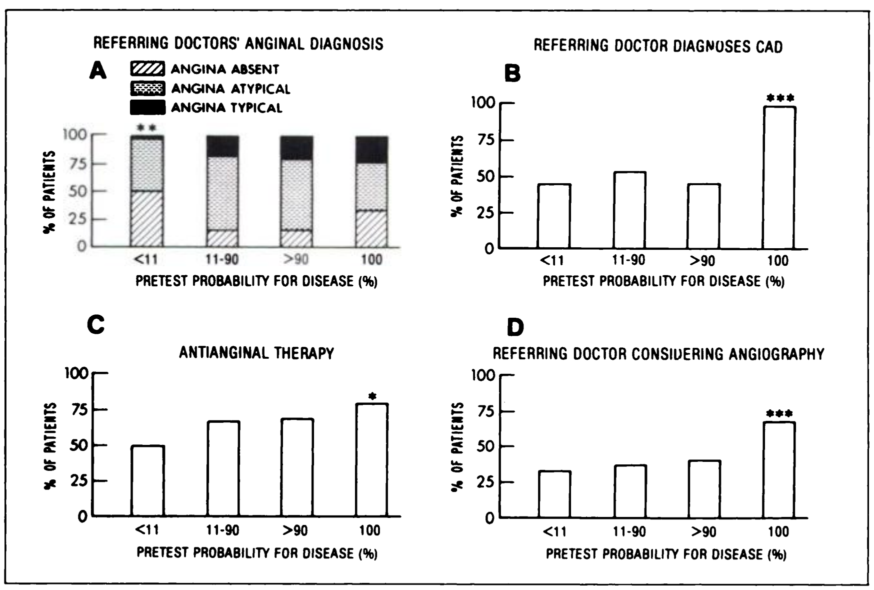

FIGURE 2. Referring physician: (A) anginal diagnosis; (B) presumes coronary artery disease is present; (C) prescribes antianginal therapy; and (D) contemplates angiography as a function of the patients' pretest probability for CAD. Physicians rarely believed that patients with probabilities for disease of <11% had typical angina, yet diagnosed CAD, prescribed antianginal therapy, and considered catheterization as often for these patients as for patients with high likelihoods for disease. Only patients with "proven" disease (100%) were treated differently. Abbreviations: CAD = coronary artery disease. $^*p < 0.05$; $^{**}p < 0.025$; $^{***}p < 0.001$ versus other likelihood categories.

Analysis by Probability Grouping

Of the 378 patients seen by the project staff, 108 had prior infarction or angiographic coronary disease, whereas 270 did not. Only 12 patients in all had previously undergone angiography. Table 1 and Figure 2A–D illustrate the referring physicians' diagnostic opinions and management plans as a function of the pre-test likelihood for disease. Referring physicians were less likely than project cardiologists to diagnose typical angina (Fig. 2A). Only 2% of patients with disease likelihoods <=10% were considered to have typical angina by referring doctors ($p < 0.025$ versus other likelihood groupings). Despite this, referring physicians were willing to diagnose coronary disease in approximately 50% of all patients without proven disease with no relationship to the pre-test likelihood for disease (Fig. 2B). Prescription of antianginal medications and consideration of the need for future angiography also bore no relationship to the pre-test likelihood for disease, with the only distinctions based on whether or not the patient had a prior infarction or disease at prior angiography (Fig. 2C–D).

Other variables that have known prognostic and diagnostic importance were examined to determine if they differed significantly by likelihood category, and thus might increase referring physicians' index of suspicion for coronary disease among the low likelihood patients. Referring physicians rarely diagnosed suspected prior infarction or left ventricular dysfunction in patients without proven disease. Furthermore, few patients were believed to have heart failure or cardiomegaly (Table 1).

TABLE 1
Data from Referring Physician about His or Her Patients

Variable	Likelihood for coronary disease <0.11	0.11–0.90	>0.90	1.00
Testing to:				
Rule in disease	45%	49%	45%	26%*
Determine disease severity	19%	22%	37%	72%
Confirm absence of disease	36%	29%	18%	2%
Testing to determine:				
Need for CABG	30%	31%	32%	66%*
If feasible to continue current treatment	51%	43%	41%	17%
Whether drugs should be modified	19%	26%	27%	17%
Previous infarction?				
No	95%	92%	91%	17%
Maybe	5%	8%	9%	6%
Yes	—	—	—	77%*
Heart Failure	4%	5%	8%	7%
Left ventricle enlarged	8%	8%	13%	21%†
Rest EF abnormal	11%	20%	9%	38%†
Exercise response expected to be abnormal	41%‡	54%	64%	85%*

Percentages are column percent. Only yes or no answers allowed except for questions regarding previous MI and purpose in testing.

CABG = coronary artery bypass grafting; EF = ejection fraction.

*,† $p < 0.001$, $p < 0.05$, respectively, for known (likelihood for disease = 1.00) versus suspected coronary disease (likelihood for disease <1.00).

‡ $p = 0.04$ for low disease likelihood versus intermediate and high disease likelihood categories.

TABLE 2
Selected Variables from Pre-test Cardiologic Evaluation

Variable	Likelihood for coronary disease <0.11	0.11–0.90	>0.90	1.0
History for hypertension	45%	48%	54%	56%
Hypercholesterolemia	9%	23%	23%	25%
Cigarette smoking	38%†	29%	14%	28%
Resting electrocardiogram				
LVH	7%	8%	9%	8%
Nonspecific ST-T changes	29%†	50%	45%	76%
Q-wave infarction	—	—	—	56%*
Prior exercise electrocardiographic stress test				
Yes	21%	14%	30%	24%
Ischemia present	33%	41%	13%	46%
Ischemia absent	33%	41%	60%	35%
Other‡	33%	18%	27%	19%

Percentages are column percent.

LVH = Left ventricular hypertrophy.

* $p < 0.001$ for known (likelihood for disease = 1.00) versus suspected coronary disease (likelihood for disease <1.00).

† $p < 0.02$ for low disease likelihood versus intermediate and high disease likelihood categories.

‡ Other = uninterpretable or inconclusive results.

The resting electrocardiogram was diagnostic of prior infarction in 56% of patients with proven coronary disease, but by definition, in none of these with <100% disease likelihood. Left ventricular hypertrophy or a conduction disturbance that could produce uninterpretable electrocardiographic exercise tests were seen infrequently (Table 2). Nonspecific ST-T-wave changes (usually ST sagging) were noted often, less frequently among patients with low likelihoods for disease than among those with higher likelihoods or proven disease (Table 2). A history for one, but not for multiple cardiac risk factors, was common, slightly more so among patients with low likelihoods for disease than among patients with higher likelihoods for disease (Table 2). Single cardiac risk factors do not significantly raise the likelihood for disease in the low prevalence population (*13*). Table 2 also shows the results of electrocardiographic exercise tests done prior to the referral for nuclear exercise tests. Only 20% of patients had previously undergone this procedure, with no significant difference in utilization or result by pre-test probability of disease. Only four patients in the low likelihood group had abnormal prior electrocardiographic exercise tests.

Impact of Tests on Perceived Need for Catheterization

The response rate to the questionnaire on post-test plans for catheterization was 49% (187 responses out of 378). Although a limited sample, there were no significant differences in referring physician or patient characteristics between the responders and nonresponders (*6*). Nuclear exercise tests did significantly reduce the perceived need for catheterization among all the patient groups, rather uniformly among patients without prior infarction or angiographically confirmed disease, and to a greater extent among patients with known disease ($p < 0.001$) (Fig. 3).

DISCUSSION

This study confirms previous reports that nuclear exercise tests are a valuable decision-making tool (*14,15*), reducing the perceived need for catheterization at all levels of pre-test probability of disease. The greatest reduction was seen among patients with proven disease, again supporting recent reports on an evolution from a diagnostic tool to a means of assessing prognosis and choosing among therapeutic options (*15*). At the other extreme, however, 15% of patients tested had likelihoods for disease of <11%. In these patients, natural history studies would suggest that no testing, or at most electrocardiographic exercise testing, would suffice for these purposes (*16*).

What accounts for this generalization of an expensive technology to a low risk subgroup? First, the evaluation of patients for possible ischemic heart disease is a particularly difficult problem since the only clinical presentation of the disease can be an infarction or sudden death (*17*). There may be dire consequences if the diagnosis is missed. Second, when a patient does have symptoms of chest discomfort, they may not be suggestive of typical angina pectoris, and there is certainly inter-physician variability in the diagnosis of even typical angina. Thus, although the history for chest pain has proven efficacy in predicting patient prognosis and the results of coronary arteriography (*2,3,9,18,19*), our data indicate that referring physicians do not have sufficient confidence in the history they themselves elicit to avoid treating these atypically symptomatic patients as if coronary disease were present. Third, electrocardiographic exercise testing was not an acceptable alternative to nuclear exercise testing in enhancing diagnostic confidence, since only 20% of patients had previously undergone this procedure (Table 2). If testing was necessary beyond the clinical evaluation, electrocardiographic stress testing could be recommended among the low prevalence patients, and electrocardiographic or nuclear exercise testing for the remaining patients. Our data on diagnosis and treatment suggest that referring physicians did not use electrocardiographic stress testing because they did not identify a low risk population in their initial evaluation. All clinical presentations as defined by our likelihood groupings were uniformly treated, with even the low likelihood patients often presumed to have disease. Viewed from this perspective of high risk, the more sensitive test (nuclear exercise test) would be required to exclude disease.

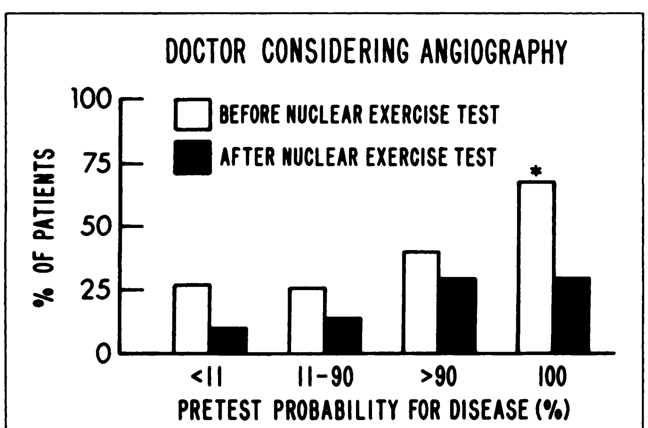

FIGURE 3. Referring physicians' pre- and post-nuclear exercise test plans for cardiac catheterization. Nuclear exercise tests reduced the perceived need for catheterization among all probability groupings, but more so for patients with proven disease. * = $p < 0.001$ versus other probability groupings.

Potential limitations to the present investigation should be addressed. Although it is not known how widespread these management practices are, a large patient and physician population from four hospitals that provide much of the care for over 1.2 million people was studied. It is possible that a selection bias for nuclear exercise test referral was responsible for the rather homogenous treatment the patients received regardless of disease likelihood or angina diagnosis. This was an outpatient population that waited two to three weeks for testing due to limited resources. However, during a thorough patient interview, examination, and search of past medical records, no clinical or test variables were discovered that would significantly alter the likelihood for disease beyond that obtained from patient age, sex, and symptoms.

The validity of the referring physician data is highly dependent on their understanding of the referral questionnaire and the care they took in completing it. The questionnaire was introduced at least three months prior to the start of the study, and repeatedly explained to the participating physicians. Objective data on the questionnaire pertaining to drug therapy and prior infarction was checked against information gathered by the project cardiologists and found to be highly concordant. There was substantial disagreement in the anginal history obtained by referring doctors and project cardiologists. Studies comparing the Rose questionnaire for angina with clinical judgement also have reported variability in angina diagnosis (*20,21*), but similar overall accuracy for the presence of coronary disease or a clinical event. Finally, we do not have data on how test results impacted on physicians' judgements regarding medical therapy or long-term follow-up to determine which patients eventually underwent catheterization after the nuclear exercise test.

In conclusion, physicians used nuclear exercise tests to assess a broad spectrum of patient presentations for ischemic heart disease. Referring physicians' actions indicated that they considered these patients to be homogenous with respect to disease risk, unless the patients had previously undergone angiography or had an infarction. Many explanations have been advanced to explain the proliferation of new diagnostic technologies beyond their original justifications. These include financial incentives, the technologic imperative (test because it is there), misunderstanding of how disease prevalence impacts on the predictive value of test results, the need to know, and fear of malpractice (*12,22*). We suggest additional explanations. Although clinicians and clinical researchers in the current study were assessing the same patients, they did not agree in their diagnoses of the patients' presenting complaints. Further studies are required to determine whether clinical judgement, questionnaires, or both for the diagnosis of angina produce the highest diagnostic accuracy, not only among clinical researchers, but more importantly among practicing physicians. At present, the referring physician is not sufficiently confident in the information derived from the preliminary evaluation to begin the process of risk stratification. Without this initial estimate of disease likelihood, a rational choice between no testing, or electrocardiographic or nuclear exercise tests could not be made. The physicians erred on the side of greater sensitivity and chose the nuclear exercise test. If this pattern continues, it may be inevitable that the next "more accurate" and likely more expensive noninvasive technology will supplant these nuclear exercise tests in the evaluation of a broad range of patients.

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(Appendix follows on next page)

CARDIOVASCULAR STUDIES: THE FOLLOWING MUST BE COMPLETED

A. EXAMINATION REQUESTED:
1. ☐ EF + Wall Motion 3. ☐ With Stress
2. ☐ Perfusion (Thallium) 4. ☐ With Stress
5. ☐ Other ______

B. REASON FOR STUDY (CHECK ONE):
1. ☐ Confirm Absence of Disease
2. ☐ Confirm Presence of Disease
3. ☐ Determine Severity of Disease
4. ☐ Monitor Therapy

C. STUDY IS TO DETERMINE NEED/ FEASIBILITY TO:
1. ☐ Continue Present Management
2. ☐ Modify Drug Therapy
3. ☐ Catheterize/Possible Surgery

D. SUSPECTED HEART DISEASE(S):
1. ☐ Ischemic
2. ☐ Congenital
3. ☐ Hypertensive Heart Disease
4. ☐ Valvular
5. ☐ Primary Myocardial
6. ☐ Other

E. ANGINA IS:
1. ☐ Absent 3. ☐ Atypical
2. ☐ Typical

IF PRESENT, CHOOSE ONE:
1. ☐ New Onset 3. ☐ Increasing Frequency and/or Severity
2. ☐ Stable

F. PREVIOUS MYOCARDIAL INFARCTION:
1. ☐ No 2. ☐ Yes 3. ☐ Maybe

G. CONGESTIVE HEART FAILURE:

	1 NO	2 YES MILD	3 YES MODERATE	4 YES SEVERE	5 MAYBE
Left					
Right					

H. PATIENT IS:
1. ☐ Asymptomatic 2. ☐ Symptomatic

SYMPTOMATIC FOR:

Angina:
1. ☐ At Rest 2. ☐ Minimal Exertion 3. ☐ Extreme Exertion

Dyspnea:
1. ☐ At Rest 2. ☐ Minimal Exertion 3. ☐ Extreme Exertion

I. ON DRUG THERAPY:
1. ☐ No 5. ☐ Anti-CHF
2. ☐ Anti-Anginals 6. ☐ Cardiotoxins
3. ☐ Antihypertensives 7. ☐ Other ______
4. ☐ Anti-Arrhythmics

J. DO YOU SUSPECT:

LEFT VENTRICLE (AT REST) I A

Size	1. ☐ Normal	2. ☐ Large
Regional Abnormalities	1. ☐ Absent	2. ☐ Present
Aneurysm	1. ☐ No	2. ☐ Yes
Ejection Fraction	1. ☐ < 30	2. ☐ 30 – 49
	3. ☐ 50 – 75	4. ☐ > 75

RESPONSE TO STRESS B
1. ☐ Normal 2. ☐ Abnormal

PERFUSION C

Rest	1. ☐ Normal	2. ☐ Abnormal
Stress	1. ☐ Normal	2. ☐ Abnormal

RIGHT VENTRICLE (AT REST) II

Size	1. ☐ Normal	2. ☐ Large
Function	1. ☐ Normal	2. ☐ Abnormal

REQUESTED BY ☐ ATTENDING ☐ HOUSE STAFF

PRINT SIGN DATE

FILLED OUT BY ☐ ATTENDING ☐ HOUSE STAFF

PRINT SIGN DATE

APPENDIX