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Diagnostic Yield of Routine Noninvasive Cardiovascular Testing in Low-Risk Acute Chest Pain Patients

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Abstract

Contemporary professional society recommendations for patients presenting to the emergency department with acute chest pain and low clinical risk encourage noninvasive testing for coronary artery disease (CAD) before, or shortly after, discharge from the emergency department. Recent reports indicate that a strategy of universal testing has a low diagnostic yield and may not be necessary. We examined data from a prospective cohort of patients who underwent evaluation of acute chest pain in our chest pain evaluation center (CPEC). Patients presenting with normal initial electrocardiogram and cardiac injury markers were eligible for observation and noninvasive testing for CAD in our CPEC. All patients were asked to participate in the prospective registry. The 213 subjects who consented were young, obese, and predominantly women (mean age 43.8 ± 12.5 , mean body mass index of 30.8 ± 7 , 64.8% women). Prevalence of diabetes was 10.3% (hypertension 37.1%, hyperlipidemia 17.8%, and current tobacco use 23.5%) Exercise treadmill testing was the primary method of evaluation ($n = 104$, 49%) followed by computed tomography coronary angiography ($n = 58$, 27%) and myocardial perfusion imaging ($n = 20$, 9%). Of 203 patients who underwent testing, 11 had abnormal test results, 4 of whom had obstructive CAD based on invasive coronary angiography. The positive predictive value for obstructive CAD after an abnormal test was 45.5%, and the overall diagnostic yield for obstructive CAD was 2.5%. In conclusion, in patients with acute chest pain evaluated in a CPEC, the yield of routine use of noninvasive testing for CAD was minimal and the positive predictive value of an abnormal test was low.

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Professional societies encourage provocative testing for low-risk chest pain patient during, or shortly after, an encounter in the emergency department (ED). Recent literature suggests that indiscriminate testing of these patients with chest pain has poor diagnostic performance. In 2011, our institution established a chest pain evaluation center (CPEC) within our ED. Patients in the CPEC were enrolled in a prospective registry to track the results of their cardiovascular evaluation. We determined the diagnostic yield of routine noninvasive cardiovascular testing in this contemporary, acute chest pain population preselected to be at low cardiovascular risk. We hypothesized that few patients would be diagnosed with coronary artery disease (CAD) and that the diagnostic yield of routine testing within this population would be low.

Methods

The design of our CPEC and the accompanying registry have been described previously.¹ The CPEC has 8 bed spaces located within the ED at our medical center. The unit is staffed by a nurse practitioner or physician assistant with specialized training in assessment and management of patients with chest pain. Supervision is provided by a member of the ED faculty. Patients were selected for observation within the CPEC if they had no known heart disease and no evidence of ischemia based on initial electrocardiogram and biomarker testing. Selection of tests for CAD were guided by a custom decision support tool that helped estimate CAD risk using the patient's symptoms, age, and risk factors. Anginal symptoms classified by the system by Diamond and Forrester² were used for CPEC selection and collected in the registry. Advanced providers are trained to supervise exercise treadmill tests (ETTs), which are performed in the unit during weekdays from 8 AM to 5 PM and from 8 AM to 12 PM on weekend days. ETT is encouraged as the primary testing technique, whereas the primary noninvasive cardiovascular imaging test is computed tomographic coronary angiography (CTCA) performed on an Aquilion One CT scanner (Toshiba, Tustin, California) with 320 detectors and images reviewed on a Vital workstation (Vitrea, Minnetonka, Minnesota) by an interdisciplinary team of radiologists and cardiologists trained in CTCA. Nuclear myocardial perfusion imaging is also available on weekdays using technetium-99m single-photon emission computed tomography.

All patients in the CPEC were asked to participate in the CPEC registry. For those who agreed and provided written informed consent, data regarding the patient's evaluation were recorded by research staff in a Web-based database using REDcap software (Vanderbilt University, Nashville, Tennessee). Data gathered included a detailed structured description of the patient's symptoms, medical history, subsequent cardiovascular testing, and test results.

ETT were classified as ischemic, nonischemic, or uninterpretable by an attending cardiologist using standard criteria for ischemia: horizontal or downsloping ST depression 1.0 mm in contiguous leads, exercise-induced hypotension, or ventricular arrhythmias; Duke treadmill scores were also calculated.³ CTCA results were classified as normal (zero calcium and no coronary lesions), non-obstructive (all coronary lesions <50% stenosis), or obstructive (at least 1 lesion ≥50% stenosis). If images were nondiagnostic, the CTCA was not categorized. The "normal testing" group included all subjects with nonischemic ETT,

those with normal or nonobstructive CTCA results, and those who did not undergo testing (i.e., their risk was so low as to not warrant testing). “Abnormal testing” was defined as all subjects with at least 1 abnormal test result: ischemic ETT, CTCA with obstructive CAD, or abnormal alternative testing. If a patient underwent more than 1 cardiovascular test or other noncardiac imaging tests (such as pulmonary embolus study or lower extremity Doppler), the patient was categorized as having multiple tests.

The primary outcome was the proportion of patients in the CPEC diagnosed with obstructive CAD after undergoing noninvasive testing. Secondly, we compared patients with and without an abnormal test result by characteristics of their angina to determine any correlation between symptoms and test results. Proportions were compared by the chi-square test and continuous data by the Student's *t* test. Statistical analyses were performed using SPSS, version 21 (IBM, Armonk, New York).

Results

A total of 213 subjects were evaluated in the CPEC and agreed to participate in the registry from December 2011 to April 2013. Approximately 20% of patients with chest pain presenting to our ED were treated in the CPEC, of which approximately 10% consented to participate in the registry. The following tests were performed: ETT for 104 (49%), CTCA for 58 (27%), other/multiple tests for 41 (19%), and no test for 10 (5%; Figure 1). The study population was young (mean age 43.8 years, range 20 to 67 years) with relatively low burden of cardiovascular risk factors (Table 1).

The numbers of each test performed exceed the number of patients in the study cohort because some patients underwent multiple tests. A total of 119 ETTs were performed, including those with ETT as the primary diagnostic strategy and some who underwent multiple tests. Only 4 ETTs demonstrated ischemia, whereas 96 were nonischemic and 19 were inconclusive. The mean Duke treadmill score was 6.6 (range –5 to 15). CTCA was performed in 71 subjects including 33 who were normal, 30 who had nonobstructive CAD, 6 who had obstructive CAD, and 1 who was inconclusive (because of mistiming of contrast bolus). Of 20 nuclear stress tests performed, only 1 had abnormal test result with a small fixed defect (summed stress score = 5, summed difference score = 0). A total of 6 patients underwent other imaging tests: 3 stress echocardiograms (none abnormal) and 3 noncardiac chest CTs. Testing was not performed for 10 of the subjects in the CPEC registry. One subject recently had normal test result at another facility, 4 were referred for outpatient follow-up, 1 left against medical advice, and the remaining 4 were felt to clinically not warrant any additional testing.

A total of 11 patients had abnormal test results (Table 2). Subsequent invasive coronary angiography was performed in 8 patients. One patient with a fixed defect on myocardial perfusion imaging did not undergo invasive angiography was presumed to have CAD and was treated medically. In total, 5 patients were diagnosed with obstructive CAD for a diagnostic yield of 2.5% (5 of 203). Ten patients who did not undergo testing were not included in our calculation. The positive predictive value of noninvasive testing in this low-risk population was 46% (5 of 11). When we compared patients with and without abnormal

test results based on angina duration, CAD risk, and symptom characteristics, none of the comparisons were significant ($p = 0.8, 0.078, \text{ and } 0.18$, respectively; Table 3).

Discussion

The results of our investigation add to a growing body of literature demonstrating a low yield of routine testing for low-risk patients with acute chest pain managed in observation or clinical decision units. This was previously demonstrated over a decade ago in a report showing that ETT was positive for 13% of low-risk patients with chest pain presenting to the ED. Only 32% had additional testing indicative of ischemia or obstructive CAD, indicating that most positive ETT in these patients were false positives.⁴ Khare et al⁵ found that 70% of coronary angiograms performed on patients with positive stress tests yielded no obstructive CAD. Of 459 patients in a study by Cotarlan et al,⁶ 62 had positive tests with 16 having obstructive CAD. Most recently, Hermann et al⁷ demonstrated that only 1.5% ($n = 63$) of 4,181 patients had obstructive disease and only 0.7% ($n = 28$) had revascularization associated with expectation of benefit (class I or IIa recommendations). Foy et al⁸ showed in 421,774 patients that risk of infarction is not different between those who do versus those who do not undergo noninvasive testing, again questioning the value of routine testing for patients in the ED with chest pain.

The reasons for the low yield of routine testing are rooted in Bayes' theorem that indicates the importance of the pretest likelihood of a diagnosis on the outcome of a test in a particular population.⁹ Our study population consisted of patients selected to be at very low pretest likelihood of cardiovascular disease. As such, a positive noninvasive test did not markedly increase the post-test likelihood of CAD, resulting in a low positive predictive value. This phenomenon is magnified when clinicians treat test results as having simple dichotomous outcomes as opposed to taking advantage of the complete diagnostic information that tests may offer. Early data on ETT, for example, show that the post-test likelihood of CAD is higher for an ETT that is markedly positive compared with one which fulfills only minimal criteria of a positive result.¹⁰

Our data raise an important question in the context of low-risk patients presenting to the ED with chest pain: how low a risk is sufficiently low to afford confidence that noninvasive testing is not warranted? In our patients, chest pain severity, duration, and character did not identify patients with positive noninvasive tests; however, the size of our study group was inadequate for conclusions in this regard. Several structured scoring systems have been developed or adapted for use in the ED. The HEART (History, ECT, Age, Risk Factors, Troponin) score appears capable of reducing indications for cardiovascular imaging, whereas the North American Chest Pain Rule does not perform as well.^{11,12} The next generation of high-sensitivity cardiac troponin assays, already in use outside the United States, may be helpful. These markers have been tested in several randomized trials on patients in the ED and consistently identified a substantial fraction of patients with acute chest pain with minimal risk of acute coronary syndrome that can be discharged without further testing.^{13,14}

The reliance on noninvasive testing for patients with acute chest pain is driven by a variety of factors. Physicians are concerned about the potential of missed diagnoses both in terms of the potential for harm to patients and liability. Of claims originating in the ED, diagnostic errors and missed myocardial infarction were among the principal reasons for malpractice claims in a large database.¹⁵ Although these are valid concerns, current data suggest that rather than indiscriminate use of noninvasive testing for all patients with chest pain, the yield may be improved if physician discretion, more accurate risk scores, and high-sensitivity biomarkers are used.^{16,17} Perspectives on the rationale of selective rather than routine functional testing for CAD in low-risk patients presenting to the ED with chest pain have recently been reviewed¹⁷; future professional society recommendations may encourage this more nuanced approach to testing.

Our investigation has several limitations. The study population is from a single center and may have selection bias through triage into the CPEC. The process of informed consent may introduce selection bias; however, the distribution of baseline characteristics is similar to a previous report of a nonselected population from our CPEC.¹ Our estimates of diagnostic yield and positive predictive value are specific to the selected low-risk population in our study and cannot be applied to a general chest pain population. As a registry and not a clinical trial, clinicians were at liberty to select which noninvasive test to use. We do not have adequate follow-up on our population and cannot estimate false negative results or the negative predictive value of our methods.

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References

1. Winchester DE, Stomp D, Shifrin RY, Jois P. Design and implementation of a stand-alone chest pain evaluation center within an academic emergency department. *Crit Pathw Cardiol.* 2012; 11:123–127. [PubMed: 22825532]
2. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. *N Engl J Med.* 1979; 300:1350–1358. [PubMed: 440357]
3. Mark DB, Hlatky MA, Harrell FE, Lee KL, Califf RM, Pryor DB. Exercise treadmill score for predicting prognosis in coronary artery disease. *Ann Intern Med.* 1987; 106:793–800. [PubMed: 3579066]
4. Amsterdam EA, Kirk JD, Diercks DB, Lewis WR, Turnipseed SD. Immediate exercise testing to evaluate low-risk patients presenting to the emergency department with chest pain. *J Am Coll Cardiol.* 2002; 40:251–256. [PubMed: 12106928]
5. Khare RK, Powell ES, Venkatesh AK, Courtney DM. Diagnostic uncertainty and costs associated with current emergency department evaluation of low risk chest pain. *Crit Pathw Cardiol.* 2008; 7:191–196. [PubMed: 18791408]
6. Cotarlan V, Ho D, Pineda J, Qureshi A, Shirani J. Impact of clinical predictors and routine coronary artery disease testing on outcome of patients admitted to chest pain decision unit. *Clin Cardiol.* 2014; 37:146–151. [PubMed: 24255007]
7. Hermann LK, Newman DH, Pleasant WA, Rojanasartikul D, Lakoff D, Goldberg SA, Duvall WL, Henzlova MJ. Yield of routine provocative cardiac testing among patients in an emergency department-based chest pain unit. *JAMA Intern Med.* 2013; 173:1128–1133. [PubMed: 23689690]

8. Foy AJ, Liu G, Davidson WR, Sciamanna C, Leslie DL. Comparative effectiveness of diagnostic testing strategies in emergency department patients with chest pain: an analysis of downstream testing, interventions, and outcomes. *JAMA Intern Med.* 2015; 175:428–436. [PubMed: 25622287]
9. Diamond GA. The wizard of odds: Bayes theorem and diagnostic testing. *Mayo Clin Proc.* 1999; 74:1179–1182. [PubMed: 10560608]
10. Rifkin RD, Hood WB. Bayesian analysis of electrocardiographic exercise stress testing. *N Engl J Med.* 1977; 297:681–686. [PubMed: 895788]
11. Mahler SA, Hiestand BC, Goff DC, Hoekstra JW, Miller CD. Can the HEART score safely reduce stress testing and cardiac imaging in patients at low risk for major adverse cardiac events? *Crit Pathw Cardiol.* 2011; 10:128–133. [PubMed: 21989033]
12. Mahler SA, Miller CD, Hollander JE, Nagurney JT, Birkhahn R, Singer AJ, Shapiro NI, Glynn T, Nowak R, Safdar B, Peberdy M, Counsellman FL, Chandra A, Kosowsky J, Neuenschwander J, Schrock JW, Plantholt S, Diercks DB, Peacock WF. Identifying patients for early discharge: performance of decision rules among patients with acute chest pain. *Int J Cardiol.* 2013; 168:795–802. [PubMed: 23117012]
13. Aldous SJ, Richards MA, Cullen L, Troughton R, Than M. A new improved accelerated diagnostic protocol safely identifies low-risk patients with chest pain in the emergency department. *Acad Emerg Med.* 2012; 19:510–516. [PubMed: 22594354]
14. Cullen L, Mueller C, Parsonage WA, Wildi K, Greenslade JH, Twerenbold R, Aldous S, Meller B, Tate JR, Reichlin T, Hammett CJ, Zellweger C, Ungerer JP, Rubini Gimenez M, Troughton R, Murray K, Brown AF, Mueller M, George P, Mosimann T, Flaws DF, Reiter M, Lamanna A, Haaf P, Pemberton CJ, Richards AM, Chu K, Reid CM, Peacock WF, Jaffe AS, Florkowski C, Deely JM, Than M. Validation of high-sensitivity troponin I in a 2-hour diagnostic strategy to assess 30-day outcomes in emergency department patients with possible acute coronary syndrome. *J Am Coll Cardiol.* 2013; 62:1242–1249. [PubMed: 23583250]
15. Brown TW, McCarthy ML, Kelen GD, Levy F. An epidemiologic study of closed emergency department malpractice claims in a national database of physician malpractice insurers. *Acad Emerg Med.* 2010; 17:553–560. [PubMed: 20536812]
16. Napoli AM. The association between pretest probability of coronary artery disease and stress test utilization and outcomes in a chest pain observation unit. *Acad Emerg Med.* 2014; 21:401–407. [PubMed: 24730402]
17. Amsterdam EA, Aman E. The patient with chest pain: low risk, high stakes. *JAMA Intern Med.* 2014; 174:553–554. [PubMed: 24515330]

Figure 1. Distribution of noninvasive testing strategy. The study population was divided into several groups based on the primary noninvasive testing strategy selected. The predominant method was exercise treadmill testing. MPI = myocardial perfusion imaging.

Table 1

Baseline demographic data for 213 patients

Age (years, mean $\pm$ SD)	43.8 $\pm$ 12.5
Body Mass Index (kg/m ²)	30.8 $\pm$ 7.5
Female	138 (65%)
Diabetes Mellitus	22 (10%)
Hypertension *	79 (37%)
Hyperlipidemia *	38 (18%)
Current Smoker	50 (24%)
Aspirin	14 (7%)
Statin	14 (7%)
Beta Blocker	13 (6%)

* Hypertension and Hyperlipidemia were extracted as data fields from the electronic health record for each patient.

Table 2

Characteristics and diagnostic evaluation of patients with abnormal noninvasive testing

Age (years)	BMI (kg/m ²)	Gender	DM	SH	HLD	CS	DST [*]	D&F [†]	Abnormal test	Coronary Angiography	Obstructive CAD
52	30.5	F	-	+	-	-	Intermediate	Typical	CTCA	+	0
47	24.4	M	-	+	-	-	Intermediate	Noncardiac	ETT	+	0
50	17.9	F	-	+	-	-	Intermediate	Atypical	CTCA	+	+
30	23.9	F	-	-	-	-	Low	Typical	ETT	0	0
48	42.5	F	+	-	-	-	High	Noncardiac	MPI	0	+
57	29.0	M	-	+	-	+	High	Noncardiac	CTCA	+	0
55	33.8	M	-	-	+	-	Intermediate	Typical	ETT	+	+
35	29.4	M	-	-	-	-	Low	Atypical	CTCA	+	0
58	41.9	M	-	+	+	-	Low	Atypical	CTCA	+	+
43	26.4	M	-	+	-	+	Low	Atypical	ETT	0	0
47	25.6	F	-	-	-	+	Intermediate	Atypical	CTCA	+	0

BMI = body mass index; CAD = coronary artery disease; Cath = invasive coronary angiography; CS = cigarette smoker; CTCA = computed tomography coronary angiography; D&F = Diamond and Forrester criteria; DM = diabetes mellitus; DST = decision support tool; ETT = exercise treadmill test; F = female; HLD = hyperlipidemia; M = male; MPI = myocardial perfusion imaging; SH = systemic hypertension.

^{*} Assessment of coronary risk based on the custom risk model used in our facility.

[†] Typicality of angina based on Diamond and Forrester criteria.

Table 3

Symptom differences between patients with normal and abnormal testing

Variable	Normal test n=202 [*]	Abnormal test n=11	p value
Angina duration[*]			
Less than a day	90 (45%)	4 (36%)	0.8
1-2 days	33 (16%)	1 (9%)	
Less than a week	32 (16%)	3 (27%)	
More than a week	43 (22%)	3 (27%)	
DST assessment			0.078
Low	120 (62%)	4 (36%)	0.18
Intermediate	65 (34%)	5 (46%)	
High	9 (5%)	2 (18%)	
Angina class			
Noncardiac	107 (54%)	3 (27%)	0.18
Atypical	48 (24%)	5 (46%)	
Typical	43 (22%)	3 (27%)	

DST = decision support tool.

^{*} Normal test group had some patients with incomplete data.