

Performance of Emergency Department Screening Criteria for an Early ECG to Identify ST-Segment Elevation Myocardial Infarction

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Background—Timely diagnosis of ST-segment elevation myocardial infarction (STEMI) in the emergency department (ED) is made solely by ECG. Obtaining this test within 10 minutes of ED arrival is critical to achieving the best outcomes. We investigated variability in the timely identification of STEMI across institutions and whether performance variation was associated with the ED characteristics, the comprehensiveness of screening criteria, and the STEMI screening processes.

Methods and Results—We examined STEMI screening performance in 7 EDs, with the missed case rate (MCR) as our primary end point. The MCR is the proportion of primarily screened ED patients diagnosed with STEMI who did not receive an ECG within 15 minutes of ED arrival. STEMI was defined by hospital discharge diagnosis. Relationships between the MCR and ED characteristics, screening criteria, and STEMI screening processes were assessed, along with differences in door-to-ECG times for captured versus missed patients. The overall MCR for all 7 EDs was 12.8%. The lowest and highest MCRs were 3.4% and 32.6%, respectively. The mean difference in door-to-ECG times for captured and missed patients was 31 minutes, with a range of 14 to 80 minutes of additional myocardial ischemia time for missed cases. The prevalence of primarily screened ED STEMIs was 0.09%. EDs with the greatest *informedness* (sensitivity+specificity-1) demonstrated superior performance across all other screening measures.

Conclusions—The 29.2% difference in MCRs between the highest and lowest performing EDs demonstrates room for improving timely STEMI identification among primarily screened ED patients. The MCR and informedness can be used to compare screening across EDs and to understand variable performance. (*J Am Heart Assoc.* 2017;6:e003528. DOI: 10.1161/JAHA.116.003528.)

Key Words: emergency department • false-negative rate • informedness • missed case rate • screening • ST-segment elevation myocardial infarction • timely care

The diagnosis of ST-segment elevation myocardial infarction (STEMI) in the emergency department (ED) is made solely by ECG. Timely diagnosis is critical to achieving timely intervention. The goal is to achieve a door-to-ECG time of 10 minutes.¹ The first 10 minutes of an ED visit, however, are administrative. To achieve timely diagnosis of patients with potential STEMI, EDs use early ECG screening criteria for all ED patients on arrival and prior to the physician evaluation.

Different EDs, however, have different criteria. The association of these criteria with missed STEMI cases and the impact of missed screening on myocardial ischemia time are unknown.

The first 10 minutes of an ED visit typically consist of intake processes (registration and triage) that usually occur well before a physician encounter (Figure 1). Consequently, ED registration and triage staff use preestablished screening

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Figure 1. Timely care goals for STEMI screening, diagnosis, and treatment: emergency department arrival to treatment. PCI indicates percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

criteria to identify patients that should receive an early ECG to diagnose STEMI (Figure 2). Given the time-sensitive nature of STEMI care, failure to identify candidates for an early ECG during ED intake processes subjects patients to diagnostic and potential treatment delay.^{1–3} Patients eventually diagnosed with STEMI present with a wide spectrum of symptoms. STEMI screening criteria are preestablished algorithms using



Figure 2. Sample emergency department early ECG screening criteria to screen for ST-segment elevation myocardial infarction. ED indicates emergency department.

a patient's arrival information. The criterion within the ED screening criteria falls on the spectrum of including only "chest pain" as the most typical symptom and variably includes consideration for more atypical symptoms or age. Identifying the most sensitive approach, balanced with specificity, could guide EDs in optimizing their STEMI screening performance.

Background

Despite decades of quality-improvement efforts, the timely diagnosis of STEMI patients in the ED presents significant operational challenges. In managing the timely care of patients with STEMI, EDs encounter 3 distinct types of patients who differ on the screening, diagnosis, and treatment continuum. First are patients who have been prediagnosed with STEMI, who have had an ECG performed and interpreted by another provider. They are usually transferred to an ED or a hospital capable of definitive treatment, most often percutaneous coronary intervention. The expectation is that treatment will be initiated on arrival. Second are prescreened patients who have been evaluated by another provider and referred to the ED with an ECG concerning for ischemia. In these cases, the diagnosis needs to be confirmed with a repeat ECG or reinterpretation of the ECG on arrival. The burden of screening for STEMI from the report of symptoms has already been met in these 2 scenarios; however, treatment has not been initiated. Third are the patients at greatest risk of delays in care: those arriving in the ED with undifferentiated symptoms who are primarily screened by that ED. In these cases, timely STEMI diagnosis is dependent on the patient's condition and symptoms triggering ED intake staff to perform an early ECG.^{4,5} The ECG is often considered the screening test for STEMI. In the context of emergency care, however, treatment is initiated with ECG evidence of STEMI, making it a diagnostic test.⁶ The true screening test is the criteria by which ED care providers initiate an ECG (Figure 2).

Overly comprehensive screening criteria for a rare disease like STEMI risks underutilization. The sole use of chest pain is user friendly but likely produces inadequate case capture. Overall, 20% to 30% of patients with STEMI will report atypical symptoms like shortness of breath and dizziness^{7–11} or will focus on associated symptoms like jaw, neck, or back pain. In addition, age positively influences the probability of STEMI, and elderly patients with STEMI more frequently report atypical symptoms.^{12–14} Shorter time to reperfusion has been shown to improve outcomes.^{15–19} Door-to-ECG time interval is the first STEMI care target toward achieving timely intervention.

Study Objective

We examined patient-oriented outcomes associated with screening performance variation for primarily ED-screened STEMI patients and the impact of a false-negative screen on myocardial ischemia time. Little is known about performance variation in contemporary ED STEMI screening, the influence of the processes that occur between ED arrival and diagnosis, or the effect of more comprehensive criteria on the quality of screening. This evidence gap was the focus of our investigation.

Methods

Study Design and Setting

This prospective historical cohort study compared the 2014 STEMI screening performance of 7 EDs (University of Pennsylvania, Brigham and Women's Hospital, Vanderbilt University, University of Wisconsin, Parkland Hospital at the University of Texas Southwestern, Oregon Health and Sciences University, and University of California Davis) selected for their geographic diversity, with considerations for US population density (see Figure 3). Our geographic and population distribution sample of US EDs and patients was selected to reduce spectrum bias from regional practice variation. The institutional review boards of all 7 participating institutions granted ethics approval for this investigation, with Vanderbilt University serving as the data coordinating center. Patient consent was waived at each institution, given the use of deidentified patient data to measure ED-level screening performance (the full study protocol is available in Data S1 and Tables S1 and S2).

Data Source and Data Collection

Data sources included summative case counts obtained from ED and hospital electronic medical record (EMR) system data reports from each hospital. Prior to data extraction, each site primary investigator met with the hospital's EMR information technology liaison to ensure that data could be obtained according to the study's data dictionary, protocol, inclusion criteria, and exclusion criteria. This involved the EMR information technology liaison developing programming code to create a data report to reliably extract the required case counts from the EMR system. The study was launched only after we received confirmation that this consistency could be achieved at all sites. To verify accuracy, each site obtained summative case counts from the hospital STEMI case review committees. Any discrepancies were adjudicated by each site primary investigator via chart review. Each institution reported



Figure 3. Study site geographic and population density distribution.

data using an online data collection tool developed within REDCap, a secure, widely used, Web-based data collection and database management application.²⁰ For the study data collection tool, see Data S1 (https://redcap.vanderbilt.ed u/surveys/?s=ET3WK99HDM).

STEMI Screening Criteria, Process, and Diagnosis

The content of each ED's screening criteria was classified into 5 categories: chest pain, atypical symptoms, associated symptoms, consideration of an age threshold, and other. Criteria comprehensiveness was defined as the number of criteria included by each ED. We qualitatively assessed the STEMI screening process by identifying the first points of contact (electronic check-in kiosk, clerks, nurses, or midlevel providers or physicians) performing early ECG screening for patients arriving via emergency medical services (EMS) versus self-transport. We confirmed that all 7 sites had established screening criteria (documented by policy or protocols for patient intake) as a fixed component of the ED patient intake and triage process and that neither the criteria nor the processes changed during the study period.

Using historical EMR data, we defined a positive screening result as having an early ECG within 15 minutes of arrival. ED arrival was defined as the first documented presence or time stamp of the patient's presence in the ED. The total number of ED patients seen included all persons registered as ED patients, including those who ultimately eloped, left without being seen, left before completing treatment, or left against medical advice. ED STEMI cases included all patients with an ED or hospital discharge diagnosis of STEMI.^{21,22} Our study door-to-ECG target was more generous than guideline recommendations; however, it reduced the likelihood that potential electronic time stamp delays would overestimate the number of missed cases. Fifteen minutes also permitted us to capture screened patients at a threshold well below the shortest mean door-to-doctor time among the participating EDs to avoid including ECGs completed after intake. To reduce misclassification bias, STEMI was defined using International Classification of Diseases, Ninth Revision codes previously used in the literature (410.01, 410.11, 410.21, 410.31, 410.41, 410.51, 410.61, 410.81, 410.91).^{13,23}

Patient Population Selection

We defined eligible ED visits as those for all patients aged \geq 18 years who were registered and evaluated in the ED from January 1 to December 31, 2014, to eliminate enrollment bias across sites using different EMR systems with different data-reporting functions. To reduce misclassification bias, we excluded prediagnosed and prescreened patients by excluding patients who arrived with an ECG from another facility or from

a transporting EMS team that was not repeated in the receiving ED.

Study Outcomes: Screening Performance Measures

We calculated the diagnostic test characteristics for STEMI screening for each individual ED and for the whole study population using ED-reported summative case counts for the total number of ED patients seen, early ECGs performed within 15 minutes of arrival (ie, positive screen), undifferentiated STEMI cases evaluated in the ED (ie, cases), and undifferentiated STEMI cases that did not receive an early ECG (ie, missed screening cases). The missed case rate (MCR), or the proportion of patients with a final diagnosis of STEMI that did not receive a timely early ECG (false-negative rate or type II error rate), was our primary performance measure outcome. We included sensitivity, specificity, accuracy, diagnostic odds ratio, and informedness as additional measures.²² Informedness is a measure that is analogous to Youden's point on a receiver operating characteristic curve. It captures the balance between a test's sensitivity and specificity (sensitivity+specificity-1) and summarizes the performance of a diagnostic test (values range from -1 to 1 with 0 representing a useless test and 1 indicating a perfect test with no false positives or false negatives).²⁴ We included positive and negative predictive values to be complete; however, these measures were not expected to differentiate the quality of ED screening performance, given the low frequency of STEMI.²⁵

Other ED Characteristics

The median door-to-ECG time and interquartile range was reported by each ED for all primarily screened STEMI patients in addition to the subgroups of captured cases (screened positive) and missed cases (screened negative). In addition, we calculated the proportion of ED patients who were evaluated for myocardial ischemia as the myocardial ischemia work-up rate to account for the frequency with which myocardial ischemia was considered in the local ED population. This rate was a proxy for the familiarity of the staff with the signs of ischemia. It included all STEMI patients as well as those who received both an ECG and serum cardiac troponin testing during their ED stay.

The reported STEMI-related clinical operations data included each institution's formalized early ECG screening criteria for STEMI (with provision of the ED policy for study team verification), total number of ED patients seen, early ECGs performed within 15 minutes of arrival (ie, screen positive), undifferentiated STEMI cases evaluated in the ED, and undifferentiated STEMI cases that did not receive an early ECG (ie, missed screening cases). This is in addition to the median door-to-ECG time and interquartile range for all primarily screened STEMI patients, the proportion of ED patients who received both an ECG and a serum cardiac troponin level during the ED visit (the myocardial ischemia evaluation rate), the first contact for ED patients who arrived via EMS and non-EMS transportation (STEMI screening agent), and the person who recorded the chief complaint of ED patients who arrived via EMS and non-EMS and non-EMS transportation. Demographic descriptors collected for each ED included annual patient volume and case mix index as measures of patient population acuity and complexity.²⁶

Statistical Analysis

With a total of 7 EDs, we performed unadjusted analyses to explore the relationship among the STEMI screening performance measures, with a focus on the MCR and factors anticipated to influence screening performance including (1) ED characteristics such as primarily screened STEMI incidence, ED volume, frequency of myocardial ischemia evaluation, and case mix index; (2) comprehensiveness of screening criteria; and (3) screening processes. We calculated Spearman rank correlation coefficients between continuous factors and the MCR as well as other STEMI screening performance measures. The Kruskal-Wallis test was used to compare STEMI screening performance across levels of categorical factors. Comprehensiveness of screening criteria was measured by the number of criteria used. The categorical data components of the screening process were documented as an ED check-in kiosk, triage registered nurse, registration clerk, greeter, and other (midlevel provider or physician). We reported frequencies, proportions, or ratios for all patient population characteristics and screening performance measures. We used the Wilcoxon signed rank test to assess whether the mean difference between each ED's median doorto-ECG time for captured and missed cases was significant. Scatter plots for the MCR and selected continuous factors were also presented for illustration purposes. All statistical analyses were conducted using R 3.1.2 (2015; R Foundation for Statistical Computing, https://www.R-project.org).

Results

In total, 472 166 adult patients were primarily screened for an early ECG to diagnose STEMI; of those, 407 were diagnosed with STEMI, for a total study population prevalence of 0.09% (95% CI 0.08–0.10%) (Table 1). Study-site STEMI prevalence ranged from 0.03% to 0.18%. This is a subset of the larger hospital STEMI population. Consequently, the prevalence of STEMI was lower than typically reported. The difference in the median door-to-ECG time between captured and missed primarily screened STEMI patients was 31 minutes (95% CI 9.7–52.3; P=0.018) of additional myocardial ischemia time (Table 2). The screening results for each ED and for the total screened population are summarized in the following sections and in Table 1.

Screening Performance: Missed Versus Captured Cases

The overall MCR was 12.8% (95% CI 9.9-16.4%), representing the frequency of delayed or missed STEMI diagnoses (Table 1). We observed a range of 3.4% to 32.6% across the 7 EDs. The mean difference between the median door-to-ECG time for captured and missed primarily screened STEMI patients in each ED ranged from 14 to 80 minutes (Table 2). We found that the MCR was strongly associated with lower STEMI prevalence (r_s =-0.929, range 0.04-0.13%, *P*=0.003). There was also a notable association with the myocardial ischemia work-up rate (r_s=-0.714, P=0.355). Higher annual patient volume (range 33 401-128 730) showed a moderately positive correlation (r_s =0.607, P=0.148). Case mix index (range 1.4-3.14) demonstrated a moderate correlation $(r_s = -0.739, P = 0.355)$ with the MCR. The comprehensiveness of the screening criteria (r_s =0.30; range 3–5) for an early ECG and accuracy ($r_s = -0.214$, P = 0.645); range 81–92%) did not demonstrate significant correlations with the MCR or other screening performance characteristics (Figure 4).

Quantifying Screening: Performance Variability

In addition to the variability noted in the MCR, the sensitivity and specificity of STEMI screening ranged from 65% to 97% and from 81% to 97%, respectively. Given the frequency with which ECGs are done and the rarity of STEMI in the broader ED population, the positive predictive value ranged from 0.29% to 5.06%, and the negative predictive value was nearly 1 with a range of 99.97% to 99.99%. Typically, this would be evidence of an excellent test;²⁷ however, given the gravity of STEMI and the resources invested to avoid missing any cases, a measure that differentiates performance beyond these parameters is required. As noted earlier, screening accuracy ranged from 81% to 97%, but the diagnostic odds ratio was more discriminatory, with a range of 17 to 860. We found that the EDs with the greatest informedness (sensitivity+specificity-1) demonstrated superior performance across all of these screening measures.

Comprehensiveness of Screening Criteria

Among the screening criteria, chest pain and atypical symptoms were used by all 7 EDs. Associated symptoms

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	ED 1	ED 2	ED 3	ED 4	ED 5	ED 6	ED 7	All
ED characteristics								
Annual patient volume	128 730	44 369	68 621	64 355	59 824	59 898	33 401	470 166
Primarily screened STEMI patients	43	23	75	61	74	72	59	407
Primarily screened STEMI prevalence (%)	0.03	0.05	0.11	0.09	0.12	0.12	0.18	60.0
MI work-up rate (%)*	19	17	19	17	19	23	16	19
Case mix index	1.4	2.01	2.09	1.4	1.67	3.14	1.98	1.96
Test characteristics								
Missed case rate [false negatives] (95% Cl)	32.6 [14] (20.1–47.5)	21.7 [5] (9.7–41.9)	20.0 [15] (12.5–30.4)	11.5 [7] (5.7–21.8)	6.8 [5] (2.9– 14.9)	5.6 [4] (2.2–13.4)	3.4 [2] (0.9– 11.5)	12.8 [52] (9.9–16.4)
True-negatives cases	118 616	38 774	55 454	55 945	51 939	54 331	32 272	407 331
True-positive cases	29	18	60	54	69	68	57	355
False positives (rate %)	10 071 (8)	5572 (13)	13 092 (19)	8349 (13)	7811 (13)	5495 (11)	1070 (3)	51 460 (13)
Sensitivity (%)	67.4 (52.5–79.5)	78.3 (58.1–90.3)	80.0 (69.6–87.5)	88.5 (78.2–94.33)	93.2 (85.1–97.1)	94.4 (86.6–97.8)	96.6 (96.6–97.0)	87.2 (83.6–90.1)
Specificity (%)	92.2 (92–92)	87 (87–88)	81 (81–81)	87 (87–87)	87 (87–87)	91 (91–91)	97 (72–73)	89 (86–87)
PPV (%)	0.29 (0.20–0.41)	0.32 (0.20-0.51)	0.46 (0.35–0.59)	0.64 (049–0.84)	0.88 (0.69–1.11)	1.22 (0.97–1.55)	5.06 (3.92–6.5)	0.69 (0.50-0.62)
NPV (%)	99.99 (99.98–99.99)	99.99 (99.97–99.99)	99.97 (99.96–99.98)	99.99 (99.97–99.99)	99.99 (99.98–1.00)	99.99 (99.98–1.00)	99.99 (99.98–1.00)	99.99 (99.98–99.99)
(+) Likelihood ratio	8.6 (6.7–10.2)	6.2 (4.6–7.2)	4.2 (3.6–4.6)	6.8 (6.0–7.3)	7.1 (6.5–7.5)	10.0 (9.4–11)	30 (27–32)	7.7 (7.4–8.0)
(-) Likelihood ratio	0.38 (0.25–0.54)	0.25 (0.11–0.48)	0.25 (0.15–0.38)	0.13 (0.07–0.25)	0.08 (0.03–0.17)	0.06 (0.02–0.15)	0.04 (0.01–0.12)	0.15 (0.12–0.19)
Diagnostic odd ratio	21 (12–39)	25 (9.6–65)	17 (9.7–30)	52 (23–112)	92 (38–220)	168 (64–444)	860 [†] (231–3201)	43 (31–55)
Accuracy (%) [†]	92 (92–92)	87 (87–88)	81 (81–81)	87 (87–87)	87 (87–87)	91 (91–91)	(20-26) (67-97) (76)	89 (89–89)
Informedness (%) ‡	57	66	61	76	80	85	97	75

Continued

Table 1. Continued

All	100%	100%	71%	86%	29%							
ED 7	Yes	Yes	Yes	No	No	3		Triage RN	Triage RN	Triage RN	Triage RN	Triage RN
ED 6	Yes	Yes	Yes	Yes	No	4		Triage RN	Reg Clerk	Triage RN	Triage RN	Triage RN
ED 5	Yes	Yes	Yes	Yes	Yes	5		Triage RN	Greeter	Triage RN	Triage RN	Triage RN
ED 4	Yes	Yes	No	Yes	No	3		Triage RN	Triage RN	Triage RN	Triage RN	Triage RN
ED 3	Yes	Yes	Yes	Yes	Yes	5		Triage RN	Reg Clerk	Triage RN	Reg Clerk	Triage RN
ED 2	Yes	Yes	Yes	Yes	No	4		Other	Reg Clerk	Other	Reg Clerk	Other
D 1 a for early ECG [§]	es sea	es a	0	es sa	0		0 minutes ^{II}	liosk	liosk	Other	riage RN	Other
E Included in screening criteria	Chest pain Y	Atypical MI Y symptoms	Associated MI N symptoms	Age threshold Y	Other	Total criteria used 3	ED patient contact in first 1	EMS arrival first K contact	Walk-in arrival K first contact	Chief complaint C recorded for EMS arrivals	Chief complaint recorded for walk-ins	Chief complaint C recorded for EMS arrivals

ED indicates emergency department; EMS, emergency medical services; MI, myocardial infarction; NPV, negative predic infarction.

*MI work-up rate=total acute coronary syndrome evaluations=troponin and ECG at any time during the ED visit.

¹Accuracy=(true positive+true negative)/(true positive+true negative+false negative). ^{*}Informedness (calculated as [sensitivity+specificity]-1) is analogous to the ideal cut point on a receiver operating characteristic curve in expressing a balance between the tradeoffs and the benefits of test sensitivity and specificity. ^{*} ves=included, no=not included.

 $^{\parallel}$ Options were greeter, automated check-in kiosk, reg clerk, triage RN, midlevel provider, physician. Numbers in parentheses represent the 95% Confidence Intervals.

Table 2. Difference in Door-to-ECG Time for Captured andMissed Cases

		All Primarily Screened ED STEMI Patients	Screen- Positive "Trigger Positive"	Screen- Negative "Trigger Negative"	
	MCR, %	Median (IQR)	Median (IQR)	Median (IQR)	Median Difference
ED 7	3.4	3 (1–5)	3 (1–5)	18 (17–19)	15
ED 6	5.6	9 (5–10)	7 (6–18)	33 (28–74)	26
ED 5	6.8	6 (3–9)	5 (2–8)	19 (18–26)	14
ED 4	11.5	5 (2–10)	4 (2–8)	26 (18–72)	22
ED 3	20.0	7 (4–16)	6 (4–7)	44 (19–117)	38
ED 2	21.7	5 (3–12)	5 (3–7)	27 (26–29)	22
ED 1	32.1	8 (5–17)	7 (5–8)	87 (21–149)	80

ED indicates emergency department; IQR, interquartile range; MCR, missed case rate; STEMI, ST-segment elevation myocardial infarction.

were included by 71%, and 86% included the consideration of an age threshold. Two EDs (ED 3 and ED 5) included all 4 screening criteria categories (Table 1) and had MCRs of 20% and 6.8%, respectively. These same EDs included other criteria in their screening process. ED 3 included considerations for the recent use of cocaine, history of a congenital heart defect, and coronary stent placement or cardiac surgery within 9 months. ED 5 included all patients on dialysis. Only ED 2 included a consideration of patient sex.

Screening Process

Physicians were not involved in STEMI screening at any of the sites. A registered nurse was most frequently the person to both assess an arriving patient and document the patient's chief complaint. No sites used check-in kiosks. The use of non–clinically trained registration clerks as the point of first contact was not associated with poorer performance by any of the screening test measures (Table 1). EDs with a triage registered nurse as the first point of contact for EMS arrival patients had lower MCRs compared with EDs with other first points of contact (P=0.034).

Discussion

Our primary study finding was an overall MCR of 12.8% for primarily screened ED STEMI patients. This rate represents the frequency of missed STEMI screening, demonstrated by a delay in door-to-ECG time. In addition, the lowest and highest performing EDs had MCRs of 32.6% and 3.4%, respectively. This 28.2% difference is clinically meaningful because it suggests patients are exposed to variable risk of diagnostic delay depending on which ED they enter for care. In addition, the cost of ineffective screening results in missed cases experiencing 14 to 80 minutes of myocardial ischemia time. This ED-level analysis is analogous to assessing the performance of a radiology or laboratory test in a population, in which the performance of 1 test is assessed as a summary of how accurately it identifies a disease in individual patients. Studies of this kind are often performed at a single center; however, we included 7 sites to strengthen our analysis and exploration of STEMI screening performance variation. In this way, we evaluated 7 different tests, serving the same function, in 7 patient populations, totaling 472 166 ED encounters.

For an acutely life-threatening disease like STEMI, for which a missed case burdens the patient with significant negative sequelae, the reliability of a negative screen is of high value. The negative predictive value can often inform the performance of this "rule out" function. For a rare condition like STEMI, however, the negative predictive value will be ≈ 1 (Table 1). An alternative is the diagnostic odds ratio, which is not influenced by incidence. It is a traditional comparative measure of screening test quality across populations but is less clinically intuitive for the average clinician than the MCR. The MCR represents the tendencies communicated by sensitivity, specificity, accuracy, and the diagnostic odds ratio with a single measure. Consequently, we propose that the MCR is a more clinically meaningful and easily interpreted performance measure for primarily screened ED patients. Its name and calculation better communicate the high stakes of a missed STEMI case while informing an understudied area of STEMI screening performance.

Informedness should also be considered a valuable performance metric. With a STEMI prevalence of 0.09% (range 0.03–0.18%), increasing the sensitivity of screening alone will produce far more physician workflow interruptions for the ECG interpretation of false-positive screens than it will improve the number of STEMI cases detected. This approach challenges the quality of care for the majority of patients because of the continual interruption of the physician's attention to interpret early ECGs. Targeting improvements in informedness (sensitivity+specificity-1) as a performance measure places value on achieving a balance between sensitivity and specificity in a manner analogous to the ideal cut point (Youden's point) on a receiver operating characteristic curve.²³ In our study, informedness demonstrated a negative correlation with the MCR. The 2 EDs with the highest informedness measures (85% and 97% [range 57-97%]) had the lowest MCRs (3.4% and 5.6% [range 3.4-32.6%]), highest sensitivity (94% and 97% [range 67–97%]), highest specificity (91% and 97% [range 81–97%]), and highest diagnostic odds ratios (168 and 860 [range 17-171]). This suggests that informedness has value as a measure of the balance in



Figure 4. Unadjusted association between missed case rate and ED characteristics. ED indicates emergency department; STEMI, ST-segment elevation myocardial infarction.

sensitivity and specificity of an ED's screening criteria and as a marker of better STEMI screening performance. MCR and informedness were not tracked previously by these EDs.

Screening criteria comprehensiveness did not have the expected influence on the MCR. The EDs with the greatest number of screening criteria-ED 3 (MCR 20.0%, 95% CI 12.5-30.4%) and ED 5 (MCR 6.8%, 95% CI 2.9-14.9%)-did not have the highest screening performance. In addition, the ED with the lowest MCR (ED 7: MCR 3.4%, 95% CI 0.9-11.5%), representing the best performance, did not have the most comprehensive screening criteria. Reporting chest pain or atypical ischemia symptoms (shortness of breath, neck or shoulder pain) uniformly triggered an early ECG in all EDs. The lowest and highest performing EDs (ED 1 and ED 7, respectively) had equivalent numbers of categories included in their screening criteria (3). Their criteria differed in that the best performer included associated symptoms and the lowest performer included an age threshold. These results are contrary to our expectation based on the results of a 2012 study that used classification and regression tree analysis to identify ideal universal screening criteria to achieve the lowest MCR in an ED.¹³ Only 1 ED included a consideration of sex in its screening criteria despite the literature noting that male sex is a risk factor for STEMI and being female increases the likelihood of reporting non-chest pain symptoms.⁸⁻¹⁰ Our findings suggest that the screening environment influences performance. In addition, the incremental value of each criterion is not well understood and requires further investigation. Detecting a relationship will require a larger ED sample or a multicenter study using patient-level data that includes screening criteria compliance, patient population, and institutional characteristics as confounders.

We anticipated that EDs with higher MCRs would have higher myocardial ischemia work-up rates and that this would be associated with a higher case mix index and annual ED patient volume. We found the myocardial ischemia evaluation rate to have a strong association with the MCR; however, this finding was not statistically significant (P=0.07). Given our small sample size, this association should be explored in a larger study. Other associations with the MCR should be considered for further exploration. Case mix index had a moderate negative correlation with the MCR. This suggests the potential influence of patient population acuity. Annual ED volume had a moderately strong inverse relationship $(r_s=0.607, P=0.167)$ with the MCR. Higher volume may reflect larger centers with more experience identifying atypical presentations of STEMI; however, this is difficult to assess through this study because all study sites were academic tertiary care facilities. It may be the case that smaller EDs, which often have less robust triage processes or shorter wait times to see a physician, have lower MCRs. Conversely, EDs with lower annual patient volumes may see fewer cases of this rare diagnosis and have higher MCRs. This particular question warrants further study.

We observed less variation than we anticipated regarding (1) the point of first contact for primarily screened ED patients

arriving via EMS (ie, ambulance) or self-transport and (2) the ED staff documenting the reason for the ED visit during intake. A triage registered nurse was the most common staff member performing intake. None of our sites used a physician in triage as the first contact for patient intake. We do not believe the involvement of physicians in intake screening for STEMI is the solution to performance improvement. STEMI is a rare disease, and in EDs where many more patients require direct physician attention for more common conditions, such an approach could cause more harm than benefit. The demonstrated lack of physician clinical decision making in this arrival process and the more common use of non–clinically trained clerks emphasizes the importance of well-developed diagnostic algorithms for timely screening and diagnosis.

Our study approach challenges the traditional characterization of ECG as a screening test for STEMI with cardiac catheterization angiography as the standard criterion. We contend that the ED screening criteria for an early ECG is the screening test. Despite its limited specificity for occlusive coronary thrombus,²⁵ the early ECG is a diagnostic test used to determine whether or not to activate the catheterization lab emergently. Our findings highlight the need to investigate the diversity of screening criteria used in clinical practice with more scrutiny. This is particularly important given that the Guidelines Applied in Practice—Door to Balloon (GAP-D2B) National Quality Initiative recommends ED physician activation of the catheterization lab for STEMI intervention as a priority process improvement.^{28–30} A multicenter patient-level study is essential to better understand what criteria are needed for an individual ED to reduce its local MCR. This further investigation should be performed with broader diversity of ED types (community practice, rural, small and medium patient volume, non-trauma centers) using patient visit data (arrival time, early ECG time, STEMI diagnosis time, type of treatment delivered, time to treatment, clinical outcomes) that include both ED characteristics (ED volume, urbanicity, academic status, case mix index, percutaneous coronary intervention center status) and patient characteristics (age, sex, race, coronary artery disease risk factors, prior use of risk factor-modifying medications or intervention, literacy, numeracy, insurance status, socioeconomic status).

In addition, considering improvements in screening quality requires a patient-centered perspective. The variable screening performance observed is not transparent to patients, referring providers, or prehospital personnel. This is primarily because existing STEMI registries and performance measures do not currently consider the quality of STEMI screening, nor do they account for the difference between the primarily screened ED STEMI patient and those who have been prescreened or prediagnosed prior to ED arrival.^{11,25,31} This distinction is necessary to inform the quality of case detection and to differentiate patients for whom the burden of ED

evaluation includes the timely consideration of myocardial ischemia. In addition, quantifying screening performance in each of these patient populations is important because the burden of action for the receiving ED is different for each STEMI patient type. Many EDs have the routine practice of "rediagnosing" prediagnosed patients so the receiving local provider can ensure that treatment is initiated appropriately. Others will direct prediagnosed patients to the coronary catheterization lab without undergoing a repeat evaluation in the receiving ED. For time-sensitive conditions like STEMI, stronger consideration should be given as to whether rediagnosis is needed with the added time delay. Future patient-level studies should explore this question with considerations for the diversity of ED types and resource settings and for those receiving percutaneous coronary intervention versus thrombolysis.

Limitations

Despite capturing STEMI screening for nearly half a million patients in a geographically diverse sample, our study includes only 407 patients with STEMI. This limits our ability to quantify the strengths of associations among ED characteristics, process, and screening performance; however, it is multicenter study focused on a subset of the larger hospital STEMI population with unique screening and diagnostic needs. We did not focus on a traditional clinical outcome. Rather, we identified novel performance measures for STEMI screening-the MCR and informedness-while considering univariate associations with contextual confounders. Each study ED uses an EMR system. This permitted reliable capture of clinical care events, time of ECG completion, and intervention. The structured event time stamping and uniform data extraction within these systems enabled quality retrospective data collection and case review. In addition, our selection of a prospective historical design reduced the potential influence of the Hawthorne effect in this processoriented study.

One must be cautious in comparing our reported MCR and STEMI prevalence with other STEMI performance studies, given our patient-centered definition of a missed case and the limitation of STEMI screening to a subset of the larger STEMI patient population. In this study of patients primarily screened by the ED for STEMI, we sought to characterize how structured screening was associated with the timeliness of STEMI identification using aggregate case counts from each ED. A follow-up study with patient visit– level data is needed to measure how consistently the local screening criteria were applied. Quantifying compliance in this manner was outside the scope of this study and cannot be informed by our study design. A patient-level study will also enable the identification of differences among the prescreened, prediagnosed, and primarily screened patient populations and risk factors associated with untimely screening.

Last, we were able to collect characterizing data for each study site but did not fully characterize the EMS and referring environment. These factors likely influenced the MCR because in a surrounding community with robust prehospital care, a patient with more typical STEMI symptoms (chest pain) may be more likely to arrive prescreened or prediagnosed. This would have led to exclusion from our study population. This aspect is important to understand because the criteria used by EDs with more robust prehospital screening may need to be tailored to include more atypical presentations. A follow-up study of the distribution of STEMI symptoms in the prescreened, prediagnosed, and primarily screened populations will help us understand the influence of prehospital care on screening performance.

Conclusion

An overall MCR of 12.8% represents missed or delayed STEMI screening, as shown by delayed initiation of the diagnostic test, the ECG. Our observed MCR range difference of 29.2% demonstrates significant variability in the timely diagnosis of STEMI in primarily screened ED patients. The impact of ineffective screening is 14 to 80 minutes of myocardial ischemia time. Inferences drawn from the diagnostic odds ratio and the informedness of the individual EDs were generally consistent with comparisons based on the MCR alone. The ability of informedness to characterize a balance between improved case detection and false negatives makes it a measure to consider for tracking STEMI screening performance across EDs, along with the MCR. This exploration identified variation requiring further research and qualityimprovement attention that can be validated in a larger sample of EDs and patients in the future.

Author Contributions

Dr Yiadom conceptualized and designed the study, and served as the lead primary investigator. She also coordinated data collection, analysis and interpretation. Conor McWade developed the online study data collection tool in REDCap, assisted with study coordination, and drafted the introduction and methods section of the manuscript. Drs Baugh, Tanski, Mills, Patterson, Salazar and Song served as study site PIs by organizing data collection from their institution's electronic medical record system and STEMI Case Review Committee, performing case adjudication for any discrepancies, and submitting study data to Dr Yiadom at the data coordinating center (Vanderbilt University). Cathy Jenkins was the biostatistician that assured consistency between the study design plan, study protocol, and data collection tool before study initiation. Dr X. Liu was the primary biostatistician for the study analysis. Dr D. Liu was the senior biostatistician for the study analysis and data presentation. Drs Wang, Dittus and Storrow contributed to the discussion, analysis, interpretation, and review of the manuscript. All co-authors have reviewed, edited and approved the final draft of this manuscript.

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Disclosures

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References

- McNamara RL, Wang Y, Herrin J, Curtis JP, Bradley EH, Magid DJ, Peterson ED, Blaney B, Frederick PD, Krumholz HM. Effect of door-to-balloon time on mortality in patients with ST-segment elevation myocardial infarction. J Am Coll Cardiol. 2006;47:2180–2186.
- Gibson CM, Pride YB, Frederick PD, Pollack CV, Canto JG, Tiefenbrunn AJ, Weaver WD, Lambrew CT, French WJ, Peterson ED, Rogers WJ. Trends in reperfusion strategies, door-to-needle and door-to-balloon times, and inhospital mortality among patients with ST-segment elevation myocardial infarction enrolled in the National Registry of Myocardial Infarction from 1990 to 2006. Am Heart J. 2008;156:1035–1044.
- Mehta RH, Bufalino VJ, Pan W, Hernandez AF, Cannon CP, Fonarow GC, Peterson ED. Achieving rapid reperfusion with primary percutaneous coronary intervention remains a challenge: insights from American Heart Association's Get with the Guidelines program. *Am Heart J.* 2008;155:1059–1067.
- 4. Brown JP, Mahmud E, Dunford JV, Ben-Yehuda O. Effect of prehospital 12-lead electrocardiogram on activation of the cardiac catheterization laboratory and

door-to-balloon time in ST-segment elevation acute myocardial infarction. Am J Cardiol. 2008;101:158–161.

- Sekulic M, Hassunizadeh B, McGraw S, David S. Feasibility of early emergency room notification to improve door-to-balloon times for patients with acute ST segment elevation myocardial infarction. *Catheter Cardiovasc Interv.* 2005;66:316–319.
- 6. Diercks DB. Triage of emergency department patients with chest pain: where should we set the bar? *Ann Emerg Med.* 2009;53:746–747.
- Canto JG, Shlipak MG, Rogers WJ, Malmgren JA, Frederick PD, Lambrew CT, Ornato JP, Barron HV, Kiefe C. Prevalence, clinical characteristics, and mortality among patients with myocardial infarction presenting without chest pain. JAMA. 2000;283:3223–3229.
- Blomkalns AL, Chen AY, Hochman JS, Peterson ED, Trynosky K, Diercks DB, Brogan GX, Boden WE, Roe MT, Ohman EM, Gibler WB. Gender disparities in the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. J Am Coll Cardiol. 2005;45:832–837.
- Milner KA, Vaccarino V, Arnold AL, Funk M, Goldberg RJ. Gender and age differences in chief complaints of acute myocardial infarction (Worcester Heart Attack Study). Am J Cardiol. 2004;93:606–608.
- Dey S, Flather MD, Devlin G, Brieger D, Gurfinkel EP, Steg PG, Fitzgerald G, Jackson EA, Eagle KA; Global Registry of Acute Coronary Events investigators. Sex-related differences in the presentation, treatment and outcomes among patients with acute coronary syndromes: the Global Registry of Acute Coronary Events. *Heart*. 2009;95:20–26.
- Brieger D, Eagle KA, Goodman SG, Steg PG, Budaj A, White K, Montalescot G; GRACE Investigators. Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: insights from the Global Registry of Acute Coronary Events. *Chest.* 2004;126:461–469.
- Panju AA, Hemmelgarn BR, Guyatt GH, Simel DL. Is this patient having a myocardial infarction? JAMA. 1998;280:1256–1263.
- Glickman SW, Shofer FS, Wu MC, Scholer MJ, Ndubuizu A, Peterson ED, Granger CB, Cairns CB, Glickman LT. Development and validation of a prioritization rule for obtaining an immediate 12-lead electrocardiogram in the emergency department to identify ST-elevation myocardial infarction. *Am Heart J.* 2012;163:372–382.
- Canto JG, Rogers WJ, Goldberg RJ, Peterson ED, Wenger NK, Vaccarino V, Kiefe Cl, Frederick PD, Sopko G, Zheng ZJ; NRMI Investigators. Association of age and sex with myocardial infarction symptom presentation and in-hospital mortality. *JAMA*. 2012;307:813–822.
- Herrin J, Miller LE, Turkmani DF, Nsa W, Drye EE, Bernheim SM, Ling SM, Rapp MT, Han LF, Bratzler DW, Bradley EH, Nallamothu BK, Ting HH, Krumholz HM. National performance on door-in to door-out time among patients transferred for primary percutaneous coronary intervention. *Arch Intern Med*. 2011;171:1879–1886.
- Wang TY, Nallamothu BK, Krumholz HM, Li S, Roe MT, Jollis JG, Jacobs AK, Holmes DR, Peterson ED, Ting HH. Associaton of door-in to door-out time with reperfusion delays and outcomes among patients transferred for primary percutaneous coronary intervention. *JAMA*. 2011;305: 2540–2547.
- O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, De Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB. 2013 ACCF/ AHA guideline for the management of ST-elevation myocardial infarction: a

report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2013;61: e78–e140.

- Rathore SS, Curtis JP, Chen J, Wang Y, Nallamothu BK, Epstein AJ, Krumholz HM. Association of door-to-balloon time and mortality in patients admitted to hospital with ST elevation myocardial infarction: national cohort study. *BMJ*. 2009;338:b1807.
- De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction every minute of delay counts. *Circulation*. 2004;109:1223–1225.
- Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42:377–381.
- Lijmer JG, Mol BW, Heisterkamp S, Bonsel GJ, Prins MH, van der Meulen JH, Bossuyt PM. Empirical evidence of designs—related bias in studies of diagnostic tests. *JAMA*. 1999;282:1061–1066.
- Reid MC, Lachs MS, Feinstein AR. Use of methodological standards in diagnostic test research: getting better but still not good. JAMA. 1995;274:645–651.
- Ward MJ, Kripalani S, Zhu Y, Storrow AB, Dittus RS, Harrell FE Jr, Self WH. Incidence of emergency department visits for ST-elevation myocardial infarction in a recent six-year period in the United States. *Am J Cardiol.* 2015;115:167–170.
- Schisterman EF, Perkins NJ, Liu A, Bondell H. Optimal cut-point and its corresponding Youden Index to discriminate individuals using pooled blood samples. *Epidemiology*. 2005;1:73–81.
- 25. McCabe JM, Armstrong EJ, Kulkarni A, Hoffmayer KS, Bhave PD, Garg S, Patel A, MacGregor JS, Hsue P, Stein JC, Kinlay S. Prevalence and factors associated with false-positive ST-segment elevation myocardial infarction diagnoses at primary percutaneous coronary intervention–capable centers: a report from the Activate-SF registry. Arch Intern Med. 2012;172:864–871.
- Perya C. Coding reponses to a case-mix measurement system based on multiple diagnoses. *Health Serv Res.* 2004;39:1027–1046.
- Powers DM. Evaluation: from precision, recall and f-measure to ROC, informedness and correlation. J Mach Learn Technol. 2011;2:37–63.
- Nissen SE, Brush JE, Krumholz HM. President's page: GAP-D2B: an alliance for quality. J Am Coll Cardiol. 2006;48:1911–1912.
- Bradley EH, Herrin J, Wang Y, Barton BA, Webster TR, Mattera JA, Roumanis SA, Curtis JP, Nallamothu BK, Magid DJ, McNamara RL. Strategies for reducing the door-to-balloon time in acute myocardial infarction. *N Engl J Med.* 2006;355:2308–2320.
- Bradley EH, Nallamothu BK, Herrin J, Ting HH, Stern AF, Nembhard IM, Yuan CT, Green JC, Kline-Rogers E, Wang Y, Curtis JP. National efforts to improve door-to-balloon time: results from the Door-to-Balloon Alliance. J Am Coll Cardiol. 2009;54:2423–2429.
- 31. Klein LW, Block P, Brindis RG, McKay CR, McCallister BD, Wolk M, Weintraub W; ACC-NCDR Registry. Percutaneous coronary interventions in octogenarians in the American College of Cardiology-National Cardiovascular Data Registry: development of a nomogram predictive of in-hospital mortality. J Am Coll Cardiol. 2002;40:394–402.

SUPPLEMENTAL MATERIAL

Data S1 – Study Protocol (AMMENDED)

Performance of Emergency Department Screening Trigger Criteria for an Early ECG to Identify STEMI

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	KJ Šong MD	University of California at Davis
INTRODUCTION	•	

Background

ST-segment elevation myocardial infarction (STEMI) is a life threatening, time-sensitive condition consisting of a sudden complete blockage of a coronary artery.¹ It requires treatment within 30-90 minutes, and the diagnosis is made via electrocardiogram (ECG). Patients suspected of STEMI are referred to an emergency department (ED) for rapid evaluation, diagnosis, and treatment. Guidelines recommend the diagnosis be made within 10 minutes of arrival.² However, the first 10 minutes of an ED visit typically consist of registration and triage. The median door-todoctor time for an ED patient is 60 minutes. As a result, ED registration and triage staff use screening criteria to identify patients who should receive an early ECG to identify STEMI. To date, the test characteristics of the screening process have not been extensively investigated. This study will examine whether there is variation in STEMI screening performance in different EDs, and whether variability is associated with the comprehensiveness of the screening criteria used.

Chest pain is the classic symptom for STEMI, however 20-30% of STEMI patients do not report chest pain.^{3,4,5,6,7} Appropriately comprehensive STEMI screening criteria, used to trigger an early ECG (trigger criteria), should include more information than chest pain presence or absence. Ideal STEMI case capture occurs when trigger criteria also includes atypical symptoms like shortness of breath and dizziness; associated symptoms like jaw pain, neck pain or back pain; and considerations of the patient's age.^{8,9,10} Previously collected data suggest the inclusion of these characteristics in different EDs trigger criteria varies significantly. We hypothesize there is variability in the screening processes between institutions, and this variability is associated with different diagnostic test characteristics.

Rationale

The ECG is often referred to as the screening test for STEMI. This is because 30-50% of patients with STEMI on ECG will not have an occlusive coronary artery thrombus when evaluated with coronary artery angiography, the criterion (gold) standard diagnostic test. Despite this limitation, the risk-benefit balance of early treatment verses further testing weighs in favor of early treatment. As a result, treatment is initiated based on the *reference diagnostic testing standard*, an ECG demonstrating STEMI. In the context of ED operations and patient flow, the trigger criteria is the

true screening test. Patients, who do not receive an early ECG from registration or triage, go on to receive typical ED care. This provides an opportunity to identify cases missed by the index test, making typical ED care an *alternative reference standard* for trigger negative patients.^{10,11}

We have looked at the STEMI screening performance at Vanderbilt University (Table S1). In doing so we considered a patient meeting <u>trigger criteria</u>, which prompts the ED registration or triage staff to initiate an early ECG, as a positive *index test*; and an <u>ECG indicating STEMI</u> as a positive *reference test*. We found that the screening process has high sensitivity and negative predictive value with poor positive predictive value and limited specificity. The likelihood ratio of positive test is 5.2 (probability of a person with a STEMI ECG screening positive via screening trigger criteria), and that of a negative test is 0.025 (probability of a person with a STEMI ECG not being identified with screening trigger criteria). This study seeks to understand these local results in the context of broader clinical practice and variability of trigger criteria between institutions.

Study Objectives

This study has two objectives. It will first examine whether the STEMI screening performance observed at Vanderbilt is generalizable. We will do this by calculating 2x2 contingency table data for patients seen in six additional EDs (in different regions of the country) individually, and then as a total population combined with Vanderbilt. Second, it will determine whether STEMI screening performance improves with more data incorporated into the trigger criteria by identifying whether there is an association between positive and negative likelihood ratios with the inclusion of associated symptoms, atypical symptoms, and age in the trigger criteria.

Potential Risks and Benefits

The ED is the unit of observation in this study. As a result, the data consists of aggregate numbers representing ED patient care events in 2014. Protected health information (PHI) and patient level data may be reviewed within the local ED to get the aggregate numbers we will use to calculate screening performance. Related data extraction will use the administrative reporting functions within the hospitals' electronic medical record systems (EMR) and review of existing summative data reports from the hospitals' STEMI case review committees. As a result there is limited potential for study-related breaches in PHI confidentiality, thus presenting minimal risk to the EDs and their patients. The participating EDs are involved in this study as a quality improvement effort with the intent to publish the results as research. The benefit to the EDs, and the patients they serve, is gaining knowledge about their local practice in the context of national peers to inform their current clinical STEMI screening practices. There is no compensation for participation.

OBJECTIVES AND OUTCOME MEASURES

This study will see whether the Vanderbilt results are generalizable by calculating 2x2 table data (see Table 1) for 7 EDs in different regions of the United States. Specifically, we will identify the sensitivity, specificity, negative predictive value, positive predictive value, false negative rate, false positive rate, likelihood ratio of being screened for an early ECG if the patient's ECG shows STEMI, likelihood ratio of triggering an early ECG if the patient's ECG is negative. STUDY DESIGN

Design

Cross sectional, retrospective cohort, multi-centered study

Subject Inclusion

All patients screened for an early ECG to identify STEMI in 2014 in seven different EDs

Data Collection

A site-PI from each ED will be responsible for extracting aggregate figures included in the study survey (Appendix I) using data from their EMR reporting functions and their hospital STEMI case review committee. To reduce misclassification bias, STEMI is defined using ICD-9 codes previously validated in the literature (410.01, 410.11, 410.21, 410.31, 410.41, 410.51, 410.61, 410.81, 410.91).¹² The EMR will provide aggregated numbers on ED care events (number of patients seen, number of patients receiving an early ECG as a result of triggering the screening criteria, etc.), while the hospital STEMI committee report will provide verifying counts for all ED STEMI cases, whether the early ECG demonstrated STEMI, and missed ED STEMI cases. For any discrepancies between the EMR and STEMI committee reports, the site PI will review the associated patient charts and make a clinical decision on whether the case was Trigger positive or negative, and STEMI positive or negative. The survey is included as appendix I, and will be sent to the site-PIs via email using REDCap. REDCap will also serve as a secure study data repository. The questionnaire has been reviewed by a biostatistician for completeness and to ensure it appropriately supports the planned analysis. (see attached)

Study Timeline

The study will begin upon receipt of IRB approval from all participating sites. We anticipate data collection will take four weeks. Analysis will begin upon receipt of data from all participating sites. The data will be analyzed with the assistance of the Department of Biostatistics at Vanderbilt.

Enrollment

Sites will be enrolled upon the submission of a completed survey and institutional IRB approval letter.

Confidentiality and Source Data

Only key study personnel at the Data Coordinating Center, Vanderbilt University, will have access to the study data from all 7 EDs.

SAMPLE SIZE

Seven EDs will be included. In 2014 these EDs saw 64353, 59929, 53165, 155000, 68621, 46378, 60000 patients. This results in a total of 507446 patients screened for STEMI. Based on previously reported data, and Vanderbilt's 2014 data, the incidence of STEMI is approximately 0.14-0.18%.^{8,12} Using the median estimate of 0.16% we anticipate 812 STEMI cases.

FINAL ANALYSIS PLAN

Two-by-two contingency tables will be calculated for each ED, and all EDs combined (Table S2). The data will be reported as sensitivity, specificity, negative predictive value, positive predictive value, false negative rate, false positive rate, likelihood ratio of being screened for an early ECG (positive index test) if the ECG demonstrates STEMI (positive reference test), likelihood ratio of being screened for an early ECG (positive index test) if the ECG does not show STEMI (negative reference test). This data will then be correlated with the inclusion of atypical symptoms, associated symptoms or age (representing yes or no as binary values) in the trigger criteria via a multi-variate logistic regression to see if there is an association.

STUDY OUTCOME

- Estimates for the screening performance of ED trigger criterion for an early ECG to identify STEMI including sensitivity, specificity, NPV, PPV, LR+, LR-, and the missed case rate (false negative rate)
- Description of whether the comprehensiveness of the criteria influences screening performance.

SIGNIFICANCE

This will be the first study to evaluate ED STEMI trigger criteria screening performance across institutions in different regions of the United States.

PERFORMANCE OF STEMI SCREENING TRIGGER CRITERIA

Online form available at:https://redcap.vanderbilt.edu/surveys/?s=ET3WK99HDM

The electrocardiogram (ECG) is often described as a screening test for ST-elevation myocardial infarction (STEMI), with coronary angiography as the criterion standard diagnostic test. However, in the emergency department (ED), treatment is initiated based on the presence of STEMI on ECG. In addition, timely diagnosis should be made within 10 minutes, well before a patient is seen by a physician and during the processes of registration and triage. As a result, in the context of ED patient care processes and flow, the ECG is the *diagnostic test* and the clinical criteria used to screen arriving ED patients for STEMI in during registration and triage (ECG trigger criteria) is the true *screening test*.

This study seeks to quantify the screening performance of the early ECG trigger criteria used to screen for STEMI across 7 geographically diverse EDs. The screening population includes all ED patients \geq 18 years of age seen in the ED from January 1, 2014 at 12:00am to December 31, 2014 at 11:59am. It assumes that all ECGs done within the first 15 minutes of an ED visit are to screen for STEMI. The **STEMI screening criteria** is the index test. Triggering an early ECG is a positive index test. An **early ECG** (performed \leq 15 minutes after patient arrival) is the <u>reference diagnostic test standard</u>. An ECG demonstrating STEMI is a positive reference test. Patients, who do not receive an early ECG from registration or triage, go on to receive typical ED care. This provides an opportunity to identify cases missed by the index test, making typical ED care an <u>alternative reference standard</u> for trigger negative patients.^{3,14}

Key Definitions

<u>Trigger positive</u> = early ECG to screen for STEMI = an ECG performed \leq 15 minutes of arrival <u>Arrival</u> = first documented presence or time-stamp of the patients presence in the ED <u>EMS</u> = patients coming to the ED via emergency medical system (EMS) ambulance or helicopter

Walk-in = patients coming to the ED via non-EMS transportation

Data Collection Sources

ED and hospital electronic medical record, or summative case counts from a hospital STEMI Case Review Committee

SURVEY

- 1) ED Name: [drop down menu]
- Select one
- Brigham and Women's Hospital
- Hospital of the University of Pennsylvania
- Vanderbilt University
- University of Wisconsin
- University of Texas Southwestern
- Oregon Health & Sciences University
- University of California Davis

2) Please upload a copy of your IRB approval letter as a pdf file.

3) In 2014, how did you identify arriving ED patients for an <u>early ECG</u> to screen for STEMI?

[drop down menu]

- Select one
- Established registration/triage criteria or protocol
- Solely at the discretion of the registration staff or triaging provider
- *EDOSG Baseline Data Collection Tool Question #41

4) If you have an established early ECG protocol that serve as your "trigger criteria," upload a PDF or MS Word document including the criteria/policy for which patients get an early ECG to screen for STEMI.

5) In addition to "chest pain" what elements are included in your early ECG screening trigger criteria to identify patients for an early ECG? Select all that apply:

• Atypical STEMI symptoms (shortness of breath, dyspnea on exertion, fatigue, nausea)

- Associated STEMI symptoms (arm pain, jaw pain, back pain, epigastric pain, abdominal pain)
- An age threshold
- Other
- Not applicable. We do not have an established trigger criteria

6) What was the total number of patients, ≥18 years of age, seen in the ED in 2014? Include all individuals registered as ED patients. Do not exclude the following ED dispositions: eloped, left without being seen, left before completing treatment, left AMA. <<Free text response>>

7) In 2014, what was the total number of patients (≥18 years of age) that had an ECG performed ≤15 minutes after their arrival in the ED? <<<Free text response>>

8) What was the total number of 2014 STEMI cases that came through the ED? Include all patients, ≥18 years of age, who were registered as ED patients? This is either all ED patients with an ED admission or hospital discharge diagnosis of STEMI (via an electronic medical record query for diagnosis "STEMI" or ICD9 codes 410.01, 410.11, 410.21, 410.31, 410.41, 410.51, 410.61, 410.81, 410.91).¹³ Confirm this number with your hospital STEMI Case Review Committee. If there is a discrepancy, review the individual patient charts. Based on Vanderbilt data, the incidence of STEMI reported in the literature, and all participant ED patient volumes, there should be no more than 5 cases that require review. <<Free text response>>

9) What was the total number of 2014 STEMI cases that came through the ED that <u>did not</u> get an early ECG (ECG \leq 15 minutes of arrival)? These are the missed screening cases. This can be obtained as an adjudicated case count from your hospital STEMI committee. Many STEMI quality improvement committees will document time-to-ECG permitting an assessment of those missed by screening. These should not include patients whose were screened, but had STEMInegative early ECGs.

<<Free text response>>

10) What was the total number of 2014 ED patients who had both an ECG performed and a serum troponin ordered and resulted. This is an estimate of the underlying "chest pain patient" burden.

<<Free text response>>

	Greeter	Check-in Kiosk	Registration Clerk	Triage RN	Midlevel Provider	Physician	Other
11) Who/what is the first contact for ED patient brought in by EMS? (select one)	0	0	0	0	0	0	0
12) Who/what records EMS arrival patients' presenting chief complaint? (select one)	0	0	0	0	0	0	0
13) Who/what is the first contact for arriving ED patients what walk-in? (select one)	0	0	0	0	0	0	0
14) Who/what records walk-in patients' presenting chief complaint? (select one)	0	0	0	0	0	0	0

15) How many hours did it take to collect the data? Please include all time spent meeting, generating reports, extracting and cleaning data by you or your proxy (IT staff or assistant). Exclude time preparing your IRB application. Round up to the nearest hour.

16) What is the median Door- to-ECG time for all primarily screened ED patients with a final hospital diagnosis of STEMI?

17) What is the 25th percentile Door-to-ECG time for all primarily screened ED patients with a final hospital diagnosis of STEMI?

18) What is the 75th percentile Door-to-ECG time for all primarily screened ED patients with a final hospital diagnosis of STEMI?

19) What is the median Door- to-ECG time for all primarily screened ED patients with a final hospital diagnosis of STEMI, who received their ECG ≤15 minutes of ED arrival?

20) What is the 25th percentile Door-to-ECG time for all primarily screened ED patients with a final hospital diagnosis of STEMI, who received their ECG ≤15 minutes of ED arrival?

21) What is the 75th percentile Door-to-ECG time for all primarily screened ED patients with a final hospital diagnosis of STEMI, who received their ECG ≤15 minutes of ED arrival?

22) What is the median Door- to-ECG time for all primarily screened ED patients with a final hospital diagnosis of STEMI, who received their ECG >15 minutes of ED arrival?

23) What is the 25th percentile Door-to-ECG time for all primarily screened ED patients with a final hospital diagnosis of STEMI, who received their ECG >15 minutes of ED arrival?

24) What is the 75th percentile Door-to-ECG time for all primarily screened ED patients with a final hospital diagnosis of STEMI, who received their ECG >15 minutes of ED arrival?

25) What was your hospital Case Mix Index (CMI) for 2014?

Table S1: Early ECG Trigger Criteria Screening Performance



Table S2: 2x2 Contingency Table Data (Question numbers included below)

		Dise ECG = Refe	ease erence Test	
		STEMI (+)	STEMI (-)	
Test Trigger Criteria	Trigger (+)	#8-#9	#7-#8+9	#7
= Index Test	Trigger (-)	#9	#6-#7-#9	#6-#7
		#8	#6-#8	#6

PROTOCOL REFERENCES:

1. Yiadom, MYAB. Emergency department treatment of acute coronary syndromes. *Emergency Medicine Clinics of North America.* 2011;4: 699-710.

2. O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *JACC*. 2013;4: e78-e140

3. Canto JG, Shlipak MG, Rogers WJ, Malmgren JA, Frederick PD, Lambrew CT, Ornato JP, Barron HV, Kiefe CI. Prevalence, clinical characteristics, and mortality among patients with myocardial infarction presenting without chest pain. *JAMA*. 2000;283:3223-3229.

4. Blomkalns AL, Chen AY, Hochman JS, Peterson ED, Trynosky K, Diercks DB, Brogan GX, Boden WE, Roe MT, Ohman EM, Gibler WB. Gender disparities in the diagnosis and treatment of non–ST-segment elevation acute coronary syndromes: large-scale observations from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines) national quality improvement initiative. *JACC.* 2005;45:832-7.

5. Milner KA, Vaccarino V, Arnold AL, Funk M, Goldberg RJ. Gender and age differences in chief complaints of acute myocardial infarction (Worcester Heart Attack Study). *Am J Cardiol.* 2004;93:606-608.

6. Dey S, Flather MD, Devlin G, Brieger D, Gurfinkel EP, Steg PG, FitzGerald G, Jackson EA, Eagle KA. Sex-related differences in the presentation, treatment and outcomes among patients with acute coronary syndromes: the Global Registry of Acute Coronary Events. *Heart.* 2009;95:20-26.

7. Brieger D, Eagle KA, Goodman SG, Steg PG, Budaj A, White K, Montalescot G. Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: insights from the Global Registry of Acute Coronary Events. *Chest.* 2004;126:461-469.

8. Panju AA., Hemmelgarn BR, Guyatt GH, Simel DL. JAMA.1998;280:1256-1263.

9. Glickman SW, Shofer FS, Wu MC, Scholer MJ, Ndubuizu A, Peterson ED, Granger CB, Cairns CB, Glickman LT. Development and validation of a prioritization rule for obtaining an immediate 12-lead electrocardiogram in the emergency department to identify ST-elevation myocardial infarction. *Am Heart J.* 2012;163:372-382

10. Lijmer JG, Mol BW, Heisterkamp S, Bonsel GJ, Prins MH, van der Meulen JH, Bossuyt PM. Empirical evidence of designs –related bias in studies of diagnostic tests. *JAMA*. 1999;282:1061-1066.

11. Carrington RM, Lachs MS, Feinstein AR. Use of Methodological standards in diagnostic test research: Getting better but still not good." *JAMA*.1995;274: 645-651.

12. Ward MJ, Kripalani S, Zhu Y, Storrow AB, Dittus RS, Harrell FE and Self WH. Incidence of emergency department visits for ST-elevation myocardial infarction in a recent six-year period in the United States. *Am J Cardiol.* 2015;115: 167-170.

13. Carrington RM, Lachs MS, Feinstein AR. Use of Methodological standards in diagnostic test research: Getting better but still not good." *JAMA*.1995;274: 645-651.