Published in final edited form as:

Am J Cardiol. 2016 December 15; 118(12): 1786–1791. doi:10.1016/j.amjcard.2016.08.066.

Comparison of the Effectiveness of Stress Echocardiography Versus Myocardial Perfusion Imaging in Patients Presenting to the Emergency Department With Low-Risk Chest Pain

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Abstract

The aim of this study was to compare clinically relevant cardiovascular outcomes and downstream resource utilization associated with stress echocardiography (SE) and myocardial perfusion imaging (MPI) in emergency department patients with low-risk chest pain. This was a retrospective analysis of health insurance claims data for a national sample of privately insured patients over the period January 1 to December 31, 2011. Subjects were selected who presented to the emergency department with a primary or secondary diagnosis of chest pain and underwent either SE or MPI. The primary end points were the percentage of patients in each group who underwent downstream cardiac catheterization, revascularization, repeat noninvasive testing, return emergency department visit with chest pain, and hospitalization for myocardial infarction. The mean length of follow-up was 190 days in both groups. Overall, 48,202 patients or 24,101 propensity-matched pairs were included in the final analysis. Compared with SE, MPI was associated with significantly higher odds of subsequent cardiac catheterization (adjusted odds ratio [AOR] 2.15; 95% confidence interval [CI] 1.99 to 2.33) and revascularization procedures (AOR 1.58; 95% CI 1.36 to 1.85) and repeat emergency department visits (AOR 1.14; 95% CI 1.11 to 1.19). The odds of repeat testing and myocardial infarction did not differ between groups. The average cost of downstream care was significantly higher in the MPI group (\$2,193.80 vs \$1,631.10, $p < 0.0001$). According to the a priori rules specified for this comparative analysis, SE is more effective than MPI for privately insured patients who present to the emergency department with chest pain. In conclusion, these findings demonstrate the importance of assessing diagnostic

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Author contributions: Drs. Foy, 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: Dr. Foy; acquisition of data: Drs. Liu and Leslie; Analysis and interpretation of data: all authors; drafting of the manuscript: Drs. Foy, Davies, Sciamanna, and Davidson; critical revision of the manuscript for important intellectual content: Drs. Davies, Davidson, and Sciamanna; Statistical analysis: Liu; study supervision: Drs. Foy and Leslie.

Disclosures

The authors have no conflicts of interest to disclose.

tests based on how they affect hard end points because identification of disease, in and of itself, may not confer any clinical advantage.

There are >8 million emergency department visits for chest pain or other symptoms concerning for myocardial ischemia each year in the United States.¹ Over time, the cost of care delivered to these patients has gone up significantly along with using advanced noninvasive cardiac testing, which increased 368% over the period 1998 to 2008.² Stress echocardiography (SE) and myocardial perfusion imaging (MPI) are 2 frequently used techniques and are given similar appropriate use scores across the continuum of symptomatic patients.² However, these techniques have not been directly compared in this patient population. We sought to compare the effectiveness of SE and MPI in patients who presented to the ED with chest pain using a national claims database. Several a priori assumptions were made to guide conclusions. First, the more effective technique would be associated with lower odds of experiencing hard cardiovascular end points of interest to patients including future/repeat stress testing, future/repeat ED visits for chest pain, and most importantly, hospitalizations for myocardial infarction (MI). Second, absent any significant differences in the odds of experiencing hard cardiovascular end points, the more effective technique would be associated with lower odds of receiving downstream catheterization and/or revascularization procedures. Our secondary aim was to compare the total cost of care associated with each technique.

Methods

This study was approved by the institutional review board at the Penn State Milton S. Hershey Medical Center. The study used Marketscan Commercial Claims and Encounters data from 2011. Marketscan is constructed and maintained by Truven Health and consists of reimbursed health care claims for employees, retirees, and their dependents of over 250 medium and large employers and their 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 de-identified 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.

A raw cohort (cohort A) of claim records for all ED visits was extracted from the year 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 subcohort (cohort C) was then extracted from cohort B to include patients who underwent noninvasive testing (inpatient or outpatient) within 7 days of their initial ED visit. *CPT* codes were used to identify receipt of exercise electrocardiography (EE) (93015, 93016 to 93018), SE (93350), MPI (78452), and coronary computed tomography angiography (CCTA) (75574). The first anatomical or functional test of coronary artery disease (CAD) the patient had after their ED presentation will be termed the “index test” in this report. A subcohort (cohort D) was extracted from cohort C to exclude patients who had an MI within

24 hours of the index encounter (*ICD-9-CM* codes 410.0 to 410.9); had a cardiac catheterization (*CPT* codes 93451 to 93464; *ICD-9-CM* codes 37.22 to 37.23), percutaneous coronary intervention (PCI) (*CPT* codes 92980 to 92996; *ICD-9-CM* codes 0.66, 36.01 to 36.09), or coronary artery bypass graft surgery (CABG) (*ICD-9-CM* codes 36.10 to 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 subcohort (cohort E) was extracted, which included only patients whose index test was SE or MPI.

All outpatient, inpatient, and pharmacy claim records within 1 year before the index test were queried to ascertain data on covariates. A history of diabetes was attributed to persons with either *ICD-9-CM* codes (250.xx) or a medication claim for any diabetes-related medication. Hyper-tension was attributed to persons with either *ICD-9-CM* codes (401 to 404) or a medication claim for any antihypertensive agent. High cholesterol 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 to 414.9). Receipt of a previous noninvasive imaging test over the 6-month period before the index chest pain encounter was attributed to persons with a *CPT* code for EE (93015, 93016 to 93018), SE (93350), MPI (78452), and CCTA (75574). Inpatient status was attributed to patients whose index chest pain encounter was associated with inpatient admission.

We applied propensity scoring to match each patient from the SE group with a patient from the MPI group in a one-to-one manner. Logistic regression was performed to estimate the propensity scores, with group ID (0 = SE; 1 = MPI) as the dependent variable and age, gender, baseline comorbidity characteristics (diabetes, hypertension, high cholesterol, and ischemic heart disease), inpatient status on index ED encounter, and stress test within previous 6 months as covariates. We obtained from the logistic regression the predicted probability of undergoing SE as the propensity score and applied stratification matching to match patients from both cohorts by the propensity scores without replacement. We were able to match a majority of the SE cohort patients at the six-digit propensity score resolution. For all remaining unmatched SE patients, we found their matches at the five-digit propensity score resolution. This final, propensity-matched cohort represents cohort F.

CAD-related procedures and hospitalizations were tracked throughout 2011, following the index test. Because patients were captured evenly over the year 2011, the average duration of follow-up was 190 days in both groups. Inpatient and outpatient claims were used to document receipt of cardiac catheterization (*CPT* codes 93451 to 93464; *ICD-9-CM* codes 37.22 to 37.23), PCI (*CPT* codes 92980 to 92996; *ICD-9-CM* codes 0.66, 36.01 to 36.09), and CABG (*ICD-9-CM* codes 36.10 to 36.19) within 1 year. *CPT* codes were used to identify receipt of EE (93015, 93016 to 93018), SE (93350), MPS (78452), and CCTA (75574). Inpatient claims only were used to document hospitalizations for acute MI within 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 1 year. Inpatient and outpatient claims were used to document

another ED encounter with a primary or secondary diagnosis of chest pain (*ICD-9-CM* code 786.50).

To assess the costs of downstream care in both groups, we measured the cost of all reimbursed inpatient, outpatient, and pharmacy claims after receipt of the index stress test. To gather information on costs before the index test, we measured the cost of all reimbursed inpatient, outpatient, and pharmacy claims within 1 year of the index test. To assess the costs of the index tests themselves, we directly measured the reimbursement. The costs of reimbursement were not included in the costs of downstream care.

We present unadjusted rates of the primary end points for propensity-matched SE and MPI groups. To test the differences in unadjusted measures for statistical significance, we directly compared the propensity-matched SE and MPI groups. For categorical variables, we used the Pearson chi-square test. For continuous variables, we compared means using Student's *t* test.

Multivariate logistic regression analyses were used to examine the relation between the SE and MPI groups and subsequent care, adjusting for potential confounders that included geographic region, age, gender, diabetes, hyper-tension, high cholesterol, ischemic heart disease, inpatient status on admission, and receipt of a noninvasive test within 6 months before the index encounter. To compare downstream spending, multivariate analysis was conducted using the earlier mentioned variables with the addition of a variable for average reimbursed health spending in the year before the index encounter. The main independent variable in these analyses was the index test (SE or MPI) and the key dependent variables were indicators of receipt of cardiac catheterization, PCI, CABG, hospitalization for acute MI, ED encounter for chest pain, future noninvasive cardiac test (EE, SE, MPI, and CCTA), and downstream reimbursed health spending. A priori subgroup analyses were conducted according to gender, inpatient/outpatient status on index ED encounter, and history of ischemic heart disease. A nonprespecified sensitivity analysis was carried out on patients based on time to index test (≥ 48 vs <48 hours).

All hypothesis tests were performed on a 2-sided basis with an α of 0.05. The lowest *p* value reported was <0.0001. Statistical analyses were performed using SAS, version 9.1.3, for data extraction and management. Forest plots were created with GraphPad Prism 6 software.

Results

In the year 2011, there were 693,212 ED encounters with a primary or secondary diagnosis of chest pain accounting for 9.2% of all encounters. After application of the inclusion and exclusion criteria, 107,055 patients were included in the final cohort before propensity matching (Figure 1). MPI (*n* = 82,954 [77.5%]) was performed significantly more often than SE (*n* = 24,101 [22.5%]). The mean length of follow-up after the index test was 190.3 days and did not significantly differ between groups. After propensity matching, 48,202 patients or 24,101 propensity-matched pairs were included in the final analysis (Figure 1). Information on baseline covariates is listed in Table 1.

Only 155 patients (0.3%) were hospitalized with an acute MI over the follow-up period. There was no significant difference in the adjusted odds of hospitalizations for MI between the SE and MPI groups (Table 2, Figure 2). Subgroup analyses did not reveal any significant differences (Figure 3).

There were 3,891 patients (8%) who had at least one repeat ED encounter for chest pain over the follow-up period. Compared with SE, patients who underwent MPI were slightly more likely to have a repeat ED encounter for chest pain (Table 2, Figure 2). This difference was observed throughout subgroups but did not reach statistical significance in the majority of them (Figure 3).

There were 7,654 patients (16%) who had at least 1 repeat noninvasive imaging test over the follow-up period. There was no significant difference in the adjusted odds of repeat testing between the SE and MPI groups (Table 2, Figure 2). Male patients and those with no history of CAD who underwent MPI were slightly more likely to experience repeat imaging compared with those who underwent SE, but no other significant differences were noted in subgroup analyses (Figure 3).

There were 3,384 patients (7%) who received a cardiac catheterization over the follow-up period. Compared with SE, patients who underwent MPI were significantly more likely to receive a cardiac catheterization (Table 2, Figure 2). The higher rate of cardiac catheterization associated with MPI was observed in all subgroups (Figure 3).

There were 775 patients (2%) who underwent revascularization over the follow-up period. Compared with SE, patients who underwent MPI were significantly more likely to undergo revascularization (Table 2, Figure 2). In subgroup analyses, the higher rate of revascularization associated with MPI was observed throughout but did not reach statistical significance in several subgroups (Figure 3).

The costs of reimbursed health claims were significantly higher in patients who underwent MPI compared with SE (\$2,193.80 vs \$1,631.10, $p < 0.0001$). Furthermore, the average reimbursed cost for MPI was significantly higher than SE (\$566.93 vs \$365.58, $p < 0.0001$). The cost of the index test itself was not considered in the cost of downstream care.

Most patients (89%) underwent testing within 48 hours of the index encounter. There were no significant differences in the magnitude or direction of the adjusted odds ratios for each of the primary end points between either group (<48 or >48 hours) and the overall cohort; however, because of the relatively small number of patients who underwent testing after 48 hours, not all odds ratios in this group reached statistical significance.

Discussion

According to the a priori rules specified to guide conclusions for this analysis, SE is more effective than MPI in privately insured patients who present to the ED with chest pain. Neither SE nor MPI were associated with significant differences in hospitalizations for MI or repeat noninvasive testing; however, SE was associated with slightly reduced odds of returning to the ED with chest pain. In addition, patients who underwent SE were

significantly less likely to undergo downstream catheterization and revascularization procedures. Based on results from this analysis, we can estimate that for every 18 patients who undergo MPI instead of SE, one will have an unnecessary cardiac catheterization and for every 125 patients who undergo MPI instead of SE, one will have an unnecessary revascularization procedure.

There are several reasons why SE may outperform MPI in patients presenting to the ED with chest pain. SE has been found repeatedly to have higher specificity for detection of obstructive CAD compared with MPI. This has been observed in studies that compared the diagnostic utility of SE and MPI in patients who underwent both tests and coronary catheterization.³ A meta-analysis that included only direct comparative studies found the specificity of SE was significantly higher than MPI (86% vs 77%, $p = 0.001$).⁴ The improved specificity of SE would result in less false-positive studies and unnecessary catheterizations, and indeed, this was observed in our study as evidenced by the revascularization to catheterization ratio being significantly higher in the SE group (27.7% vs 20.2%, $p = 0.0008$).

The odds of revascularization were also significantly higher in the MPI group (1.9% vs 1.3%, $p < 0.0001$) that likely reflects the detection of incidental CAD. Overdiagnosis is a term used to describe the detection and treatment of disease that would not harm the patient if left undetected. 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.⁵ We feel it is mechanistically plausible that MPI leads to the overdiagnosis of asymptomatic CAD compared with SE.

Although MPI and SE reach the correct diagnostic conclusion, a similar percentage of the time, they often differ on a patient-by-patient basis. Quinones et al³ found that MPI and SE agreed on the final diagnosis in only 76.8% of patients. MPI and SE assess different targets along the ischemic cascade. Disruption of coronary flow, identified by MPI, occurs earlier than systolic dysfunction, identified by SE, and the latter may represent a more important target for identification and treatment. We believe the findings of our investigation reinforce the need for diagnostic tests to be evaluated based on how they affect hard end points because identification of disease, in and of itself, may not necessarily confer any clinical advantage and could even be disadvantageous.

There are several important limitations of this study. Although propensity matching was used to normalize the SE and MPI groups to the best ability afforded by claims data, unmeasured variables may still have contributed to the differences between groups that were observed. Although not supported by the most recent appropriate use criteria for multimodality imaging, patient-specific characteristics may have driven test selection so that those perceived to have a higher pretest probability of CAD more often received MPI.² We attempted to control for pretest probability status by accounting for age, gender, traditional cardiovascular risk factors, history of CAD that included recent MI, recent prior stress testing, and inpatient status on index admission, but it is possible that inability to assess specific chest pain characteristics, the electrocardiogram at rest, and other clinical

information related to patient status affected our ability to normalize the groups. Although this explanation is possible and may be contributing to the results, we feel it is more likely that test selection was driven by provider-specific factors as opposed to patient-specific ones. This is supported by the significant regional variation observed in the use of SE and MPI in this analysis. The North Central and South were the largest regions represented, and there was a significant difference in test distribution. In the South region, MPI and SE accounted for a 67.1% and 32.9% share of testing compared with a 39.0% and 61.0% share of testing in the North Central region ($p < 0.0001$). The higher reimbursement rate for MPI is one provider-specific variable that could have driven the use of MPI relative to SE as the average cost of reimbursement across the country was \$566.93 for MPI compared with \$365.58 for SE.

An additional limitation is our inability to control for the variable of pharmacologic or exercise testing that cannot be captured sufficiently with claims data. If patients who underwent MPI compared with SE were less likely to exercise and truly unable to, this reduced exercise capability could have contributed to the differences between groups that were observed. We were also unable to capture smoking and obesity status; both covariates, if unevenly distributed in the MPI group could have contributed to the differences between groups that were observed. However, given the even distribution of the other covariates, after propensity matching, it is unlikely that smoking and obesity would have preferentially plagued one group or the other. Although obesity presents an additional challenge to cardiovascular imaging, it negatively affects both MPI and SE and providers prone to perform one test or the other would have little reason to change strategies due to obesity.

Because of limitations of claims data, we did not assess overall mortality. Given the age of the cohort and the low rate of MI, we feel it is unlikely that cardiac death would have significantly contributed to differences in follow-up events. Patients in the ROMICAT-II trial were similar in presenting features, age, and risk factor profile to our cohort, and there were no recorded deaths at any time in the trial.⁶

Finally, in this patient population, cardiac stress testing has not been found to improve clinically relevant patient end points and its utility in this setting has been questioned.^{7,8} Foy et al⁹ recently reported that early cardiac stress testing was not associated with lower rates of MI during 190 days of follow-up in patients who presented to the ED with chest pain, but it was associated with higher rates of downstream testing and revascularization procedures. Therefore, deferral of early cardiac stress testing in favor of close outpatient follow-up may be the most appropriate strategy.¹⁰ Because in this patient population, cardiac stress testing remains a IIa recommendation in the newest iteration of the American College of Cardiology/American Heart Association Guideline for the Management of Patients With NoneST-Elevation Acute Coronary Syndromes, it will remain a common practice which is why comparative effectiveness research on different cardiac stress testing strategies remains an important topic.¹¹

Acknowledgments

This study was supported by grant UL1 TR000127 from the National Institutes of Health. 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.

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FURTHER POINTS

- Any (grey) halftones (photographs, micrographs, etc.) are best viewed on screen, for which they are optimized, and your local printer may not be able to output the greys correctly.
- If the PDF files contain colour images, and if you do have a local colour printer available, then it will be likely that you will not be able to correctly reproduce the colours on it, as local variations can occur.
- If you print the PDF file attached, and notice some ‘non-standard’ output, please check if the problem is also present on screen. If the correct printer driver for your printer is not installed on your PC, the printed output will be distorted.

Figure 1.

Flow diagram. Ex ECG = exercise electrocardiography.

Figure 2.
Forest plot for primary end points (SE reference).

Figure 3.
Forest plots for subgroup analyses (SE reference).

Table 1

Baseline risk factors (n = 107,055)

Variable	MPI (unmatched) 82,954	MPI (matched) 24,101	Stress Echo 24,101
Location			
Northeast	17.5%	8.2%	15.7%
North Central	25.8%	28.8%	44.9%
South	43.3%	51.3%	25.1%
West	9.9%	11.4%	9.5%
Unknown	3.5%	0.3%	4.9%
Gender			
Female N *	44,168%	13,269 (55)%	13,253 (55)%
Male N *	39,111%	10,832 (45)%	10,893 (45)%
Age (years)			
Age (mean) *	50.9%	48.9%	48.8%
<34	3.4%	5.9%	6.3%
35-44	19.2%	25.1 %	24.7%
45-54	39.0%	39.2%	39.2%
55-64	38.4%	29.7%	29.7%
Risk factors			
Diabetes Mellitus N *	21,490%	4,178 (17)%	4,187 (17)%
Hypertension N *	48,493%	11,125 (46)%	11,054 (46)%
High Cholesterol N *	43,143%	9,984 (41)%	9,990 (41)%
Ischemic Heart Disease N *	4,655%	600 (3)%	622 (3)%
Additional covariates			
Inpatient status *	13,325%	2,152 (9)%	2,208 (9)%
Stress test in prior 6 months *	4,718%	799 (3)%	783 (3)%

* Statistical significant difference (p <0.05) between the unmatched MPI and stress echo groups.

Table 2

Results Myocardial Perfusion Imaging (MPI) versus Stress Echocardiogram (SE)

Variable	MPI	SE	AOR*	P
Cardiac Catheterization 3384 (7%)	9.4%	4.7%	2.2	<.0001
Coronary Revascularization procedure 775 (2%)	1.9%	1.3%	1.6	<.0001
Coronary Revascularization procedure to Cardiac Catheterization ratio	20.2%	27.7%	—————	.0008
Repeat ED visit 3891 (8%)	8.1%	8.0%	1.1	.003
Repeat test 7654 (16%)	16.6%	15.1%	1.0	0.84
Myocardial Infarction 155 (0.3%)	0.34%	0.30%	1.2	0.20

* Adjusted odds ratio; MPI versus SE, SE is reference.