

Early Echocardiography Can Predict Cardiac Events in Emergency Department Patients With Chest Pain

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Study objective: Accurate diagnosis in emergency department patients with possible myocardial ischemia is problematic. Two-dimensional echocardiography has a high sensitivity for identifying patients with myocardial infarction (MI); however, few studies have investigated its diagnostic ability when used acutely in ED patients with possible myocardial ischemia. Therefore we investigated the ability of ED echocardiography for predicting cardiac events in patients with possible myocardial ischemia.

Methods: Echocardiography was performed within 4 hours of ED presentation in 260 patients with possible myocardial ischemia, and was considered positive if there were segmental wall motion abnormalities or the ejection fraction was less than 40%. ECGs were considered abnormal if there was an ST-segment elevation or depression of greater than or equal to 1 mm, or ischemic T-wave inversion. Cardiac events included MI and revascularization.

Results: Of the 260 patients studied, 45 had cardiac events (23 MI, 19 percutaneous transluminal angioplasty, 3 coronary bypass surgery). The sensitivity of echocardiography for predicting cardiac events was 91% (95% confidence interval 79% to 97%), which was significantly higher than the ECG (40% [95% CI 27% to 55%]; $P < .0001$), although specificity was lower (75% [95% CI 69% to 81%] versus 94% [95% CI 90% to 97%]; $P < .001$). Addition of the echocardiography results to baseline clinical variables and the ECG added significant incremental diagnostic value ($P < .0001$). With use of multivariate analysis, only male gender ($P < .03$, odds ratio [OR] 2.4 [1.1 to 5.3]), and a positive echocardiographic finding ($P < .0001$, OR 24 [9 to 65]) predicted cardiac events. Excluding patients with abnormal ECGs (N=30) did not affect sensitivity (85%) or specificity (74%) of echocardiography.

Conclusion: Echocardiography performed in ED patients with possible myocardial ischemia identifies those who will have cardiac events, is more sensitive than the ECG, and has significant incremental value when added to baseline clinical variables and the ECG.

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INTRODUCTION

Each year more than 5 million patients are evaluated in emergency departments for chest pain or other symptoms suggestive of myocardial ischemia.¹ Because of the limitations of historical, physical, and ECG data, many of these patients are admitted to the hospital, although the majority are later determined to have nonischemic causes of their symptoms.² Despite this low threshold for admission, up to 8% of patients with acute myocardial infarction (MI) are discharged to home,^{3,4} with a significant associated mortality rate.³ Although some of the inadvertently discharged patients have ongoing infarction, others may have unstable angina that subsequently evolves into MI. The significant short-term risk for cardiac morbidity and mortality associated with unstable angina underscores the importance of identifying these patients.^{5,6}

Previous studies have demonstrated that two-dimensional echocardiography is a sensitive tool for identifying patients with MI.⁷⁻⁹ However, there are limited data on the use of early echocardiography in patients with ischemia without MI.¹⁰ The objectives of this study were as follows: (1) to investigate the ability of ED echocardiography to identify patients at risk for cardiac events, (2) to determine the accuracy in patients without abnormal ECGs, and (3) to determine whether echocardiography provides incremental diagnostic information when added to historical and ECG variables.

METHODS

All patients presenting to our ED with chest pain or other symptoms suggestive of myocardial ischemia underwent an evaluation by housestaff and attending physicians that included a history, physical examination, and ECG. If, after the initial evaluation, the emergency physician thought that myocardial ischemia was a possible cause for the presenting symptoms, the patient was treated according to a diagnostic pathway. This study included consecutive patients evaluated between 7 AM and 7 PM weekdays. All patients gave informed consent, and the study was approved by the Committee on the Conduct of Human Research. All patients who were approached for study enrollment agreed to participate; the few patients (<2%) who did not undergo echocardiography were excluded because of the inability to perform the echocardiogram in a timely fashion.

Further evaluation was completed using a previously described diagnostic and triage protocol.¹¹ In brief, high-risk patients were admitted to the CCU for exclusion of MI. Moderate-risk patients were admitted for a "fast-track rule-in" protocol after undergoing rest myocardial perfusion imaging with technetium-99m sestamibi (Dupont Pharma). Low-risk patients underwent rest perfusion imaging in the ED. Those with negative results after rest perfusion imaging were discharged and scheduled to return for follow-up stress testing within the next 48 hours, whereas those with positive results after rest perfusion imaging were admitted to the CCU. All admitted patients underwent serial myocardial marker sampling. Additional diagnostic evaluation was left to the discretion of the CCU attending physician.

Echocardiography

Two-dimensional echocardiograms were obtained (Hewlett-Packard model 500, 1000, or 1500 ultrasound systems, Palo Alto, California) by a cardiology fellow or trained cardiac sonographer within 4 hours of the patients' arrival in the ED. Parasternal long- and short-axis, and two- and four-chamber views were recorded on .5-inch VHS videotape and were later interpreted by two experienced echocardiographers blinded to patients' clinical status and outcome. Patients were excluded if two or more of the four views were not interpretable. A wall motion score index (WMSI) was calculated according to a 16-segment wall motion score system,¹² and ejection fraction was visually estimated. Echocardiographic findings were considered positive if they showed the following: (1) abnormal wall motion of two or more contiguous segments, (2) abnormal wall motion of one segment visible in two different views, or (3) global hypokinesis with an estimated ejection fraction less than 40%. The few disagreements between the two echocardiographers were resolved by a third echocardiographer. All physicians involved in the care of the patient were blinded to the echocardiography results.

Endpoints and Definitions

Endpoints included MI and revascularization (percutaneous transluminal coronary angioplasty [PTCA] or coronary artery bypass surgery [CABG]) during the initial hospital evaluation. Long-term cardiac endpoints included cardiac death or MI more than 1 week after the initial evaluation. Cardiac death was defined as death as a result of MI, arrhythmia, or an unexpected death of unknown cause. Long-term cardiac endpoints were assessed by chart review, scripted telephone interviews, and death registry data from the Virginia Division of Health Statistics.

ECGs were considered abnormal if they revealed 1 mm or more of ST-segment elevation or depression in two con-

tiguous leads, or ischemic T-wave inversion. Myocardial infarction was confirmed if at least two of the following were present: symptoms consistent with myocardial ischemia, evolving diagnostic ECG changes, or elevation of the creatine kinase-MB (CK-MB) isoenzyme subunit concentration greater than or equal to 8.0 ng/dL with a relative index of 4.0 or more (relative index=[CK-MB/total CK]×100). Typical symptoms included chest pain described as chest pressure, tightness, burning, heaviness, squeezing, crushing, or indigestion, shortness of breath, and symptoms similar to prior angina or infarction. Only the initial visit was used for patients presenting more than once during the study period.

Statistical Analysis

Results are presented as mean±1SD. Proportional and continuous variables were compared using χ^2 analysis and Student's *t* test, respectively. A *P* value less than or equal to .05 was considered significant. Logistic regression analysis using forward, backward, stepwise, all subsets via score statistic, and Akaike Information Criterion (AIC) criteria (SAS version 6.11) were performed using MI and revascularization as endpoints. Candidate variables included those that have previously been shown to identify ED patients with MI: gender, age 60 years or older, previous MI, and typical chest pain. The ECG and echocardiographic results (both considered as dichotomous variables) were also entered. To determine the incremental diagnostic value of a positive echo-

cardiogram, clinical variables were considered as a group. Subsequently the ECG and the echocardiographic results were entered. The incremental diagnostic value was determined by significant changes in the likelihood ratio test.

RESULTS

From August 1994 to December 1994, 598 patients were evaluated in the ED for possible myocardial ischemia or infarction, of whom 262 (43%) had early echocardiography performed as part of the study protocol. Two (.7%) studies were uninterpretable and were excluded, leaving 260 patients who formed the study cohort. The 336 patients who did not undergo echocardiography had similar baseline clinical characteristics and outcomes, including age (53±15 versus 54±14 years), male gender (48% versus 51%), number of risk factors (1.6±1.1 versus 1.6±1.1), and the incidence of MI (8.3% versus 9.0%) or revascularization (7.4% versus 8.0%).

Patient Characteristics With and Without Events

Forty-five patients (17%) had cardiac events. Events occurred in 35 of the 76 patients initially considered high-risk, 7 of the 49 moderate-risk, and 3 of the 135 low-risk patients. Myocardial infarction occurred in 23, 13 of whom presented with ST-segment elevation. Revascularization was performed in an additional 22 (2 CABG, 20 PTCA). Two patients died of complications related to acute MI during

Table 1.
Comparison of patients with and without cardiac endpoints.

Characteristic	With Cardiac Events (N=45) No. (%)	No Cardiac Events (N=215) No. (%)	<i>P</i> Value	Odds Ratio (95% CI)
Age ≥60 years	24 (53)	68 (32)	.006	2.5 (1.3-5.0)
Male	31 (69)	102 (47)	.008	2.5 (1.3-4.7)
Hypertension	25 (56)	109 (51)	.55	1.2 (.6-2.3)
Diabetes	13 (29)	42 (20)	.16	1.7 (.8-3.5)
Elevated cholesterol	14 (31)	63 (29)	.81	1.1 (.5-2.2)
Family history	7 (16)	43 (20)	.49	.7 (.3-1.8)
Tobacco use	14 (31)	95 (44)	.11	.6 (.3-1.1)
Total risk factors (mean±SD)	1.6±1.4	1.6±1.0	.88	NA
Previous MI	15 (33)	46 (21)	.09	1.8 (.9-3.7)
Typical symptoms	38 (84)	157 (73)	.11	2.0 (.8-4.7)
Chest pain duration (hr) (25th, 75th percentile)	2.5 (1,8)	3 (1,6)	NS	NA
Abnormal ECG	18 (40)	12 (5.6)	<.0001	11.3 (4.9-26)
Abnormal echocardiogram	41 (91)	53 (25)	<.0001	31 (11-92)
WMSI	1.63±.51	1.2±.46	<.0001	NA
Ejection fraction (mean±SD)	42±15	54±14	<.0001	NA

NA, Not applicable.

Data presented as number of patients, unless otherwise indicated. Cardiac endpoints refer to MI, cardiovascular death, or revascularization.

the initial hospital admission; both had positive echocardiographic findings. Patients with cardiac events were more likely to be older, be male, have abnormal ECGs and echocardiographic results, and have higher WMSIs and lower ejection fractions (Table 1).

Echocardiography and ECG Results

Of the 45 patients with cardiac events, 41 (91%) had positive echocardiographic findings and 18 (40%) had abnormal ECGs ($P<.0001$). Positive echocardiograms were more frequent than abnormal ECGs in patients with MI (96% [22/23] versus 65% [15/23], $P<.0001$) and with revascularization (86% [19/22] versus 17% [3/22], $P<.0001$). Mean WMSI ($1.6\pm.4$ versus $1.7\pm.6$), ejection fraction (43% $\pm 15\%$ versus 41% $\pm 15\%$) and percent with positive echocardiographic findings (96% versus 86%) were not significantly different between patients with MI and those with revascularization. Sensitivity of echocardiography was not affected by the presence or absence of symptoms at the time of imaging for either MI (100% versus 92%) or revascularization (82% versus 91%).

Only 4 of the 166 patients (2.4%) with negative echocardiographic findings had cardiac events; all were considered high-risk patients at the time of the initial evaluation. One patient had an MI (peak CK level of 231 U/L); the ECG was normal. The other three underwent PTCA for single-vessel disease. Two of these 3 patients had chest pain duration of less than 1 hour and had imaging while pain-free. One patient had a normal ECG; the other two had ECG evidence of prior MI but did not have ischemic changes.

Fifty-three (25%) of the 215 patients with positive echocardiographic findings did not have cardiac events. Of these, 75% had historical or echocardiographic evidence of previous MI ($N=29$), significant coronary disease on coronary angiography ($N=3$), or severe global hypokinesia with an estimated ejection fraction of less than or equal to 25% ($N=8$).

Echocardiography provided alternative explanations for symptoms in two patients, which included significant outflow tract obstruction and severe aortic regurgitation requiring aortic valve replacement. Additional diagnoses in two other patients included unsuspected significant aortic valve stenosis necessitating valve replacement and a left ventricular apical thrombus.

Predictive Value of Early Echocardiography

The sensitivity, 91% (95% CI 79% to 97%), and negative predictive value, 98% (95% CI 94% to 99%), of ED echocardiography for predicting MI or revascularization were significantly higher than that of the ECG, 40% (95% CI 27% to 55%; $P<.0001$), and 88% (95% CI 83% to 92%; $P<.001$), respectively. Specificity of echocardiography, 75% (95% CI 69% to 81%), was significantly lower than that of the ECG, 94% (95% CI 90% to 97%) ($P<.001$). Positive predictive values (44%, 95% CI 34% to 54%, and 60%, 95% CI 42% to 76%, $P=.12$) were not significantly different. Excluding patients with historical or ECG evidence of previous MI significantly improved specificity of echocardiography to 84% (95% CI 78% to 89%, $P<.04$) compared with all patients) with a nonsignificant increase in sensitivity to 97% (95% CI 82% to 99%).

Table 2.

Comparison of patients with and without cardiac events excluding those with abnormal ECGs.

Characteristic	With Cardiac Events (N=27) No. (%)	No Cardiac Events (N=203) No. (%)	P Value	Odds Ratio
Age ≥ 60 years	13 (48)	63 (31)	.08	2.1 (.9-4.7)
Male	17 (63)	97 (48)	.17	1.8 (.7-4.1)
Hypertension	17 (63)	99 (49)	.17	1.8 (.8-4.1)
Diabetes	8 (30)	39 (19)	.21	1.8 (.7-4.3)
Elevated cholesterol	10 (37)	59 (29)	.40	1.4 (.6-3.3)
Family history	6 (22)	40 (20)	.76	1.2 (.4-3.1)
Tobacco use	7 (26)	87 (43)	.09	.5 (.2-1.2)
Total risk factors (mean \pm SD)	1.8 \pm 1.4	1.6 \pm .8	.51	NA
Previous MI	11 (41)	45 (22)	.04	2.4 (1.0-5.6)
Typical symptoms	21 (78)	149 (73)	.63	1.3 (.5-3.3)
Abnormal echocardiogram	23 (85)	49 (24)	<.0001	18 (6.0-55)
WMSI (mean \pm SD)	1.7 \pm .2	1.29 \pm .5	.0002	NA
Ejection fraction (mean \pm SD, %)	41 \pm 17	54 \pm 14	.0004	NA

NA, Not applicable.

Data presented as number (%) of patients, unless otherwise indicated.

All models used demonstrated that the only independent predictors of MI or revascularization were male gender ($P<.03$; odds ratio (OR) 2.4, 95% CI 1.1 to 5.3) and positive echocardiographic findings ($P<.0001$; OR 24, 95% CI 9.0 to 65). Pearson's test for goodness of fit demonstrated a satisfactory fit without need for an interaction term ($P=.09$). Alternate estimates of the OR based on jackknife statistics were similar.¹³ Adding the ECG results to a model that included the baseline historical and clinical risk factors significantly improved the ability to predict cardiac events ($\chi^2=48$, $P<.0001$). The addition of the echocardiography results to the combination of clinical, historical, and ECG variables significantly increased the overall predictive ability of the model ($\chi^2=88$, $P<.0001$).

Patients Without Ischemic ECGs

The accuracy of echocardiography was not affected by excluding the 30 patients with abnormal ECGs (Table 2). Cardiac events occurred in 23 of 72 patients (32%) with positive echocardiographic findings, compared with only 4 of 158 patients (2.5%) with negative echocardiographic findings. A positive echocardiographic finding was the only independent multivariate predictor of cardiac endpoints ($\chi^2=38$, $P<.0001$; OR 14.4, 95% CI 5.2 to 39). Sensitivity (85%, 95% CI 67% to 94%), specificity (76%, 95% CI 69% to 81%), and positive (33%, 95% CI 23% to 45%) and negative predictive values (97%, 95% CI 94% to 99%) of echocardiography in this subgroup were not significantly different than those of all patients. By definition, the sensitivity and positive predictive value of the ECG was 0%.

Discharged Patients

One hundred twenty-one of the 260 patients studied were discharged from the ED after the initial evaluation. Of these, 114 (94%) were discharged based on the combination of a low clinical suspicion for MI or unstable angina, a nonischemic ECG, and negative tests after rest perfusion imaging. Echocardiographic findings were positive in 8 of these patients (7%). Three additional patients were discharged after rest perfusion imaging demonstrated a perfusion defect unchanged from previous studies; echocardiographic findings were positive in all, and later stress perfusion imaging demonstrated fixed defects. One patient was discharged despite positive perfusion imaging. Echocardiographic findings were negative. Three patients were discharged without rest perfusion imaging. Two had negative echocardiographic findings; results of coronary angiography performed 1 and 40 days later were normal in both. The third patient had nonspecific abnormalities on the ECG and

a WMSI of 1.19 on echocardiography; no events occurred during 13 months of follow-up.

Long-Term Events

Late follow-up (mean 9.6 ± 4.1 months) was obtained in 243 of the 258 (94%) patients who survived to discharge. Twelve patients experienced 14 cardiac events (2 MI, 2 MI and death, and 8 cardiac deaths), which occurred a mean of 175 days (range 18 to 494 days) after the index evaluation. Long-term endpoints occurred in 1.3% of patients with negative echocardiographic findings and 12% of patients with positive echocardiographic findings (OR 15, 95% CI 1.7 to 134, $P<.001$). After excluding the 45 patients who had short-term cardiac events, 5 (9.4%) of 53 patients with positive echocardiographic findings had long-term cardiac events, compared with 1 (0.6%) of 162 patients who had negative echocardiographic findings (OR 9.0, 95% CI 1.7 to 134, $P<.001$).

DISCUSSION

We found that two-dimensional echocardiography performed in the ED on patients presenting with possible myocardial ischemia reliably identified those who had MI or underwent revascularization. The sensitivity of echocardiography was significantly higher than that of the initial ECG and was not reduced after excluding patients with abnormal ECGs. Importantly, the echocardiography results added significant incremental value when combined with the historical, clinical, and ECG variables.

In the evaluation of any new diagnostic technique, it is important that the results be interpreted in light of all the available information, not considered in isolation.¹⁴ The true impact of a particular test is the incremental value it adds to known information. We found that echocardiography provided significant incremental diagnostic value and markedly improved the ability to identify patients at risk of cardiac events, even after consideration of clinical, historical, and ECG variables.

Most studies performed in ED patients with possible myocardial ischemia, including those using echocardiography, have attempted to identify only those with MI.^{8,9,15} However, identifying patients with unstable angina is also important. The number of patients admitted with unstable angina has increased,¹⁶ and is similar to that of patients with MI.^{2,17} Focusing on excluding MI alone may result in failure to identify patients with ongoing ischemia, who have a significant risk for short- and long-term cardiovascular morbidity and mortality. Early identification of patients with unstable angina may significantly reduce the risk of MI.¹⁸

Although the ECG is the most commonly used risk stratification, it is diagnostic in only a minority of ED patients with chest pain.² Myocardial markers of necrosis also lack sensitivity for identifying patients with unstable angina.¹⁹ These limitations have led to investigation of other tools, including serial ST-segment monitoring²⁰ and myocardial perfusion imaging.¹¹ In this study, we found that echocardiography can also be used to identify patients at risk of cardiac events other than MI.

Comparison With Other Studies

Previous studies have shown that wall motion abnormalities are present in 90% to 100% of patients with transmural infarction^{8,9,21} and in approximately 86% of patients with non-Q-wave MI.²² Comparison studies of the two techniques in CCU patients have shown that the sensitivity of echocardiography is significantly higher than that of the ECG for identifying patients with MI.^{9,21,22}

Few studies have systematically examined the diagnostic ability of ED echocardiography. Sabia et al⁸ performed echocardiography within 4 hours of presentation in 180 consecutive patients with chest pain. Among the 169 patients with interpretable studies, 82 had either normal wall motion or global systolic dysfunction, of whom only 2 (4%) had MIs. In contrast, 27 of the 87 patients (31%) who had regional wall motion abnormalities had diagnoses with MI. The sensitivity of echocardiography was significantly higher than that of the ECG. The results from the current study extend those of Sabia et al. Using more liberal criteria for defining abnormal ECGs (ST-segment elevation and depression and ischemic T-wave inversion) and for positive echocardiography (ejection fraction <40% in addition to regional wall motion abnormalities), we found that the sensitivity of echocardiography was still significantly higher than that of the ECG.

Peels et al²¹ performed ED echocardiography in 43 patients who presented to the ED with chest pain and non-ischemic ECGs. They found a sensitivity of 92% for identifying patients with MI. The specificity was 53% when MI was the only endpoint considered, but it increased to 78% when significant coronary disease was also considered as an endpoint. These results are comparable to those of the current study.

In contrast, Gibler et al²⁰ found that echocardiography had limited sensitivity but excellent specificity in 901 patients who underwent echocardiography as part of a diagnostic pathway for low-risk patients with chest pain. This study, however, included a lower-risk patient population than other studies, with fewer than 5% having either MI or unstable angina. The low sensitivity may also have resulted from performing echocardiography at the end of

the 9-hour rule-out protocol, by which time wall motion abnormalities may have resolved.

Considerations in Use of ED Echocardiography

Early echocardiography must be performed by a trained operator and interpreted by a physician experienced in wall motion analysis. Although images may be poor in some patients, adequate images are obtainable in more than 90%,^{8,23,24} indicating that echocardiography is applicable to most ED patients with chest pain. The use of echocardiography requires prompt interpretation to affect patient management. This is now possible by telephonic transmission of digitized images. Computer software and hardware is now available that allows transmission of images over standard telephone lines.²⁵

Wall motion may be normal in patients with small infarctions.²⁶ However, these patients have a low risk of complications^{8,27,28} and their care can be assigned at triage to lower-intensity observation or stepdown units rather than high-cost ICU beds. In the setting of a low clinical suspicion, patients with normal wall motion can safely undergo immediate stress testing.²⁹ Echocardiography may also provide additional, unanticipated information,³⁰ as well as diagnose other nonischemic causes of chest pain (though the frequency of such disorders was low in the current study).

The presence or absence of symptoms at the time of imaging is unlikely to affect diagnostic accuracy in patients with MI. However, the presence,³¹ duration,³² and severity of ischemia, as well as the extent of the ischemic zone, are likely to have important effects on the persistence of wall motion abnormalities in patients with unstable angina. Wall motion abnormalities may persist in patients who have imaging after prolonged, severe ischemia,^{33,34} which may explain why we found that sensitivity was not significantly decreased in patients whose had imaging performed while they were symptom-free. However, others have found that imaging performed after symptom resolution may be associated with reduced sensitivity.^{20,31} This implies that optimal exclusion of myocardial ischemia may require provocative testing in patients with normal wall motion who have imaging performed in the absence of symptoms.

An additional limitation of echocardiography is the inability to distinguish between acute infarction, old infarction, and acute ischemia. Elevations in early cardiac markers can rapidly identify patients with ongoing infarction, but differentiating between ischemia and prior infarction is more difficult. However, patients with prior infarction are at an increased risk of cardiovascular complications,^{15,17} and early discharge is not usually appropriate. The presence of moderately or severely reduced systolic function may

also result in “false-positive” results. Although these patients may have a low risk of acute events,⁸ the presence of left ventricular systolic dysfunction is associated with an increased risk of long-term cardiovascular events and provides independent prognostic information even after clinical, historical, and ECG variables are considered.^{35,36} Identification of these patients also offers the opportunity to initiate appropriate medical management.³⁷

Limitations of the Current Study

Not all patients were admitted to the hospital. As part of the risk stratification process used at our institution, low-risk patients undergo early myocardial perfusion imaging and are discharged home if the study result is negative. However, 96% of patients either were admitted and underwent serial myocardial marker analysis or were discharged from the ED on the basis of a combination of a low clinical suspicion, negative results after rest perfusion imaging, and a nonischemic ECG. The likelihood of MI in the presence of negative perfusion imaging results is low (<1%),¹¹ making it unlikely that a significant number of patients with MI were inadvertently discharged. We used revascularization as a surrogate for unstable angina, an endpoint that has been used in previous studies.^{38,39} Despite the potential for bias, revascularization implies the presence of significant coronary disease and may provide a more objective endpoint for unstable angina than clinical diagnosis alone. Although patients enrolled were not consecutive, baseline characteristics and cardiac outcomes were similar to those not having echocardiography, and thus the cohort included in this study should be a representative subgroup of all patients.

In conclusion, our results suggest that ED echocardiography performed in patients with a broad range of risk of myocardial ischemia identifies those at high risk of cardiac events and provides significant incremental diagnostic value when added to baseline clinical, historical, and ECG variables. Sensitivity was higher than that of the initial ECG and remained high when patients with abnormal ECGs were excluded. Echocardiography in the ED is easily performed, and has the potential to enable more accurate risk stratification and more effective triage of patients to more appropriate levels of care.

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