Limited Use of Outpatient Stress Testing in Young Patients With Atypical Chest Pain

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Low prevalence of coronary artery disease within this population suggests that younger patients may not require stress testing for chest pain evaluations as long as pretest likelihood is low.

The decision to perform stress testing in the evaluation of chest pain is often based on the pretest likelihood of coronary artery disease (CAD).[1-7] Cardiac risk scores, which incorporate smoking status, blood pressure, diabetes mellitus, and cholesterol levels, also may provide further risk stratification.[8-11] Assuming that the prevalence of CAD increases with age, young adults could be deemed low risk, not warranting cardiac screening.[12]

Professional society guidelines from the American College of Cardiology/American Heart Association and American College of Physicians[4,5] recommend stress testing as the initial diagnostic test for CAD in symptomatic patients; additionally, the guidelines also suggest that screening stress tests may confer primary prevention benefit in intermediate-risk asymptomatic patients.[9,13] Exercise treadmill testing is considered the initial modality of choice, given its technical ease and lower cost, compared with stress echocardiography.[14]

Previously published reports have shown the limited use of stress testing to screen young asymptomatic adults.[15-17] Because this patient demographic typically has a low pretest likelihood of CAD, positive stress tests are often false-positive results.[7,18] The consequence of false-positive testing may be unnecessary additional cardiac testing, potentially leading to more patient harm than benefit.[18,19] For active-duty service members, false-positive testing also has the potential to affect worldwide deployability and/or sea duty status while further risk stratification is performed; as a result, mission readiness may be impacted.

Although the number of clinic visits for chest pain has declined, there has been a discordant increase in the rates of stress testing in the US.[20-22] Additionally, the rate of stress testing among young adults, specifically in the 25- to 34-year age group, has increased in recent years. Given the rising use of stress tests in the young patient population, the clinical use of stress testing needs to be reassessed.

Although much of the literature has already demonstrated the low value of stress testing in young asymptomatic adults, no data currently exist regarding its outpatient use in evaluating young symptomatic patients. The military represents a predominantly young cross-section of the general population suitable for exploring this topic. Using a cohort of active-duty service members, we aimed to determine the use of outpatient stress testing in evaluating young patients with atypical chest pain.

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METHODS

The US Department of Defense (DoD) Military Health System Database Repository (MDR) and Comprehensive Ambulatory Professional Encounter Record (CAPER) were the data sources for this study. The MDR contains continually updated, longitudinal electronic medical records (EMRs) for nearly 1.4 million active-duty service members and is composed of administrative, medical, pharmacy, and clinical data. The Naval Medical Center Portsmouth (NMCP) Institutional Review Board approved this study.

Study Cohort

We performed chart reviews of service members aged 18 to 35 years who received cardiac stress testing at NMCP, an academic tertiary care center, within 30 days after an office visit for atypical chest pain between October 1, 2010, and September 30, 2015. Atypical chest pain was defined as any outpatient claim with ICD-9 code, 786.5x, in the primary diagnosis field (Table 1).[4] Cardiac stress testing was identified using CPT codes. Additional cardiac testing occurring within 1 year of patients' index stress test also was documented. Exclusion criteria were known CAD as well as inpatient and emergency department stress testing. Results were tallied for the entire study period (2010-2016).

Demographics and cardiac risk factors (ie, hypertension, hyperlipidemia, diabetes mellitus, and smoking status) were assessed prior to index chest pain evaluations and defined via ICD-9 codes within outpatient records.

Cardiac Testing Outcomes

Patients were initially categorized by the results of baseline electrocardiograms (ECG) and index stress tests (ie, exercise treadmill or stress echocardiography, exercise or Lexiscan myocardial perfusion imaging, dobutamine stress echocardiography). Positive tests were defined as those having electrical or structural ischemic changes. Chronotropic changes were infrequent and nonpathologic and were not counted. Patient endpoints were either additional cardiac testing or negative index stress test without additional testing.

Statistical Analysis

The agreement between both baseline ECG and index stress test as well as index stress test and additional cardiac testing were analyzed using McNemar test and matched-pair odds ratios (ORs) with corresponding 95% CIs. Analyses were stratified by demographics and cardiac risk factors to assess for potential confounding. Analyses were performed using SAS version 9.4 (Cary, NC).

RESULTS

A total of 1,036 patients were evaluated for atypical chest pain and had index stress testing between October 1, 2010 and September 30, 2015. The study cohort was 69% male with a mean (SD) age of 27.3 (4.7) years. More than 60% of the cohort was older than aged > 25 years. The most prevalent cardiac risk factor among the study group was smoking (23%), followed by hypertension (15%) and hyperlipidemia (10%) (Table 2). More than 94% of study patients were referred for index stress testing by their primary care provider.

In the initial testing cohort, exercise treadmill test (59.3%) and exercise echocardiogram (37.1%) were the most common stress testing modalities. The mean (SD) metabolic equivalents (METS) achieved among individuals who performed exercise stress testing was 13.9 (2.8). There were 65 patients who had a positive baseline ECG/negative index stress test, 958 patients had a negative ECG/negative index test, and 8 patients had a negative ECG/positive index test. The difference between the first

Table 1. Clinical Classification of Chest Pain[4]

Typical angina (definite)	(1) Substernal chest discomfort with a characteristic quality and duration that is (2) provoked by exertion or emotional stress and (3) relieved by rest or nitroglycerin.
Atypical angina (probable)	Meets 2 of the above characteristics.
Noncardiac chest pain	Meets 1 or none of the typical angina characteristics.

Table 2. Demographics, Risk Factors, and Referral Source of 1,036 Study Patients

Age, mean, y (SD)	27.3 (4.7)
Age category, No. (%)	
18-20 y	74 (7)
21-25 y	334 (32)
26-30 y	323 (31)
31-35 y	305 (30)
Gender, No. (%)	
Male	719 (69.4)
Female	317 (30.6)
Cardiac risk factors, No. (%)	
Smoker	238 (23.0)
Hypertension	159 (15.3)
Hyperlipidemia	100 (9.7)
Diabetes mellitus	5 (0.5)
Chronic kidney disease	1 (0.1)
Referral source, No. (%)	
Primary care provider	979 (94.5)
NMCP emergency department	52 (5.0)
Community emergency department	2 (0.2)
Pulmonology clinic	2 (0.2)
Walk-in	1 (0.1)

Abbreviation: NMCP, Naval Medical Center Portsmouth.

Table 3. Cardiac Testing Characteristics and Outcomes

Index Stress Testing		
Modality	**No.**	**%**
Exercise, treadmill	614	59.3
Exercise, stress echocardiography	384	37.1
Exercise, myocardial perfusion imaging	18	1.7
Lexiscan myocardial perfusion imaging	18	1.7
Dobutamine stress echocardiography	2	0.2
Results	**Mean**	**SD**
Metabolic equivalents[a]	13.9	2.8
Baseline Electrocardiogram	**Positive Index Test, No.**	**Negative Index Test, No.**
Positive	5	65
Negative	8	958
Additional Cardiac Testing		
	Yes	**No**
Patients with additional testing, No.	102	934
Modality[b]	**No.**	**%**
Computed tomography angiography	48	42.8
Exercise, stress echocardiography	43	38.3
Exercise, treadmill	5	4.5
Transthoracic echocardiography	5	4.5
Exercise, MPI	3	2.7
Left heart catheterization	2	1.8
Lexiscan MPI	2	1.8
Cardiac magnetic resonance imaging	1	0.9
Dobutamine stress echocardiography	1	0.9
Event monitor	1	0.9
Holter monitor	1	0.9
	Positive Additional Test, No.	**Negative Additional Test, No.**
Positive index stress test	2	11
Negative index stress test	1	88

Abbreviations: METS, metabolic equivalents; MPI, myocardial perfusion imaging.
[a]Average metabolic equivalents for patients who had exercise stress testing.
[b]Restricted to patients who had additional cardiac testing; tests are not mutually exclusive, some patients had more than 1 test.

2 groups (6.27% vs 0.77%) was statistically significant, given $\chi^2 = 44.5$; $P < .001$ (McNemar test); matched-pair OR, 8.125 (95% CI 3.9-16.93, $P < .05$). There was 93% concordance for the dual negative tests group (Table 3).

There were 102 patients (10%) who performed additional cardiac testing. Among this subgroup, 13 patients (1.3%) had additional testing for further evaluation of a positive index stress test (Table 4) and 89 patients (8.6%) had testing for continuing atypical chest pain despite a negative index stress test. The number of additional tests performed exceeded 102 because some patients underwent multiple tests. There were 11 patients that had a positive index stress test/negative additional test, 1 patient had a negative index test/positive additional test, and 88 patients had a negative index test/negative additional test. The difference between the first 2 groups (10.8% vs 0.9%) was statistically significant, ($\chi^2 = 8.33$, $P < .004$ by McNemar test; matched pair OR, 11 [95% CI 1.42-85.2, $P < .05$]). There was 88% concordance for the dual negative tests group.

Coronary computed tomography angiography (CCTA) demonstrated nonobstructive CAD in 3 patients (0.3%) within the study cohort. There was no obstructive CAD identified in our cohort. Two patients had negative left heart catheterizations (LHC). One of these patients had a negative LHC and a negative Lexiscan after a CCTA showed CAD; all 3 of these additional tests were performed for evaluation of continued chest pain despite negative index stress testing. The positive predictive value of cardiac stress testing for nonobstructive CAD in this low-risk population was 15.4% (2 of 13). Stratification by demographics, CAD risk factors, and cardiac test results revealed no presence of confounding factors during analyses.

DISCUSSION

In this retrospective, observational study of 1,036 young patients with atypical chest pain who had stress testing, there was relatively strong agreement between baseline ECG and index stress test results. Individuals also were 8 times more likely to have positive baseline ECGs and negative stress testing than having the opposite finding. Additional cardiac testing similarly demonstrated congruency with index stress testing and showed the propensity for false-positive stress tests. Further testing with CCTA demonstrated minimal nonobstructive CAD in < 1% of the study cohort and 2 LHC were negative. Despite the low prevalence of CAD and apparent low diagnostic use of stress testing in our young cohort, symptomatic service members still require stress testing to determine deployment suitability.

The low yield of outpatient stress testing in our young population is rooted in Bayes' theorem, which highlights the importance of pretest likelihood in the diagnosis of CAD.[7,23] Because our cohort had a low prevalence and low pretest likelihood of CAD, positive index stress tests were often false-positive results and consequently did not increase the posttest likelihood of CAD, resulting in low positive predictive value.

Additional cardiac testing had limited clinical value in our cohort. The 3 cases of nonobstructive CAD were unlikely to be pathologic given the minimal degree

Table 4. Characteristics of Patients With Abnormal Stress Testing

Age, y	Cardiac Risk Factors	Baseline ECG Result	Stress Test Result	Additional Test(s) Result
18	None	Normal	ETT, < 1 mm upsloping inferior ST depressions	ESE, normal
21	Hypertension	Nonspecific ST abnormality	ETT, 1 mm infero-lateral ST depressions	CCTA, normal
25	None	Normal	ETT, 1.5-2 mm horizontal inferior ST depressions	ESE, normal
25	None	Normal	ETT, 1.5 mm downsloping inferior ST depressions, T-wave inversions	TTE, normal
27	None	Normal	ETT, 2 mm horizontal ST depression in AVR	ESE, normal
27	None	Normal	ETT, 0.5-1 mm horizontal inferior ST depressions	CCTA, normal
28	None	Nonspecific T-wave abnormality	ETT, infero-lateral T wave inversions	ESE, normal
31	None	Nonspecific T-wave inversions	ETT, < 1 mm upsloping anterior ST depressions	CCTA, minimal soft plaque in LAD, < 30% stenosis
32	Hypertension	Nonspecific ST depressions	ETT, infero-lateral T-wave inversions	CCTA, normal
32	None	Lateral T-wave inversions	ETT, 1 mm inferior ST depressions	ESE, normal
33	Hypertension Hyperlipidemia	Nonspecific T-wave inversions	ETT, 1-1.5 mm horizontal infero-lateral ST depressions	CCTA, nonobstructive soft plaque in LAD, 30-50% stenosis
34[a]	Hypertension	Normal	ETT, normal	CCTA, nonobstructive calcific plaque in LAD, < 30% stenosis LHC, normal Lexiscan, normal
35	None	Normal	ETT, 1 mm horizontal infero-lateral ST depressions, T-wave inversions	ESE, normal
35	None	Nonspecific T-wave inversions	ETT, nonspecific 1 mm upsloping ST depression	Patient declined ESE

Abbreviations: CCTA, coronary CT angiography; ESE, exercise stress echocardiography; ETT, exercise treadmill test; LHC, left heart catheterization; TTE, transthoracic echocardiography.
[a]This patient had a normal index stress test but abnormal additional CCTA testing.

of observed stenosis and the 2 LHC did not require revascularization. These results are similar to those shown by Christman and colleagues and Mudrick and colleagues, which highlighted the low yield of additional cardiac studies and low rate of revascularization among symptomatic patients without known cardiac disease, respectively.[18,19]

This is the first study, to our knowledge, to quantitatively demonstrate the low use of outpatient stress testing for young adults with atypical chest pain. Previous studies that assessed stress testing for young patients with chest pain in acute settings such as emergency departments and chest pain observation units, similarly demonstrated minimal yield of routine diagnostic testing.[23,24] This further highlights the premise that outpatient and even emergent-setting stress testing in low cardiac risk individuals may be of limited value and not always necessary.

Limitations

There were several study limitations. As a single-center, cross-sectional review, we may not be able to extrapolate our findings to the general population. However, given the low prevalence of CAD in young adults, stress testing would likely have limited value regardless of the sample distribution; so it may be possible to extend our findings beyond our cohort. Also, neither baseline ECG nor index stress test (irrespective of modality) could be given a diagnostic value in predicting ischemia alone; doing so would require comparison with the gold standard—heart catheterization. Although referral bias has been associated with diagnostic performance of stress testing, we did not adjust for this phenomenon.[25] Given the higher average metabolic equivalents achieved in our cohort, this potential bias likely did not affect diagnostic performance.

CONCLUSION

There was low diagnostic use of outpatient stress testing and additional cardiac testing for CAD among young patients with atypical chest pain. The limited value of cardiac stress testing is likely a function of the low CAD prevalence within this population, suggesting that younger patients may not necessarily require stress testing for chest pain evaluations as long as pretest likelihood is low. Despite our results, we maintain that the decision to perform stress testing should still be guided by clinical judgment, but perhaps our findings may alleviate physicians' concerns over the urgency of when to refer low-risk patients for testing. Although we are cautious in inferring our findings to the general population, the similarity it shares with those from other published reports may suggest its applicability beyond our study cohort.

Author disclosures

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Disclaimer

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