ORIGINAL INVESTIGATION

Yield of Routine Provocative Cardiac Testing Among Patients in an Emergency Department–Based Chest Pain Unit

Luke K. Hermann, MD; David H. Newman, MD; W. Andrew Pleasant, MD; Dhanadol Rojanasarntikul, MD; Daniel Lakoff, MD; Scott A. Goldberg, MD; W. Lane Duvall, MD; Milena J. Henzlova, MD

Importance: The American Heart Association recommends routine provocative cardiac testing in accelerated diagnostic protocols for coronary ischemia. The diagnostic and therapeutic yield of this approach are unknown.

Objective: To assess the yield of routine provocative cardiac testing in an emergency department–based chest pain unit.

Design and Setting: We examined a prospectively collected database of patients evaluated for possible acute coronary syndrome between March 4, 2004, and May 15, 2010, in the emergency department–based chest pain unit of an urban academic tertiary care center.

Participants: Patients with signs or symptoms of possible acute coronary syndrome and without an ischemic electrocardiography result or a positive biomarker were enrolled in the database.

Exposures: All patients were evaluated by exercise stress testing or myocardial perfusion imaging.

Main Outcomes and Measures: Demographic and clinical features, results of routine provocative cardiac testing and angiography, and therapeutic interventions were recorded. Diagnostic yield (true-positive rate) was calculated, and the potential therapeutic yield of invasive therapy was assessed through blinded, structured medical record review using American Heart Association designations (class I, IIa, IIb, or lower) for the potential benefit from percutaneous intervention.

Results: In total, 4181 patients were enrolled in the study. Chest pain was initially reported in 93.5%, most (73.2%) were at intermediate risk for coronary artery disease, and 37.6% were male. Routine provocative cardiac testing was positive for coronary ischemia in 470 (11.2%), of whom 123 underwent coronary angiography. Obstructive disease was confirmed in 63 of 123 (51.2% true positive), and 28 (0.7% overall) had findings consistent with the potential benefit from revascularization (American Heart Association class I or IIa).

Conclusions and Relevance: In an emergency department–based chest pain unit, routine provocative cardiac testing generated a small therapeutic yield, new diagnoses of coronary artery disease were uncommon, and false-positive results were common.

JAMA Intern Med. 2013;173(12):1128-1133.
Published online May 20, 2013.
doi:10.1001/jamainternmed.2013.850

Author Affiliations: Department of Emergency Medicine (Drs Hermann, Newman, Pleasant, Rojanasarntikul, Lakoff, and Goldberg) and Division of Cardiology, Department of Internal Medicine (Drs Duvall and Henzlova), Mount Sinai School of Medicine and Mount Sinai Medical Center, New York, New York. Dr Rojanasarntikul is now with the Department of Emergency Medicine, King Chulalongkorn Memorial Hospital, Chulalongkorn University, Bangkok, Thailand.

CHEST PAIN AND OTHER symptoms that may represent cardiac ischemia are common reasons for emergency department (ED) visits. The American Heart Association (AHA)[1] recommends a strategy that incorporates provocative cardiac testing into the evaluation of this patient group, to further risk stratify patients who have negative results on cardiac biomarker testing and to identify patients who may benefit from revascularization. However, emerging literature suggests that this group is one that may not benefit from further risk stratification.[2-4] Therefore, the identification of patients who have obstructive coronary artery disease (CAD) and patients who could potentially benefit from revascular-

CME available online at jamanetworkcme.com and questions on page 1046

See Invited Commentary at end of article

See also page 1056

ization may become an increasingly important rationale for routine provocative testing in this population.

Recently published consensus guidelines outline coronary anatomic features associated with the potential benefit of provocative testing (AHA class I or IIa) and features associated with a lack of benefit or harm (AHA class IIb or III).[5] Using data from a chest pain unit population during a 6-year period, we applied this classification to identify the number and proportion of cases in which an accelerated diagnostic pathway with provocative testing led to the accurate detection of obstructive coronary disease. We hypothesized that both the potential therapeutic yield and the diagnostic yield of routine provocative testing in the chest pain observation unit would be low.

METHODS

STUDY DESIGN

We examined a prospectively collected database of ED patients with potential ischemic chest pain admitted to the ED chest pain unit and used formal medical record review methods applied to a post hoc question examining the proportion and nature of coronary angiography findings and percutaneous coronary interventions performed. The study was approved by the institutional review board of the Mount Sinai Medical Center.

SETTING

Initial data collection was conducted in the noninvasive cardiology laboratory of an urban academic tertiary care center between March 4, 2004, and May 15, 2010. The annual ED census was between 80 000 and 100 000 patients during this period, and the chest pain unit evaluated more than 700 patients annually for potential acute coronary syndrome.

ELIGIBILITY CRITERIA

All patients without a known history of CAD who were admitted to the chest pain unit for the evaluation of possible acute coronary syndrome and who completed provocative testing during the study period were considered eligible for study. Admission criteria for the chest pain unit are based on previously published risk factors for adverse events among ED patients.[6] The attending emergency physician determined the probability of major adverse events related to myocardial ischemia according to initial symptoms based on the presence or absence of the following published high-risk features: clinical evidence of heart failure, worsening of previously stable angina, initial systolic blood pressure of 100 mm Hg or higher, pain the same as with a previous myocardial infarction, electrocardiography (ECG) evidence of myocardial ischemia or infarction (new or not known to be old), ST-segment depression of more than 0.1 mV measured 80 milliseconds from the J point or inverted T waves of more than 0.3 mV, and ST-segment elevation of more than 0.1 mV measured 80 milliseconds from the J point in 2 or more contiguous leads or Q waves of 30 milliseconds and 0.1 mV in depth. There were no upper or lower age limits for study inclusion eligibility.

Briefly, the chest pain unit protocol as initiated by the emergency physician includes serial ECG, telemetry monitoring, serial serum troponin measurements, and (following 2 sets of negative serum troponins during a 6-hour period) provocative cardiac testing. The specific testing modality is chosen by the cardiologist in charge of the service at the time of evaluation. By laboratory protocol, patients younger than 50 years who are capable of exercise and have no exclusionary baseline ECG abnormalities first undergo exercise ECG testing without imaging. If the result of the exercise ECG study is positive (defined as ≥1-mm horizontal or downsloping ST segment depression in 3 consecutive beats occurring >80 milliseconds after the J point), the patient receives a dose of intravenous sestamibi isotope, and stress myocardial perfusion imaging is performed.

Standard imaging, exercise, and pharmacologic protocols as defined by the American Society of Nuclear Cardiology[7] were used. Exercise testing was performed according to the Bruce or modified Bruce protocol, with heart rate, blood pressure, and 12-lead ECG recorded before, during, and after exercise. Exercise was terminated for limiting cardiac symptoms or for greater than 2-mm horizontal or downsloping ST-segment depression measured 80 milliseconds after the J point over at least 3 consecutive beats.

A cardiologist interpreted all provocative studies in accord with American Society of Nuclear Cardiology[7] guidelines. A normal myocardial perfusion imaging study was defined as the absence of perfusion defects on stress images considered a summed stress score of less than 3. Per unit protocol, patients with abnormal provocative studies (any study not read by the interpreting cardiologist as "no evidence for inducible ischemia") were evaluated by the cardiology service, and an individualized determination was made regarding coronary angiography and potential percutaneous intervention vs admission for further management vs discharge with a plan for medical management and outpatient follow-up observation.

OUTCOMES

Our primary aims were to assess the proportion of overall observation unit patients found to have newly diagnosed anatomic coronary disease for which revascularization would be considered beneficial (AHA class I or IIa), as well as the proportion deemed to have coronary disease for which revascularization would be nonbeneficial or harmful (AHA class IIb or III). As secondary aims, we planned to characterize the nature of suggested benefits and to describe diagnostic yield according to the criterion standard (coronary angiography) for the diagnosis of obstructive CAD. We defined this as the proportion of positive and negative results on coronary angiography following a positive result on nuclear stress testing. While this meant that only a fraction of patients with positive stress test results would be included (because most do not undergo angiography), we chose this outcome because it was likely to represent an overestimate of accuracy based on the established selection biases inherent in referral for coronary angiography[8-10] and would be a conservative (ie, optimistic) assessment of the accuracy of positive findings on stress imaging in the overall cohort.

DATA COLLECTION

Prospective

All patients undergoing provocative testing were approached before stress testing by a trained cardiology nurse or cardiology fellow. All data were collected using a structured data form, including information on symptoms, presentation, medical history, ECG findings, demographic information, and traditional cardiac risk factors (**Table 1**). Pretest probability of CAD (very low, low, intermediate, or high) was determined on the basis of American College of Cardiology and AHA guidelines.[11]

Table 1. Prospective Data Collection

Patient Demographic	Value (N = 4181)
Age, mean, y	55
Sex, No. (%)	
Male	1570 (37.6)
Female	2611 (62.4)
Cardiac risk factors, No. (%)	
Diabetes mellitus	858 (20.5)
Hypertension	2340 (56.0)
Hyperlipidemia	1584 (37.9)
Family history of CAD	498 (11.9)
Smoking	2013 (48.1)
Pretest probability of CAD, No. (%)[a]	
Very low	149 (3.6)
Low	651 (15.6)
Intermediate	3062 (73.2)
High	319 (7.6)
Initial symptoms, No. (%)	
Chest pain	3908 (93.5)
Shortness of breath	2464 (58.9)
Type of stress test, No. (%)	
Stress ECG alone	517 (12.4)
Perfusion imaging	3664 (87.6)
Stressor, No. (%)	
Exercise	2581 (61.7)
Pharmacologic	1600 (38.3)
Perfusion results, No. (%)	(n = 3664)
Normal	3194 (87.2)
Abnormal	470 (12.8)

Abbreviations: CAD, coronary artery disease; ECG, electrocardiogram.
[a] Adapted from Gibbons et al.[11] Very low is less than 5%, low is 5% to 10%, intermediate is greater than 10% to 90%, and high is greater than 90%.

As part of initial data collection, patients were followed up to determine if coronary angiography or further cardiac imaging studies had been performed. A summed stress score (a validated mechanism for quantifying ischemic myocardium found on perfusion imaging[12]) was calculated and documented for each patient.

Medical Record Review

Because one of our primary study questions was generated after the prospective data collection mechanism was constructed, we undertook a formal review of data elements to minimize bias. Data were reviewed and abstracted from the study database by research assistants blinded to study hypothesis. Assistants were trained by one of us (W.A.P.) during a detailed training session, including familiarization with the database, definition of all terms, and group review of the data form. Following abstraction, 10% of data points were reabstracted by the trainer (W.A.P.) and reviewed for accuracy. No elements of disagreement were found between abstractors and the trainer. Three investigators (W.A.P., D.L., and S.A.G.) performed a review of cases for designation according to the AHA guideline classification of benefit vs nonbenefit, and disagreements were resolved by consensus and rereview.

STATISTICAL ANALYSIS

We used simple descriptive statistics with 95% CIs for all proportions. $P < .05$ was considered statistically significant for all comparisons.

RESULTS

A total of 4181 patients (age range, 22-97 years) met eligibility criteria, underwent stress testing (512 ECG stress tests and 3669 perfusion imaging studies), and were analyzed in the study (**Figure**). Of these, 470 (11.2%) had provocative studies that were positive for inducible myocardial ischemia. Of these 470 patients, 123 (26.2%) underwent subsequent coronary angiography, while 347 patients (73.8%) (after evaluation by a cardiologist) were discharged home with a presumptive diagnosis of CAD and a plan for medical management (**Table 2**). These 2 groups (catheterization vs discharge) were compared by age, the number of traditional cardiac risk factors, and the mean summed stress score difference (percentage of inducible ischemic myocardium by imaging study) (Table 2 and **Table 3**). Only the mean summed stress score difference was significantly different between the groups and was higher among the group that underwent cardiac catheterization (11.1% [95% CI, 9.4%-12.6%] vs 5.1% [95% CI, 5.5%-6.5%]).

Among 123 patients who underwent coronary angiography, 63 had obstructive disease (≥50% left main CAD or ≥70% non–left main CAD) (**Table 4**), which was further classified according to AHA criteria as follows: 28 patients were classified as having disease that would potentially benefit from revascularization (AHA class I or IIa), 9 as uncertain benefit (AHA class IIb), and 26 as harm (AHA class III). Among 59 patients who underwent catheterization but had no obstructive disease, 31 had normal angiography findings, while 28 had nonobstructive disease.

DISCUSSION

The yield of provocative cardiac testing in the chest pain unit, as defined by the ability to identify obstructive disease with the potential to benefit from revascularization and the predictive values of the test, was extremely low. While AHA guidelines suggest that provocative testing risk stratifies patients to a potentially near-zero short-term adverse event rate, there is increasing recognition that a negative result on serial biomarker evaluation (typically a prerequisite for provocative testing) may also achieve this goal, making further risk stratification attempts redundant or inherently difficult.[2-4,13] Therefore, the potential therapeutic and diagnostic yield of provocative testing may take on an increasingly central role in determining the usefulness of provocative testing for low-risk and moderate-risk patients with chest pain evaluated in accelerated diagnostic protocols.

For the objectives of our study, we defined a potentially beneficial revascularization as one occurring in a patient for whom coronary anatomic features suggested a class I or IIa recommendation by recently published AHA criteria. The class of AHA recommendation for each anatomic variant of obstructive disease differs based on the revascularization technique used (coronary artery bypass graft vs percutaneous coronary intervention). For the purposes of establishing benefit in our study, the highest potential class of recommendation for each anatomic variant was chosen by default. Among 4181 patients referred to the chest pain unit for an accelerated

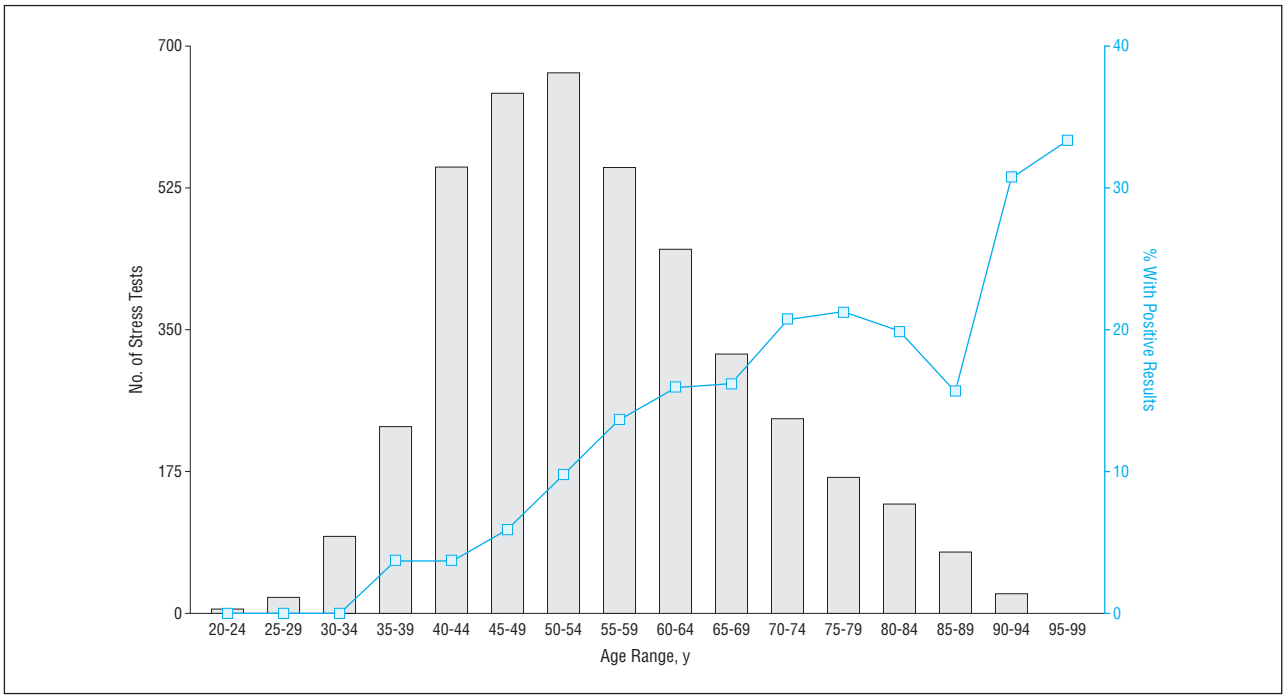

Figure. Number of stress tests and percentage with positive results by age range.

Table 2. Among the Overall Cohort, 470 Patients for Whom Routine Provocative Cardiac Testing Was Positive for Coronary Ischemia and 347 Patients Who Were Discharged Home With a Presumptive Diagnosis of CAD and a Plan for Medical Management

Patient Demographic	Overall Cohort (N = 4181)	Positive Result on Provocative Testing (n = 470)	Discharged Home (n = 347)	Coronary Angiographies Among Patients With Positive Result on Provocative Testing		
				Overall (n = 123)	Positive Result (n = 63)	Negative Result (n = 60)
Age, mean, y	55	62	63	60	61	59
Sex, No./total No. (%)						
Male	1570/4181 (37.6)	234/470 (49.8)	162/347 (46.7)	72/123 (58.5)	40/63 (63.5)	28/60 (46.7)
Female	2611/4181 (62.4)	236/470 (50.2)	185/347 (53.3)	51/123 (41.5)	23/63 (36.5)	32/60 (53.3)
Framingham risk factors, mean, No.	2.0	2.0	2.0	2.0	2.4	1.8
Pretest probability of CAD, No./total No. (%)[a]						
Very low	149/4181 (3.6)	5/470 (1.1)	4/347 (1.2)	1/123 (0.8)	1/63 (1.6)	0/60
Low	651/4181 (15.6)	32/470 (6.8)	26/347 (7.5)	6/123 (4.9)	2/63 (3.2)	4/60 (6.7)
Intermediate	3062/4181 (73.2)	362/470 (77.0)	269/347 (77.5)	93/123 (75.6)	48/63 (76.2)	45/60 (75.0)
High	319/4181 (7.6)	73/470 (15.5)	48/347 (13.8)	23/123 (18.7)	12/63 (19.0)	11/60 (18.3)
Summed stress score difference, mean	Not available	6	5	9	11	8

Abbreviation: CAD, coronary artery disease.
[a] Adapted from Gibbons et al.[11]

diagnostic protocol, less than 1% could potentially benefit according to AHA revascularization criteria. A statistically equivalent proportion (<1%) was found to have anatomic disease for which revascularization would lead to harm according to criteria. This seems to be consistent with an increasing evidence base suggesting that revascularization may offer little or no benefit compared with medical management for many patients with obstructive CAD.[14,15] Moreover, our cohort (patients having acute chest pain with negative serial biomarker results) represents a group for whom prior meta-analyses[15,16] suggest no benefit from invasive therapy and who may experience increased mortality.

Most importantly, the potential to identify obstructive CAD to guide future management may, in some cases, be considered reason enough to include provocative testing as a routine part of screening for acute coronary syndrome. However, this potential benefit must be precisely delineated and ultimately weighed against the potential harms inherent to testing, including considerations such as radiation exposure, false-positive results, adverse effects (eg, nephropathy), and resource utilization.[17]

Among 4181 patients in our study without known CAD, only 28 patients had CAD meeting guideline criteria for revascularization at the conclusion of their diagnostic evaluation, while 347 patients had a positive pro-

Table 3. Coronary Angiography Results by Patient Age, Sex, the Number of Framingham Risk Factors, Pretest Probability of CAD, and the Summed Stress Score Difference

Patient Demographic	Positive Result on Coronary Angiography (n = 63)	Unprotected Left Main CAD (n = 7)	3-Vessel CAD (n = 15)	2-Vessel CAD With Proximal LAD (n = 4)	2-Vessel CAD Without Proximal LAD (n = 13)	1-Vessel CAD With Proximal LAD (n = 4)	1-Vessel CAD Without Proximal LAD (n = 26)
Age, mean, y	61	58	62	62	60	57	63
Sex, No./total No. (%)							
Male	40/63 (63.5)	5/7 (71.4)	10/15 (66.7)	3/4 (75.0)	9/13 (69.2)	2/4 (50.0)	14/26 (53.8)
Female	23/63 (36.5)	2/7 (28.6)	5/15 (33.3)	1/4 (25.0)	4/13 (30.8)	2/4 (50.0)	12/26 (46.2)
Framingham risk factors, mean, No.	2.3	2.9	2.2	2.3	2.5	1.5	2.3
Pretest probability of CAD, No./total No. (%)[a]							
Very low	1/63 (1.6)	1/7 (14.3)	1/15 (6.7)	0/4	0/13	0/4	0/26
Low	5/63 (7.9)	0/7	1/15 (6.7)	0/4	1/13 (7.7)	0/4	1/26 (3.8)
Intermediate	46/63 (73.0)	5/7 (71.4)	11/15 (73.3)	3/4 (75.0)	10/13 (76.9)	2/4 (50.0)	21/26 (80.8)
High	11/63 (17.5)	1/7 (14.3)	2/15 (13.3)	1/4 (25.0)	2/13 (15.4)	2/4 (50.0)	4/26 (15.4)
Summed stress score difference, mean	11	19	14	15	11	22	6

Abbreviations: CAD, coronary artery disease; LAD, left anterior descending coronary artery.
[a] Adapted from Gibbons et al.[11]

Table 4. Yield of Routine Provocative Cardiac Testing Before Discharge Among Patients in the Emergency Department–Based Chest Pain Unit

Variable	No./Total No. (%)
Positive provocative study result	470/4181 (11.2)
Confirmed true positive by angiography	63/123 (51.2)
Confirmed false positive by angiography	60/123 (48.8)
Angiography results	
New diagnosis of obstructive CAD	63/4181 (1.5)
Anatomic disease classified as having potential for benefit via revascularization, AHA class I or IIa	28/4181 (0.7)
Disease classified as AHA class I or IIa if coronary artery bypass graft performed	28/4181 (0.7)
Disease classified as AHA class I or IIa if percutaneous coronary intervention performed	7/4181 (0.2)

Abbreviations: AHA, American Heart Association; CAD, coronary artery disease.

vocative study result that was not followed by catheterization. The decision to undergo catheterization after provocative testing was made by a cardiologist, who evaluated and tailored management for each patient with a positive study result. Although we did not collect these data specifically, presumably patients thought to be at highest risk of significant obstructive CAD were typically referred for angiography, a presumption supported by the significantly higher percentage of ischemic myocardium according to myocardial perfusion imaging in this group. However, in our study this subgroup of presumably higher-risk patients had no evidence of obstructive CAD in almost half the cases and had normal coronary arteries in 25.2%. Patients with positive stress test results who were not referred for angiography seem likely to have an equal or lower incidence of obstructive CAD, which suggests that half or more of patients with positive stress test results in our cohort who did not undergo angiography (approximately 173 patients, or 4.1% of the cohort) were discharged with an erroneous diagnosis of obstructive CAD.

Regarding radiation exposure, despite a protocol that emphasized ECG stress testing alone whenever possible, the presence of exclusionary features for such testing led to the performance of nuclear imaging in 87.6% of our patients. Although radiation exposure was not calculated for this particular cohort, it has been done so in the past at the study institution and in the ED setting.[18,19] Recent literature places the effective dose to the patient of a standard rest-stress myocardial perfusion imaging study at around 11 mSv, with stress-only studies ranging from 3 to 8 mSv depending on administered activity, and upward of 24 mSv for dual-isotope myocardial perfusion imaging studies.[20] By comparison, conventional coronary angiography is reported to impart about 7 mSv.[21] Similarly, although we did not conduct a detailed cost analysis of our protocol, the addition of provocative testing before discharge clearly increased the cost of that visit. In the study institution, an ECG stress test, a myocardial perfusion study, and diagnostic coronary angiography carry charges of $640, $2200, and $6800, respectively.

There are important limitations to our study. All patients were evaluated at a single center; therefore, it is unclear the degree to which these findings can be generalized to other centers. This also meant that interpretation of provocative testing results was performed by a single physician group, and cardiac stress testing may be performed differently in some centers. There was no direct patient follow-up assessment of clinical outcomes or management in the outpatient setting, making it unclear whether patients who were discharged with a pre-

sumptive diagnosis of CAD retained this diagnosis or were treated for this diagnosis. Therefore, it is possible that the diagnosis of CAD as confirmed by provocative testing led to long-term benefits via the initiation of medical management for the disease. In addition, a substantial proportion of patients in our cohort did not undergo coronary angiography, rendering criterion standard determination of anatomic disease unavailable. However, this shortcoming may also represent a more pragmatic, real-world approximation of patient management decisions in chest pain unit settings. Furthermore, we used coronary angiography as our criterion standard, while emerging technologies (including intravascular ultrasonography and fractional flow reserve calculation) may at some point eclipse this modality. Finally, our review of the examination of the potential benefit vs nonbenefit based on coronary anatomy represents a medical record review design and the inherent biases associated with this. We addressed this problem by ensuring abstractor blinding and all other available bias-minimizing procedures available to medical record review methods. In addition, the concrete nature of the primary outcome in this portion of the study (coronary anatomy findings on angiography) suggests that typical medical record review biases should not have appreciably affected our findings.

In conclusion, we evaluated a large, single-center cohort of ED chest pain unit patients undergoing an accelerated diagnostic protocol and provocative cardiac testing. Few patients were found to have CAD meeting guideline criteria for revascularization, few were newly diagnosed as having obstructive CAD, and false-positive results were common.

Accepted for Publication: January 21, 2013.
Published Online: May 20, 2013. doi:10.1001/jamainternmed.2013.850
Correspondence: Luke K. Hermann, MD, Department of Emergency Medicine, Mount Sinai School of Medicine, One Gustave L. Levy Place, PO Box 1149, New York, NY 10029 (luke.hermann@mssm.edu).
Author Contributions: *Study concept and design:* Hermann, Newman, and Rojanasarntikul. *Acquisition of data:* Hermann, Newman, Rojanasarntikul, Lakoff, Goldberg, Duvall, and Henzlova. *Analysis and interpretation of data:* Hermann, Newman, Pleasant, and Lakoff. *Drafting of the manuscript:* Hermann, Newman, Rojanasarntikul, and Lakoff. *Critical revision of the manuscript for important intellectual content:* Hermann, Newman, Pleasant, Rojanasarntikul, Goldberg, Duvall, and Henzlova. *Statistical analysis:* Hermann, Newman, and Lakoff. *Administrative, technical, and material support:* Hermann, Newman, Pleasant, Goldberg, and Duvall. *Study supervision:* Hermann, Rojanasarntikul, Duvall, and Henzlova.
Conflict of Interest Disclosures: None reported.

REFERENCES

1. Amsterdam EA, Kirk JD, Bluemke DA, et al; American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee of the Council on Clinical Cardiology, Council on Cardiovascular Nursing, and Interdisciplinary Council on Quality of Care and Outcomes Research. Testing of low-risk patients presenting to the emergency department with chest pain: a scientific statement from the American Heart Association. *Circulation*. 2010;122(17):1756-1776.
2. Redberg RF. Coronary CT angiography for acute chest pain. *N Engl J Med*. 2012;367(4):375-376.
3. Scheuermeyer FX, Innes G, Grafstein E, et al. Safety and efficiency of a chest pain diagnostic algorithm with selective outpatient stress testing for emergency department patients with potential ischemic chest pain. *Ann Emerg Med*. 2012;59(4):256-264, e3.
4. Kosowsky JM. Approach to the ED patient with "low-risk" chest pain. *Emerg Med Clin North Am*. 2011;29(4):721-727, vi.
5. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions [published correction appears in *Circulation*. 2012;125(8):e412]. *Circulation*. 2011;124(23):e574-e651.
6. Goldman L, Cook EF, Johnson PA, Brand DA, Rouan GW, Lee TH. Prediction of the need for intensive care in patients who come to the emergency departments with acute chest pain. *N Engl J Med*. 1996;334(23):1498-1504.
7. Hansen CL, Goldstein RA, Berman DS, et al. Quality Assurance Committee of the American Society of Nuclear Cardiology. Myocardial perfusion and function single photon emission computed tomography. *J Nucl Cardiol*. 2006;13(6):97-120.
8. Philbrick JT, Horwitz RI, Feinstein AR. Methodologic problems of exercise testing for coronary artery disease: groups, analysis and bias. *Am J Cardiol*. 1980;46(5):807-812.
9. Diamond GA, Rozanski A, Forrester JS, et al. A model for assessing the sensitivity and specificity of tests subject to selection bias: application to exercise radionuclide ventriculography for diagnosis of coronary artery disease. *J Chronic Dis*. 1986;39(5):343-355.
10. Cecil MP, Kosinski AS, Jones MT, et al. The importance of work-up (verification) bias correction in assessing the accuracy of SPECT thallium-201 testing for the diagnosis of coronary artery disease. *J Clin Epidemiol*. 1996;49(7):735-742.
11. Gibbons RJ, Balady GJ, Bricker JT, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). *Circulation*. 2002;106(14):1883-1892.
12. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. *Circulation*. 2003;107(23):2900-2907.
13. Hamm CW, Goldmann BU, Heeschen C, Kreymann G, Berger J, Meinertz T. Emergency room triage of patients with acute chest pain by means of rapid testing for cardiac troponin T or troponin I. *N Engl J Med*. 1997;337(23):1648-1653.
14. Stergiopoulos K, Brown DL. Initial coronary stent implantation with medical therapy vs medical therapy alone for stable coronary artery disease: meta-analysis of randomized controlled trials. *Arch Intern Med*. 2012;172(4):312-319.
15. Hoenig MR, Aroney CN, Scott IA. Early invasive versus conservative strategies for unstable angina and non-ST elevation myocardial infarction in the stent era. *Cochrane Database Syst Rev*. 2010;3(3):CD004815.
16. O'Donoghue M, Boden WE, Braunwald E, et al. Early invasive vs conservative treatment strategies in women and men with unstable angina and non-ST-segment elevation myocardial infarction: a meta-analysis. *JAMA*. 2008;300(1):71-80.
17. Pauker SG, Kassirer JP. The threshold approach to clinical decision making. *N Engl J Med*. 1980;302(20):1109-1117.
18. Duvall WL, Croft LB, Ginsberg ES, et al. Reduced isotope dose and imaging time with a high-efficiency CZT SPECT camera. *J Nucl Cardiol*. 2011;18(5):847-857.
19. Duvall WL, Wijetunga MN, Klein TM, et al. Stress-only Tc-99m myocardial perfusion imaging in an emergency department chest pain unit. *J Emerg Med*. 2012;42(6):642-650.
20. Henzlova MJ, Duvall WL. The future of SPECT MPI: time and dose reduction. *J Nucl Cardiol*. 2011;18(4):580-587.
21. Einstein AJ, Moser KW, Thompson RC, Cerqueira MD, Henzlova MJ. Radiation dose to patients from cardiac diagnostic imaging. *Circulation*. 2007;116(11):1290-1305.