Original Investigation

Comparative Effectiveness of Diagnostic Testing Strategies in Emergency Department Patients With Chest Pain
An Analysis of Downstream Testing, Interventions, and Outcomes

Andrew J. Foy, MD; Guodong Liu, PhD; William R. Davidson Jr, MD; Christopher Sciamanna, MD; Douglas L. Leslie, PhD

IMPORTANCE Patients presenting to the emergency department (ED) with chest pain whose evaluation for ischemia demonstrates no abnormalities receive further functional or anatomical studies for coronary artery disease; however, comparative evidence for the various strategies is lacking and multiple testing options exist.

OBJECTIVE To compare chest pain evaluation pathways based on their association with downstream testing, interventions, and outcomes for patients in EDs.

DESIGN, SETTING, AND PARTICIPANTS Retrospective analysis of health insurance claims data for a national sample of privately insured patients from January 1 to December 31, 2011. Individuals with a primary or secondary diagnosis of chest pain in the ED were selected and classified into 1 of 5 testing strategies: no noninvasive testing, exercise electrocardiography, stress echocardiography, myocardial perfusion scintigraphy, or coronary computed tomography angiography.

MAIN OUTCOMES AND MEASURES The proportion of patients in each group who received a cardiac catheterization, coronary revascularization procedure, or future noninvasive test as well as those who were hospitalized for an acute myocardial infarction (MI) during 7 and 190 days of follow-up.

RESULTS In 2011, there were 693 212 ED visits with a primary or secondary diagnosis of chest pain, accounting for 9.2% of all ED encounters. After application of the inclusion and exclusion criteria, 421 774 patients were included in the final analysis; 293 788 individuals did not receive an initial noninvasive test and 127 986 did, representing 1.7% of all ED encounters. Overall, the percentage of patients hospitalized with an MI was very low during both 7 and 190 days of follow-up (0.11% and 0.33%, respectively). Patients who did not undergo initial noninvasive testing were no more likely to experience an MI than were those who did receive testing. Compared with no testing, exercise electrocardiography, myocardial perfusion scintigraphy, and coronary computed tomography angiography were associated with significantly higher odds of cardiac catheterization and revascularization procedures without a concomitant improvement in the odds of experiencing an MI.

CONCLUSIONS AND RELEVANCE Patients with chest pain evaluated in the ED who do not have an MI are at very low risk of experiencing an MI during short- and longer-term follow-up in a cohort of privately insured patients. This low risk does not appear to be affected by the initial testing strategy. Deferral of early noninvasive testing appears to be reasonable.

JAMA Intern Med. doi:10.1001/jamainternmed.2014.7657
Published online January 26, 2015.

Editor's Note

Author Affiliations: Division of Cardiology, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania (Foy, Davidson); Department of Public Health Sciences, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania (Liu, Leslie); Division of Internal Medicine, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania (Sciamanna).

Corresponding Author: Andrew J. Foy, MD, Division of Cardiology, Penn State Milton S. Hershey Medical Center, 500 University Dr, PO Box 850 H047, Hershey, PA 17033 (afoy@hmc.psu.edu).

Approximately 6 million patients are evaluated in the emergency department (ED) annually for chest pain or other symptoms suggestive of myocardial ischemia. The estimated cost to the US economy for this event is $10 billion to $12 billion.[1,2] Patients without objective evidence of ischemia have been shown[3] to be at low risk for a major adverse cardiovascular event. Most of these patients do not have a cardiac cause for their symptoms, and an optimal management strategy is unknown.[4]

The American Heart Association has endorsed the safety and usefulness of noninvasive cardiac imaging to provoke ischemia or detect anatomical coronary artery disease before or within 72 hours after discharge.[5] However, there is no evidence that noninvasive testing reduces the risk of future cardiac events compared with a more conservative approach. Furthermore, multiple options for noninvasive testing exist, and there may be specific advantages and disadvantages associated with each modality. Exercise electrocardiography (EE) is low cost, does not expose the patient to radiation, and is acceptable as an initial diagnostic strategy in patients capable of exercising whose resting electrocardiogram (ECG) results are interpretable; however, EE lacks sensitivity and specificity in relation to other testing modalities.[6,7] Stress echocardiography (SE) is also relatively low cost, free of radiation exposure, and can be used when the resting ECG results are not interpretable; SE has the highest specificity of all modalities.[7] Myocardial perfusion scintigraphy (MPS) has high sensitivity but exposes the patient to radiation and is of higher cost compared with the other tests.[7] Coronary computed tomography angiography (CCTA) may expedite the triage of low-risk patients with chest pain and has a high sensitivity for detecting anatomical disease; however, it too exposes the patient to radiation.[8,9] The consequences of these differences for patients evaluated in the ED for chest pain may be important, and, to our knowledge, this issue has not yet been explored.

We sought to compare the association between an initial strategy of EE, SE, MPS, CCTA, or no noninvasive testing with downstream cardiac catheterizations, revascularization procedures, future noninvasive imaging tests, and hospitalizations for myocardial infarction (MI). The study was conducted in a national cohort of privately insured patients evaluated in the ED for chest pain.

Methods

Data Sources

The study was approved by the institutional review board at Penn State Milton S. Hershey Medical Center. The study used MarketScan Commercial Claims and Encounters data from January 1 to December 31, 2011. MarketScan, which is constructed and maintained by Truven Health Analytics, consists of reimbursed health care claims for employees, retirees, and their dependents of more than 250 medium- and large-sized employers and health plans from across all 50 states and the District of Columbia. The database includes a population of approximately 58 million and captures administrative claims with patient-level deidentified data from inpatient and outpatient visits and filled prescriptions. Diagnosis codes use the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*). Procedures are identified by *ICD-9-CM* codes in the inpatient files and by *Current Procedural Terminology* (*CPT*) codes in the carrier and outpatient claims files.

Patient Cohort

A raw cohort (cohort A) of claims records for all ED visits was extracted from the 2011 MarketScan outpatient and inpatient database. A subcohort (cohort B) of ED patients with a primary or secondary diagnosis of chest pain (*ICD-9-CM* code 786.50) was extracted from cohort A. A second subcohort (cohort C) was then extracted from cohort B to include patients who underwent 1 of the 4 noninvasive cardiac tests (EE, SE, MPS, and CCTA) as inpatients or outpatients within 7 days of their initial ED visit. The *CPT* codes were used to identify receipt of EE (93015, 93016-93018), SE (93350), MPS (78452), and CCTA (75574). The first anatomical or functional test of coronary artery disease that patients underwent after their ED presentation was termed the *index test* in this study. A third subcohort (cohort D) was extracted from cohort C to exclude patients who developed an MI within 24 hours of the index encounter (*ICD-9-CM* codes 410.0-410.9); who underwent a cardiac catheterization (*CPT* codes 93451-93464 and *ICD-9-CM* codes 37.22-37.23), percutaneous coronary intervention (PCI) (*CPT* codes 92980-92996 and *ICD-9-CM* codes 0.66, 36.01-36.09), or coronary artery bypass graft (CABG) surgery (*ICD-9-CM* codes 36.10-36.19) after the ED visit but before a noninvasive cardiac test was performed; and who did not maintain continuous enrollment during the covered period. From cohort D, a fourth subcohort (cohort E) was extracted, which included all outpatient and inpatient claims records within 1 year before and after the initial noninvasive cardiac test.

A fifth subcohort (cohort F) was extracted from cohort B to include patients who did not receive any of the noninvasive tests described above within 7 days of their initial ED visit. A sixth subcohort (cohort G) was extracted from cohort F that excluded patients who received a primary diagnosis of acute MI (*ICD-9-CM* codes 410.XX) within 24 hours of their index chest pain encounter. This was done to ensure that patients who were admitted for chest pain with a recognized MI were not included in the no-testing cohort. Patients were also excluded from this cohort if they received a cardiac catheterization (*CPT* codes 93451-93464 and *ICD-9-CM* codes 37.22-37.23), PCI (*CPT* codes 92980-92996 and *ICD-9-CM* codes 0.66, 36.01-36.09) or CABG surgery (*ICD-9-CM* codes 36.10-36.19) within 24 hours of their index chest pain encounter. This was done to ensure that patients admitted with chest pain who had catheterization and/or revascularization performed immediately were not included in the no-testing cohort. Finally, patients were excluded if they received a primary or secondary diagnosis of pneumonia and influenza (*ICD-9-CM* codes 480-488), chronic obstructive pulmonary disease or allied conditions (*ICD-9-CM* codes 490-496), other diseases of the respiratory system (*ICD-9-CM* codes 510-519), acute respiratory tract infection (*ICD-9-CM* codes 460-466), aortic dissection (*ICD-9-CM* codes 441), diseases of pulmonary circulation (*ICD-9-CM* codes 415-417), acute pericarditis (*ICD-9-CM* codes 420),

and heart failure (*ICD-9-CM* codes 428). From cohort G, a final subcohort (cohort H) was extracted, which included all outpatient and inpatient claims records within 1 year before and after the initial noninvasive cardiac test.

All outpatient, inpatient, and pharmacy claims records within 1 year before the index test were queried to ascertain baseline risk factors. A history of diabetes mellitus was attributed to persons with either *ICD-9-CM* codes (250.xx) or a medication claim for any diabetes-related medication. Hypertension was attributed to persons with either *ICD-9-CM* codes (401-404) or a medication claim for any antihypertensive agent. High cholesterol level was attributed to persons with either *ICD-9-CM* codes (272.0, 272.2, and 272.4) or a medication claim for any cholesterol-lowering medication. Ischemic heart disease was attributed to persons with *ICD-9-CM* codes for acute MI (410.xx), old MI (412), or ischemic heart disease (414.8-414.9).

Receipt of a noninvasive imaging test during the 6-month period before the index chest pain encounter was attributed to persons with a *CPT* code for EE (93015, 93016-93018), SE (93350), MPS (78452), and CCTA (75574). Inpatient status was attributed to patients whose index chest pain encounter was associated with hospital admission.

Episodes of Care

Coronary artery disease–related procedures and hospitalizations were tracked for up to 1 year following the index test. Inpatient and outpatient claims were used to document receipt of cardiac catheterization (*CPT* codes 93451-93464 and *ICD-9-CM* codes 37.22-37.23), PCI (*CPT* codes 92980-92996 and *ICD-9-CM* codes 0.66, 36.01-36.09), and CABG surgery (*ICD-9-CM* codes 36.10-36.19) within 7 days and 1 year. The *CPT* codes were used to identify receipt of EE (93015, 93016-93018), SE (93350), MPS (78452), and CCTA (75574). Inpatient and outpatient claims were used to document hospitalizations for acute MI within 7 days and 1 year. Hospitalizations for acute MI were identified as either a primary diagnosis of acute MI (*ICD-9-CM* codes 410.XX) or a primary diagnosis of a complication of an acute MI (*ICD-9-CM* codes 785.51, 785.59, 429.5, 429.6, and 429.71), with a secondary diagnosis of acute MI. Inpatient and outpatient claims were used to document receipt of another noninvasive cardiac imaging study within 7 days and 1 year.

Statistical Analysis

We determined unadjusted rates of subsequent test and procedure use across the 5 types of initial management strategies. To test the differences in unadjusted measures for statistical significance, we used joint tests across all 5 groups. For categorical variables, we used the Pearson χ^2 test. For continuous variables, we compared means across the 5 groups using analysis of variance.

Multivariate logistic regression analyses were used to examine the relationship between the 5 testing groups and subsequent care, adjusting for potential confounders, including geographic region, age, sex, diabetes, hypertension, high cholesterol level, ischemic heart disease, inpatient status on admission, and receipt of a noninvasive test within 6 months before the index encounter. The main independent variable in these analyses was the initial management strategy, including no testing, EE, SE, MPS, and CCTA; the key dependent variables were indicators of receipt of cardiac catheterization, PCI, CABG surgery, hospitalization for acute MI, or future noninvasive cardiac testing (EE, SE, MPS, and CCTA). Subgroup analyses were carried out for female and male patients.

All hypothesis tests were performed on a 2-sided basis with an α level of .05. The lowest *P* value reported was <.001. Statistical analyses were performed using SAS, version 9.1.3 (SAS Institute Inc), for data extraction and management. Forest plots were created with Prism 6 software (GraphPad Software, Inc).

Results

In 2011, there were 693 212 ED encounters with a primary or secondary diagnosis of chest pain, accounting for 9.2% of all ED encounters. After application of the inclusion and exclusion criteria, 421 774 patients were included in the final analysis; 293 788 individuals did not receive a noninvasive test within 7 days of their index encounter and 127 986 did undergo testing, representing 1.7% of all ED encounters (**Figure 1**). In patients who underwent initial noninvasive testing, MPS was the most frequently used diagnostic modality (82 954 individuals [64.8%]), followed by SE (24 101 [18.8%]), EE (18 206 [14.2%]), and CCTA (2725 [2.1%]). The mean length of follow-up after the index test was 190.3 days. Patients in the CCTA group had a shorter length of follow-up (184.3 days) in relation to MPS (*P* = .001) and EE (*P* = .02). The other groups' follow-up times did not differ significantly.

The mean age of the noninvasive imaging cohort was 49.9 years, and 52.7% were female. Patients who underwent initial noninvasive testing were older, had more comorbid conditions, were more likely to be hospitalized on their index chest pain encounter, and were more likely to have undergone noninvasive testing within 6 months before their index chest pain encounter (**Table 1**).

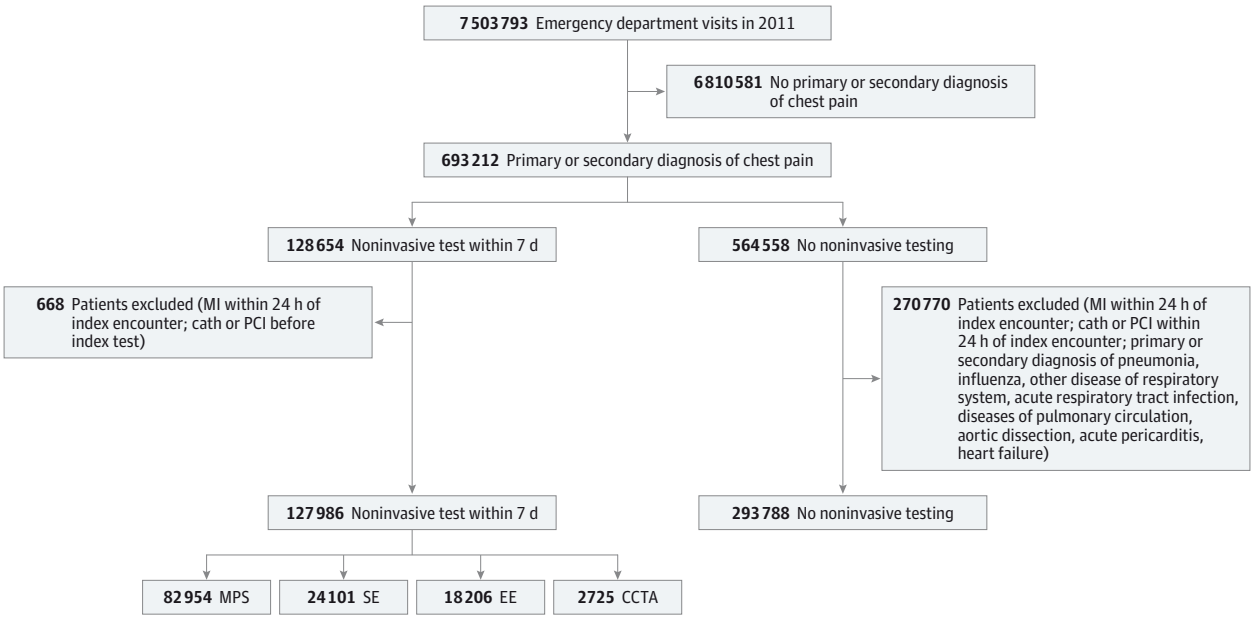
Hospitalizations for Acute MI

Only 464 patients (0.11%) and 1396 patients (0.33%) were hospitalized with an acute MI during 7 and 190 days of follow-up, respectively. Compared with the no-testing cohort, there were no significant differences in hospitalizations for MI in any of the noninvasive imaging groups (**Table 2** and **Figure 2**). Subgroup analyses also did not reveal any significant differences (**Table 3**).

Subsequent Cardiac Catheterization

A total of 12 608 patients (3%) and 22 388 patients (5.3%) received a cardiac catheterization during 7 and 190 days of follow-up, respectively. Compared with the no-testing cohort, patients who underwent an initial strategy of noninvasive imaging were significantly more likely to receive a cardiac catheterization during 7 days of follow-up; however, at 190 days of follow-up this significant difference was no longer evident in those undergoing an initial strategy of SE (Table 2 and Figure 2). In subgroup analyses, the higher rate of cardiac catheterization associated with CCTA was not significant for female patients during 190 days of follow-up (Table 3).

Figure 1. Flow Diagram of Cohort Selection Process



Cath indicates coronary catheterization; CCTA, coronary computed tomography angiography; EE, exercise electrocardiography; MI, myocardial infarction; MPS, myocardial perfusion scintigraphy; PCI, percutaneous coronary intervention; and SE, stress echocardiography.

Subsequent Revascularization Procedure

A total of 3078 patients (0.7%) and 5668 patients (1.3%) underwent revascularization during 7 and 190 days of follow-up, respectively. Compared with the no-testing cohort, after 7 days of follow-up, patients undergoing initial noninvasive testing had higher rates of revascularization; however, during 190 days of follow-up, this significant difference was no longer evident in those undergoing an initial strategy of SE (Table 2 and Figure 2). In subgroup analyses, the higher rate of revascularization associated with CCTA was not statistically significant for female patients during 190 days of follow-up (Table 3).

Subsequent Noninvasive Cardiac Testing

A total of 24 141 (5.7%) and 55 534 (13.2%) of patients received a future noninvasive test during 7 and 190 days of follow-up, respectively. Compared with the no-testing cohort, during 190 days of follow-up, patients undergoing initial noninvasive testing had significantly higher rates of subsequent noninvasive testing (Table 2 and **Figure 3**).

Discussion

This cohort of privately insured patients evaluated in the ED for chest pain without MI had very low rates of MI and revascularization during short-term and longer-term follow-up. The low risk of MI did not appear to be affected by the initial testing strategy, and deferral of noninvasive testing appeared to be a reasonable approach. For patients receiving an initial noninvasive test, SE was associated with the lowest rate of downstream catheterizations and revascularization procedures. This finding suggests that, of the noninvasive testing strategies, SE is the most efficacious in this population of patients. Furthermore, the significant increase in revascularization associated with MPS, CCTA, and EE without a concomitant reduction in MI suggests that overdiagnosis is a legitimate concern in this patient population.

Several important limitations apply to this analysis. The no-testing cohort was significantly younger and had fewer comorbid conditions than the cohort undergoing an initial noninvasive test. In addition, within the noninvasive testing cohort, patients undergoing MPS were older and had slightly higher rates of diabetes mellitus, hypertension, high cholesterol level, and ischemic heart disease. Although we controlled for these variables in our statistical analyses, we cannot rule out bias from unmeasured confounders, such as chest pain characteristics and presenting ECG features (eg, ST-segment depression or T-wave inversion), that could have affected the rates of downstream testing and treatment. To limit confounding as much as possible, strict exclusion criteria were applied to the cohorts to make them representative of low-risk patients with chest pain. For example, patients in the noninvasive testing cohort were excluded if they had an MI on the same visit as were patients who underwent cardiac catheterization, PCI, or CABG surgery before the index test. This exclusion was done to ensure, as best as possible, that patients admitted with MI were not included in the cohort since it is not uncommon for these patients to undergo noninvasive testing as part of a conservative management strategy before catheterization. It is also not uncommon for patients who are admitted with an MI or unstable angina to undergo noninvasive imaging after catheterization if there are multiple lesions and the responsible vessel is not easily identifiable. We believe that our strict exclusion criteria limited confounding from these types of patients as much as possible. Strict exclusion criteria were also applied to the no-testing cohort to ensure that patients with an MI or un-

Table 1. Baseline Risk Factors

Characteristic	Cohort		Noninvasive Test			
	No Test	Noninvasive Test	MPS	SE	EE	CCTA
No. (%) of patients	293 788 (69.7)	127 986 (30.3)	82 954 (64.8)	24 101 (18.8)	18 206 (14.2)	2725 (2.1)
Region, %						
Northeast[a]	57 289 (19.5)	23 165 (18.1)	14 517 (17.5)	3784 (15.7)	4424 (24.3)	474 (17.4)
North Central[a]	66 396 (22.6)	36 476 (28.5)	21 402 (25.8)	10 821 (44.9)	3532 (19.4)	676 (24.8)
South[a]	115 459 (39.3)	50 043 (39.1)	35 919 (43.3)	6049 (25.1)	6682 (36.7)	1373 (50.4)
West[a]	45 537 (15.5)	13 695 (10.7)	8212 (9.9)	2290 (9.5)	3077 (16.9)	161 (5.9)
Unknown	9107 (3.1)	4608 (3.6)	2,903 (3.5)	1,181 (4.9)	492 (2.7)	41 (1.5)
Sex, No. (%)						
Female[a]	157 915 (53.8)	67 408 (52.7)	44 168 (53)	13 253 (54.9)	8732 (47.8)	1410 (51.2)
Male[a]	135 873 (46.2)	60 578 (47.3)	39 111 (47)	10 893 (45.1)	9542 (52.2)	1342 (48.8)
Age, %, y						
Mean, y[a]	41.3	49.9	50.9	48.8	47.2	47.3
0-17	16 746 (5.7)	128 (0.1)	0	24 (0.1)	127 (0.7)	8 (0.3)
18-34	76 972 (26.2)	6399 (5.0)	2820 (3.4)	1518 (6.3)	1802 (9.9)	232 (8.5)
35-44	63 752 (21.7)	27 517 (21.5)	15 927 (19.2)	5,953 (24.7)	4879 (26.8)	738 (27.1)
45-54	73 741 (25.1)	49 531 (38.7)	32 352 (39.0)	9,448 (39.2)	6627 (36.4)	1071 (39.3)
55-64	59 933 (20.4)	44 411 (34.7)	31 854 (38.4)	7,158 (29.7)	4788 (26.3)	676 (24.8)
Comorbid conditions, No. (%)						
Diabetes mellitus[a]	30 524 (10.4)	29 212 (22.8)	21 490 (25.9)	4187 (17.4)	3073 (16.9)	462 (17.0)
Hypertension[a]	72 913 (24.8)	69 181 (54.1)	48 493 (58.5)	11 054 (45.9)	8310 (45.6)	1324 (48.6)
High cholesterol level[a]	53 487 (18.2)	61 694 (48.2)	43 143 (52.0)	9990 (41.5)	7378 (40.5)	1183 (43.4)
Ischemic coronary disease[a]	6084 (2.1)	5930 (4.6)	4655 (5.6)	622 (2.6)	551 (3.0)	102 (3.7)
Other baseline risk factors						
Inpatient status[a]	19 000 (6.5)	17 646 (13.8)	13 325 (16.1)	1906 (7.9)	2108 (11.6)	307 (11.3)
Stress test in prior 6 mo[a]	7533 (2.6)	5960 (4.7)	4718 (5.7)	759 (3.2)	305 (1.7)	178 (6.5)

Abbreviations: CCTA, coronary computed tomography angiography; EE, exercise electrocardiography; MPS, myocardial perfusion scintigraphy; SE, stress echocardiography.

[a] Denotes a statistically significant difference ($P < .05$) between cohorts.

stable angina were not included. In addition, patients were excluded if a nonischemic condition that could have caused chest pain was diagnosed. We believe that the low rates of MI in all groups within 7 and 190 days of follow-up support our assumption that this was a uniformly low-risk cohort.

Because of limitations of MarketScan, which does not capture data on mortality, we could not assess for death among our cohort. Given the age of the cohort and the low rate of MI, it is unlikely that cardiac death would have significantly contributed to differences in follow-up events. Data from the Rule Out Myocardial Infarction/Ischemia Using Computer Assisted Tomography trial[8] would support this assumption of a minor effect of cardiac death because their patient cohort was similar in presenting features, age, and risk-factor profile to ours and there were no recorded deaths at any time in the trial. In addition, we did not try to assess for rates of clinical angina after the index test, which could be an important metric. Because MarketScan does not include Medicare patients, these results cannot be generalized to individuals older than 65 years.

Despite the limitations of this analysis, we believe these findings have important implications for the management of care for patients presenting to the ED with chest pain and no evidence of an MI. First, these patients are at low risk for experiencing an MI in the near future, and the risk does not seem to increase significantly with more comorbid conditions. The absolute rates of MI at 7 and 190 days of follow-up between patients in the no-testing and MPS cohorts differed by only 0.1% and 0.2%, respectively, despite a 9.6-year age difference and more than doubling of the number of comorbid conditions in the MPS cohort (Table 1). When the risk of an event is low, it is difficult to reduce it further. The results of this study do not support the idea that future MIs can be significantly reduced with early noninvasive testing. This finding is consistent with that of Chan et al,[10] who prospectively studied 962 consecutive patients with low-risk chest pain who were admitted and monitored with telemetry. The investigators found no significant difference in 30-day cardiovascular events among patients who received a stress test, either as an inpatient or an outpatient, and those who did not. Safavi et al[11] found significant variation between hospitals in the use of advanced imaging in patients with suspected acute coronary syndrome without acute MI. Hospitals with higher imaging rates (35% vs 6%) did not have lower readmission rates for acute MI but were significantly more likely to admit patients and perform angiography.

Our results also suggest that initial deferment of noninvasive testing does not deny revascularization for patients who may benefit from it. During a mean of 190 days of follow-up, there was no significant difference in the adjusted odds ratio

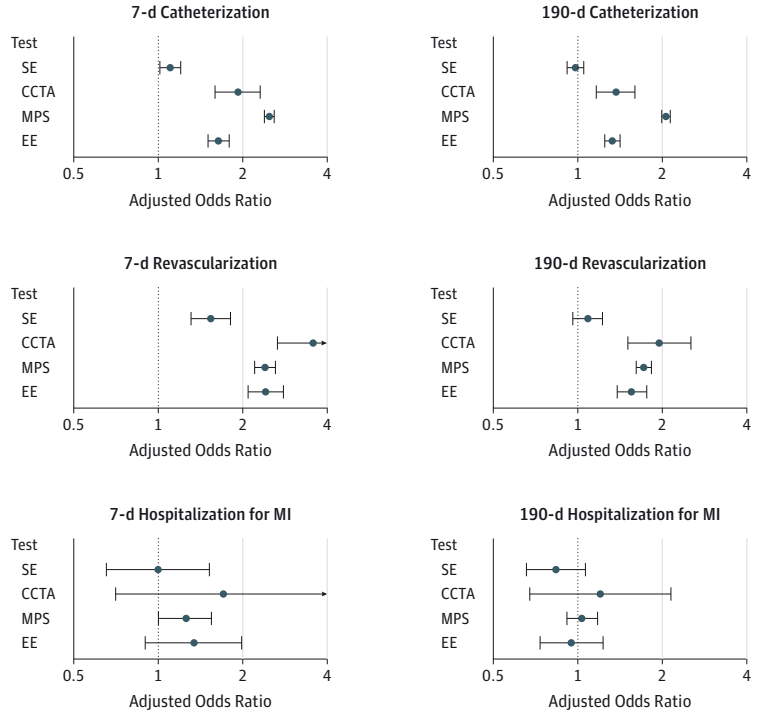
Table 2. Primary End Points and AOR of Noninvasive Testing Strategies Compared With the No-Testing Cohort

End Point	Intervention During 7 d, %	AOR (95% CI)	Intervention During 190 d, %	AOR (95% CI)
Catheterization				
No test	1.7	1 [Reference]	3.4	1 [Reference]
SE	2.5	1.10 (1.01-1.20)	4.7	0.98 (0.92-1.05)
EE	3.7	1.63 (1.50-1.78)	6.0	1.33 (1.25-1.42)
MPS	7.5	2.48 (2.38-2.58)	12.0	2.06 (2.00-2.13)
CCTA	4.7	1.91 (1.59-2.30)	6.8	1.37 (1.17-1.60)
Revascularization				
No test	0.4	1 [Reference]	0.8	1 [Reference]
SE	0.8	1.54 (1.31-1.81)	1.3	1.08 (0.96-1.22)
EE	1.3	2.41 (2.09-2.80)	1.9	1.55 (1.38-1.75)
MPS	1.9	2.40 (2.21-2.61)	3.0	1.71 (1.61-1.82)
CCTA	1.9	3.56 (2.65-4.76)	2.4	1.95 (1.51-2.52)
Second stress test[a]				
No test	0	NA	9.5	1 [Reference]
SE	14.5	NA	16.6	1.47 (1.42-1.52)
EE	12.1	NA	16.7	1.63 (1.56-1.70)
MPS	22.9	NA	24.1	2.31 (2.26-2.36)
CCTA	11.1	NA	16.3	1.58 (1.42-1.75)
MI				
No test	0.1	1 [Reference]	0.3	1 [Reference]
SE	0.1	0.99 (0.65-1.51)	0.3	0.83 (0.65-1.06)
EE	0.2	1.33 (0.89-1.98)	0.4	0.94 (0.73-1.22)
MPS	0.2	1.25 (1.00-1.54)	0.5	1.03 (0.91-1.17)
CCTA	0.2	1.70 (0.70-4.14)	0.4	1.20 (0.67-2.13)

Abbreviations: AOR, adjusted odds ratio; CCTA, coronary computed tomography angiography; EE, exercise electrocardiography; MI, myocardial infarction; MPS, myocardial perfusion scintigraphy; NA, not applicable; SE, stress echocardiography.

[a] By definition, the no-testing cohort did not undergo noninvasive testing within 7 days of their index encounter; therefore, follow-up testing during 7 days cannot be compared between the no-testing cohort and the others.

Figure 2. Adjusted Odds Ratios for Cardiac Catheterization, Revascularization, and Hospitalizations for Myocardial Infarction (MI) During 7 and 190 Days of Follow-up vs No Testing



CCTA indicates coronary computed tomography angiography; EE, exercise electrocardiography; MPS, myocardial perfusion scintigraphy; and SE, stress echocardiography. Vertical lines indicate the reference group (those who did not receive initial testing); limit lines, 95% CI.

Table 3. Subgroup Analyses of Primary End Points and AORs for Male and Female Patients Compared With the No-Testing Cohort

	Total Cohort		Females		Males	
End Point	%	AOR (95% CI)	%	AOR (95% CI)	%	AOR (95% CI)
Catheterization						
No test	3.4	1 [Reference]	2.5	1 [Reference]	4.5	1 [Reference]
SE	4.7	0.98 (0.92-1.05)	4.1	1.12 (1.03-1.24)	5.3	0.87 (0.80-0.95)
EE	6.0	1.33 (1.25-1.42)	4.9	1.41 (1.27-1.57)	7.0	1.27 (1.17-1.34)
MPS	12.0	2.06 (2.00-2.13)	10.0	2.21 (2.10-2.32)	14.1	1.94 (1.86-2.03)
CCTA	6.8	1.37 (1.17-1.60)	4.1	1.01 (0.77-1.32)	9.6	1.64 (1.36-1.99)
Revascularization						
No test	0.8	1 [Reference]	0.4	1 [Reference]	1.3	1 [Reference]
SE	1.3	1.08 (0.96-1.22)	0.8	1.25 (1.01-1.55)	1.9	1.01 (0.87-1.17)
EE	1.9	1.55 (1.38-1.75)	0.9	1.35 (1.06-1.73)	2.8	1.61 (1.41-1.85)
MPS	3.0	1.71 (1.61-1.82)	1.7	1.71 (1.53-1.92)	4.5	1.70 (1.58-1.83)
CCTA	2.4	1.95 (1.51-2.52)	1.0	1.42 (0.83-2.44)	3.9	2.17 (1.62-2.91)
Follow-up noninvasive testing						
No test	9.5	1 [Reference]	8.6	1 [Reference]	10.6	1 [Reference]
SE	16.6	1.47 (1.42-1.52)	17.0	1.66 (1.58-1.75)	16.1	1.28 (1.21-1.35)
EE	16.7	1.63 (1.56-1.70)	17.4	1.88 (1.78-2.00)	16.1	1.41 (1.33-1.49)
MPS	24.1	2.31 (2.26-2.36)	24.4	2.61 (2.53-2.69)	23.8	2.02 (1.96-2.09)
CCTA	16.3	1.58 (1.42-1.75)	16.4	1.72 (1.49-1.99)	16.2	1.44 (1.24-1.67)
Hospitalization for MI						
No test	0.3	1 [Reference]	0.2	1 [Reference]	0.4	1 [Reference]
SE	0.3	0.83 (0.65-1.06)	0.2	0.96 (0.65-1.40)	0.4	0.75 (0.54-1.04)
EE	0.4	0.94 (0.73-1.22)	0.2	0.82 (0.51-1.32)	0.5	1.00 (0.73-1.35)
MPS	0.5	1.03 (0.91-1.17)	0.3	0.84 (0.67-1.05)	0.8	1.13 (0.97-1.31)
CCTA	0.4	1.20 (0.67-2.13)	0.4	1.35 (0.55-3.30)	0.5	1.09 (0.52-2.32)

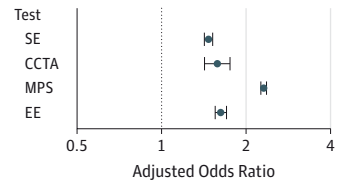
Abbreviations: AOR, adjusted odds ratio; CCTA, coronary computed tomography angiography; EE, exercise electrocardiography; MI, myocardial infarction; MPS, myocardial perfusion scintigraphy; SE, stress echocardiography.

of revascularization between the initial no-testing and SE cohorts (Figure 2). More appropriate decisions regarding the use of noninvasive testing may be made given the passage of time. Because most patients with suspected acute coronary syndrome do not have a cardiac cause for their symptoms,[12] initial deferment of noninvasive testing could allow for symptom clarification. Deferral of early noninvasive testing could allow for more appropriate and selective use of noninvasive testing in the outpatient setting. During 190 days of follow-up, only 9.5% of patients in the no-testing cohort underwent a future noninvasive test, but their adjusted odds ratio of revascularization was similar to that of the SE cohort.

Providing reassurance is one reason often cited for routine diagnostic testing in low-risk patients; however, Rolfe and Burton[13] found that diagnostic testing in such patients did not reduce anxiety or improve symptom status. Our findings support those of Rolfe and Burton because patients who underwent an initial strategy of noninvasive testing in our study were more likely to receive subsequent noninvasive testing.

Stress echocardiography would appear to be the most efficacious noninvasive test based on the results of this investigation since it was associated with the least number of catheterization and revascularization procedures and no significant difference in hospitalizations for MI. Coronary computed tomography angiography may be particularly limited in men in this population because it appears to be associated with the highest adjusted odds of revascularization. This finding is consistent with prior studies. In the ROMICAT II trial,[8] CCTA compared with usual care led to more diagnoses of obstructive coronary artery disease and more revascularization procedures without improving hard cardiovascular end points.

Figure 3. Adjusted Odds Ratios for Second Noninvasive Testing During 190 Days of Follow-up



CCTA indicates coronary computed tomography angiography; EE, exercise electrocardiography; MPS, myocardial perfusion scintigraphy; and SE, stress echocardiography. Vertical lines indicate the reference group (those who did not receive initial testing); limit lines, 95% CI.

Overall, our results suggest that in a cohort of patients presenting to the ED with chest pain, the increased detection and treatment of coronary artery disease via CCTA, MPS, and EE may be of little or no value. *Overdiagnosis* is a term used to describe the detection and treatment of disease that would not

harm the patient if left undetected. Relevant examples include the increased detection of breast cancer with mammographic screening, prostate cancer with prostate-specific antigen testing, and pulmonary embolism with computed tomography pulmonary angiography.[14-16] Consequences of overdiagnosis include the negative effects of unnecessary labeling, the harms of unneeded tests and therapies, and the opportunity cost of wasted resources that could be better used to treat genuine illness.[17]

Using data from the present analysis, we estimate that for every 27 patients who undergo MPS instead of an initial strategy of no testing, 1 patient will undergo an unnecessary catheterization, and for every 71 patients who undergo CCTA instead of no testing, 1 individual will undergo an unnecessary catheterization. When viewed in the broader context of the approximately 6 million ED visits annually for a chief symptom chest pain, for every 100 000 patients who undergo MPS instead of an initial strategy of no testing, approximately 3700 patients will undergo an unnecessary catheterization. In addition, for every 100 000 patients who undergo CCTA instead of an initial strategy of no testing, approximately 800 individuals will have an unnecessary revascularization procedure performed.

Conclusions

More studies need to be conducted to clarify the best testing strategy for low-risk patients being evaluated for chest pain in the ED. A randomized trial comparing a no-testing strategy with different noninvasive testing strategies with an emphasis on hard end points could definitively address this need. Given today's concerns regarding health care cost growth, especially the portion attributable to noninvasive cardiac imaging, and patient safety issues related to radiation exposure as well as overdiagnosis, performing such a study should be a priority.[18]

ARTICLE INFORMATION

Accepted for Publication: November 16, 2014.

Published Online: January 26, 2015. doi:10.1001/jamainternmed.2014.7657.

Author Contributions: Drs Liu and Leslie had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Foy, Davidson, Sciamanna, Leslie.
Acquisition, analysis, or interpretation of data: Foy, Liu, Davidson, Leslie.
Drafting of the manuscript: Foy, Sciamanna.
Critical revision of the manuscript for important intellectual content: Foy, Liu, Davidson, Leslie.
Statistical analysis: Foy, Liu, Leslie.
Obtained funding: Foy.
Administrative, technical, or material support: Davidson.
Study supervision: Foy, Sciamanna, Leslie.

Conflict of Interest Disclosures: None reported.

Funding/Support: This study was supported in part by grant UL1 TR000127 from the National Institutes of Health.

Role of the Funder/Sponsor: The National Institutes of Health had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Previous Presentation: This research was presented as a moderated poster at the ACC 2014 Scientific Sessions; March 31, 2014; Washington, DC.

REFERENCES

1. Nawar EW, Niska RW, Xu J. *National Hospital Ambulatory Medical Care Survey: 2005 Emergency Department Summary: Advanced Data From Vital and Health Statistics; No. 386*. Hyattsville, MD: National Center for Health Statistics; 2007.

2. Pitts SR, Niska RW, Xu J, Burt CW. National hospital ambulatory medical care survey: 2006 emergency department summary. *Natl Health Stat Report*. 2008;7(7):1-38.

3. Hamm CW, Braunwald E. A classification of unstable angina revisited. *Circulation*. 2000;102(1):118-122.

4. Pope JH, Aufderheide TP, Ruthazer R, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med*. 2000;342(16):1163-1170.

5. 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.

6. Qaseem A, Fihn SD, Williams S, Dallas P, Owens DK, Shekelle P; Clinical Guidelines Committee of the American College of Physicians. Diagnosis of stable ischemic heart disease: summary of a clinical practice guideline from the American College of Physicians/American College of Cardiology Foundation/American Heart Association/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons. *Ann Intern Med*. 2012;157(10):729-734.

7. Garber AM, Solomon NA. Cost-effectiveness of alternative test strategies for the diagnosis of coronary artery disease. *Ann Intern Med*. 1999;130(9):719-728.

8. Hoffmann U, Truong QA, Schoenfeld DA, et al; ROMICAT-II Investigators. Coronary CT angiography versus standard evaluation in acute chest pain. *N Engl J Med*. 2012;367(4):299-308.

9. Min JK, Shaw LJ, Berman DS. The present state of coronary computed tomography angiography a process in evolution. *J Am Coll Cardiol*. 2010;55(10):957-965.

10. Chan GW, Sites FD, Shofer FS, Hollander JE. Impact of stress testing on 30-day cardiovascular outcomes for low-risk patients with chest pain admitted to floor telemetry beds. *Am J Emerg Med*. 2003;21(4):282-287.

11. Safavi KC, Li SX, Dharmarajan K, et al. Hospital variation in the use of noninvasive cardiac imaging and its association with downstream testing, interventions, and outcomes. *JAMA Intern Med*. 2014;174(4):546-553.

12. Lindsell CJ, Anantharaman V, Diercks D, et al; EMCREG-International i*trACS Investigators. The Internet Tracking Registry of Acute Coronary Syndromes (i*trACS): a multicenter registry of patients with suspicion of acute coronary syndromes reported using the standardized reporting guidelines for emergency department chest pain studies. *Ann Emerg Med*. 2006;48(6):666-677.

13. Rolfe A, Burton C. Reassurance after diagnostic testing with a low pretest probability of serious disease: systematic review and meta-analysis. *JAMA Intern Med*. 2013;173(6):407-416.

14. Miller AB, Wall C, Baines CJ, Sun P, To T, Narod SA. Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial. *BMJ*. 2014;348:g366.

15. Etzioni R, Penson DF, Legler JM, et al. Overdiagnosis due to prostate-specific antigen screening: lessons from US prostate cancer incidence trends. *J Natl Cancer Inst*. 2002;94(13):981-990.

16. Wiener RS, Schwartz LM, Woloshin S. Time trends in pulmonary embolism in the United States: evidence of overdiagnosis. *Arch Intern Med*. 2011;171(9):831-837.

17. Moynihan R, Doust J, Henry D. Preventing overdiagnosis: how to stop harming the healthy. *BMJ*. 2012;344:e3502. doi:10.1136/bmj.e3502.

18. Shaw LJ, Marwick TH, Zoghbi WA, et al. Why all the focus on cardiac imaging? *JACC Cardiovasc Imaging*. 2010;3(7):789-794.