Sensitivity and specificity of the Vectraplex electrocardiogram system with a cardiac electric biomarker in the diagnosis of ST-elevation myocardial infarction

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ABSTRACT

ST-elevation myocardial infarction (STEMI) is a clinical diagnosis based on a compatible history and characteristic electrocardiographic changes. In the current era, STEMI is treated emergently with angiography, leading to percutaneous coronary intervention. However, false-positive electrocardiograms (ECGs) occur, resulting in unnecessary emergent catheterizations. We hypothesized that the Vectraplex cardiac electrical biomarker (CEB) would increase the specificity for the diagnosis of STEMI. We studied 50 patients who were identified by standard of care (clinical history, physical exam, and 12-lead ECG) as suspected to have STEMI and tested the sensitivity and specificity of the Vectraplex ECG system. Using the final clinical diagnosis (based on history, ECGs, troponin values, and angiographic findings) as the gold standard, we found the CEB value to be quite dynamic, with a reasonable sensitivity and a good positive predictive value but generally poor specificity and negative predictive value. It offered only a 20% improvement compared to 50-50 performance on receiver operator curves.

KEYWORDS Cardiac electric biomarker; electrocardiogram; percutaneous coronary intervention; ST-elevation myocardial infarction

ST-elevation myocardial infarction (STEMI) is a clinical diagnosis based on a compatible history and characteristic electrocardiographic (ECG) changes. In the current era, STEMI is treated emergently with angiography, leading to percutaneous coronary intervention (PCI). However, false-positive ECGs occur, resulting in unnecessary emergent catheterizations. Studies have shown that 10% to 30% of presumed STEMI are found to have an alternative diagnosis.^{1,2} We previously reported data from an 18-month period in which 28% of patients believed to have STEMI referred for angiography did not require PCI, with many found to have an alternative diagnosis.¹ Similarly, in a large statewide STEMI system of nearly 4000 catheterization laboratory activations, nearly 30% were either deemed inappropriate or did not require interventional therapy.² Thus, more accurate diagnosis by ECG or another technology is a significant clinical need. The US Food and Drug Administration approved the Vectraplex ECG system, which records skin-surface cardiac electrical activity, producing a derived 15-lead ECG.

However, unlike a standard ECG, the Vectraplex ECG system, utilizing supplementary proprietary analysis (eigenvalue modeling of the various vectors, quantifying dipolar and multipolar forces),^{3,4} yields additional information, dubbed the “cardiac electrical biomarker” (CEB), that is proposed to add to the sensitivity and specificity of findings. The Vectraplex ECG system has been previously studied in retrospective patient groups and compared to traditional ECG computer and human analysis.⁵ Others have correlated a rise in CEB with a subsequent rise in serum troponin measurements.⁶ We hypothesized that the Vectraplex CEB would increase the *specificity* of the diagnosis of STEMI while maintaining sensitivity.

METHODS

To evaluate the hypothesis, we selected 50 patients who were identified by standard of care (clinical history, physical exam, and 12-lead ECG) as suspected of having STEMI and who would therefore be referred for emergent coronary

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angiography. Once identified, a rapid “STEMI activation” was performed and the patient was transferred emergently to the cardiac catheterization laboratory. After arriving in the catheterization laboratory, but prior to initiation of angiography, we placed the five-electrode Vectraplex monitoring system onto the patient’s skin at the appropriate locations, in addition to standard monitoring electrodes. The Vectraplex system was set to begin recording all data prospectively in a continuous fashion from prior to start of the procedure until the completion of the case. Angiography, and PCI if indicated, was carried out for standard indications and in the usual fashion, with treatment decisions left to the discretion of the interventional cardiologists, without knowledge of the information from the Vectraplex system.

The study received approval by the Scott & White institutional review board. Informed consent was obtained by a clinical research nurse or clinical research coordinator. The institutional review board, recognizing the unstable clinical situation of many of these patients and the fact that very rapid care was needed, allowed consent to be obtained after the catheterization. No care decisions were made based on information obtained from the novel diagnostic system; the studied instrument only recorded information, with no potential for harm. The data were securely stored but not analyzed until informed written consent was provided by the patient, typically 4 to 24 hours after the procedure, after clinical stability was assured and anesthesia was fully resolved. If the patient did not grant consent, his or her Vectraplex information was deleted and not analyzed.

Data were collected in the Vectraplex ECG system prior to being exported to SAS 9.4 and R Ver. 3.1.0 for cleaning, management, and data analysis. Descriptive statistics were reported with counts, minimum, 25th percentile, median, mean, 75th percentile, maximum, and standard deviation for continuous variables. Categorical variables were described as counts (percentages). Sensitivity, specificity, positive and negative predictive values, and accuracy were calculated with 95% confidence intervals to compare possible cutoff points from the Vectraplex ECG system in determining whether patients had a STEMI diagnosis. Receiver operating characteristics (ROC) were calculated for the chosen cutoff point and for the continuous measures using logistic regression models.

RESULTS

Fifty patients were studied over a period of 6 months, from February 2015 to August 2015. All patients were referred for emergent cardiac catheterization at a single institution on the basis of standard clinical criteria. Two patients were withdrawn after consent was obtained and one patient was lost due to an error in recording the data, leaving 47 patients for final analysis. Baseline demographic and clinical characteristics are presented in [Table 1](#).

A final diagnosis was determined based on ECG review, cardiac catheterization findings, and serial troponin I

measurements. The final clinical diagnosis was STEMI in 83% of the 47 patients included in the study, indicating that 17% of patients with suspected STEMI were found to have another diagnosis. The other diagnoses included unstable angina ($n = 2$, both with prior Q waves and persistent ST elevation), stress cardiomyopathy ($n = 3$), myocarditis ($n = 1$), atrial tachycardia ($n = 1$), and erroneous ECG interpretation ($n = 1$).

Angiographic and ECG findings are recorded in [Table 2](#). We measured the CEB constantly throughout angiography and, if performed, PCI. CEB measurements were obtained at periodic intervals as well as when significant changes occurred. Because the goal was to assess the incremental value of the Vectraplex ECG in the early diagnosis and management of STEMI, we evaluated the earliest parts of the recordings (i.e., at the time closest to when the ECG was being utilized to diagnose STEMI). Because of a tendency toward excessive noise upon first placing the electrodes, minutes 3 to 8 were analyzed (before angiography actually

Table 1. Baseline demographic and clinical characteristics of 48 patients with suspected ST-elevation myocardial infarction

Characteristics	Number (%) or median (range)
Male	31 (65%)
Age (years)	62 (29–90)
Body mass index (kg/m ²)	28.3 (19.8–45.2)
Hypertension	38 (79%)
Diabetes mellitus	
Absent	31 (65%)
Oral controlled	11 (23%)
Insulin	6 (13%)
Chronic kidney disease	6 (13%)
Prior CABG	2 (4%)
Prior myocardial infarction	7 (15%)
LVH (by echo)	15 (31%)
Bundle branch block	
No	42 (88%)
Right	1 (2%)
Left	1 (2%)
Other (IVCD, other)	4 (8%)
Left ventricular wall thickness (mm)	13.0 (12–16)
Baseline heart rate (bpm)	82.5 (52–120)
Maximum ST elevation (mm)	2.0 (1.0–9.0)
Total ST elevation (mm)	5.0 (2.25–25)
Peak troponin I (ng/mL)	27.61 (0–369)

CABG indicates coronary artery bypass grafting; LVH, left ventricular hypertrophy; IVCD, intraventricular conduction delay.

Table 2. Electrocardiographic and angiographic characteristics of 48 patients with suspected ST-elevation myocardial infarction

Characteristic	
Location of injury pattern (<i>n</i> = 45)	
Anteroseptal	33%
Lateral	7%
Inferior	56%
Posterior	4%
Culprit coronary artery (<i>n</i> = 41)	
LAD	41%
LC	15%
Right	44%
TIMI flow before catheterization (<i>n</i> = 21)	
0	63%
1	2%
2	5%
3	29%
TIMI flow after catheterization (<i>n</i> = 41)	
0	0%
1	5%
2	2%
3	93%
Presence of collateral vessels (<i>n</i> = 47)	
No	87%
Yes	13%

LAD indicates left anterior descending; LC, left circumflex; TIMI, Thrombolysis in Myocardial Infarction.

commenced). Curves could be generated, showing the distribution of CEB values over the entire time of angiography, as shown in [Figure 1](#).

Previous guidance from the company, generated from a patient population predominantly with suspected acute coronary syndrome (ACS), suggested that a CEB <66 was normal, 66 to 94 was intermediate risk, and >94 was abnormal. To maximize sensitivity, we combined all values ≥66 as possibly suggestive of a STEMI, whereas values <66 would be inconsistent with a STEMI. Because the CEB was quite dynamic, we analyzed CEB values as minimum, median, mean, and maximum values, with the hypothesis that minimum values would accentuate specificity, whereas maximum values would increase sensitivity. CEB values are described in [Table 3](#).

Using the final clinical diagnosis (determined by the primary author) as the gold standard, based on all clinical data (history, ECGs, troponin values, and angiographic

findings) available, we compared the performance of various CEB assessments ([Table 4](#)). Using the statistical calculations for accuracy or ROC, the CEB median or CEB mean performed the best, but even these only performed moderately well, with a positive predictive value of 82% to 85% and a negative predictive value of 11% to 23%.

Initially we evaluated the first 10 minutes of the recordings. Subsequently we reanalyzed the data utilizing only minutes 3 to 8 (in an attempt to exclude any noise that may have been present at the beginning of the recording and as the procedure unfolded), but we found no significant difference in the results. We also subsequently analyzed the data after using a data smoothing process in an attempt to mitigate some of the variability of the data (that we speculate could be influenced by motion or noise), but again the results were not significantly changed.

DISCUSSION

The need to accurately diagnose an acute coronary occlusion in the setting of STEMI is paramount in order to allow appropriate life-saving and myocardium-saving therapies to be delivered. However, therapies are expensive, require specialized personnel and equipment, and are associated with a low but real risk of complications. The ability of history, physical exam, ECG, and point-of-care lab testing to predict an acute coronary occlusion is imperfect, with studies showing that the suspected diagnosis is correct only 70% to 90% of the time. New tools would be welcomed if they could increase the accuracy of the diagnosis of STEMI and/or the need for PCI.

We studied 47 patients who were clinically suspected to have a STEMI and in whom all of the data were available to assuredly confirm or refute the diagnosis and assessed the incremental value of the Vectraplex ECG system. Because we hypothesized that the measured CEB could aid in and enhance the decision to pursue emergent angiography, we chose to evaluate the first few minutes of the recordings (before angiography was performed). CEB values were varied and dynamic, and that compelled us to analyze the information in various ways, including minimum values (e.g., suspecting that all patients with STEMI would have a CEB level >94, or at least >66). Maximum CEB values were also analyzed, as well as statistically determined means and medians.

Sensitivity was lowest for CEB min, whereas specificity was lowest for CEB max. All measurements suffered from a low negative predictive value, but this is likely due to the relatively rare patient who did not have a STEMI (i.e., a STEMI-enriched population was preselected). However, though the positive predictive values were consistently high, the ROC analyses suggested only, at best, 59.5%. A value of 50% would be equivalent to a chance occurrence, so this finding suggests only a 20% improvement over chance. Beyond the initial analysis, we explored other

Figure 1. Representative cardiac electrical biomarker (CEB) curves. **(a)** Patient 7, with a prior inferior myocardial infarction (MI), who presented with a large anterior MI, Thrombolysis in Myocardial Infarction (TIMI) 0 flow at the time of initial angiography. **(b)** Patient 11, with a large MI due to a proximal left anterior descending (LAD) occlusion, with TIMI 0 flow at the time of initiation of angiography, which concluded with TIMI 3 flow. Q waves were present on the initial electrocardiogram (ECG) (although clinically the event was acute with no prior history of MI); no collateral vessels to the LAD were present at onset. Notice the variability in the CEB values, despite their overall elevated values. **(c)** Patient 16, who presented with a posterior MI due to occlusion of a left circumflex. Minimal ST elevation was present on surface ECG. TIMI 1 flow was present at the onset of the procedure, and TIMI 3 flow was ultimately restored. The vessel was not opened until 800 to 1000 seconds after initiation of the recording. **(d)** Patient 21, with 3-mm ST

Table 3. Measured values of the cardiac electrical biomarker in 47 patients with suspected ST-elevation myocardial infarction^a

Variable	Minimum value	Median value	Mean value	Maximum value
CEB min	2.00	48.00	93.41	533
CEB median	13.00	155.75	224.54	819
CEB mean	14.53	177.90	239.79	805.50
CEB max	44.00	394.00	489.22	1298.00

CEB indicates cardiac electrical biomarker; CEB min, minimum measured CEB from one patient's data; CEB median, median value from one patient's data; CEB mean, mean value from one patient's data; CEB max, maximum measured value from one patient's data.

^aMultiple CEB values were recorded for each patient, comprising a data set for each individual patient.

analyses based on hypotheses that might account for irregularities within the data, but ultimately these yielded the same conclusions.

The study was a small pilot study, with a limited number of patients. Additionally, the clinical scenario is challenging, because patient care and treatment take top priority, and patient pain, movement, perspiration, inadequate skin preparation, and other factors could all influence the quality of the data recording, especially given the stringent system requirements for excellent data recording quality. Normal or expected CEB values for patients suffering a STEMI are not known and could be different from those expected from data derived from patients with non-ST-elevation ACS. Because there are no published reports for the dynamic nature of the CEB in this scenario, the proper timing of assessment is not known.

In conclusion, we used the Vectraplex ECG system to evaluate 47 patients who were believed to be suffering a STEMI in order to assess its ability to add prognostic or diagnostic information. Among these patients, 83% in fact proved to have a STEMI upon retrospective assessment, a figure consistent with prior published reports.^{1,2} We found the CEB value to be quite dynamic and, utilizing multiple assessments of it, we found it to have reasonable sensitivity with a good positive predictive value but generally poor specificity and negative predictive value. This resulted in only a 20% improvement compared to a 50-50 chance diagnosis.

elevation in leads V1 to V3, who was found to have a thrombotic occlusion of an old LAD stent with TIMI 2 flow initially. ST elevation subsequently resolved. Definitive vessel treatment did not commence until after 500 seconds. **(e)** Patient 30, who presented with chest pain and ST elevation in the precordial leads. However, angiography revealed no significant coronary artery disease, and there was no rise in troponin. Subsequent echocardiography revealed left ventricular systolic dysfunction consistent with a nonischemic cardiomyopathy.

Table 4. Performance of the cardiac electrical biomarker compared with the final clinical diagnosis

Variable	Sensitivity 95% CI	Specificity 95% CI	PPV 95% CI	NPV 95% CI	Accuracy 95% CI	AUC
CEB min	32.5% 18.6–49.1	62.5% 24.5–91.5	81.3% 54.4–96.0	15.6% 5.3–32.8	37.5% 24.0–52.7	47.6%
CEB median	75.0% 58.8–87.3	37.5% 8.5–75.5	85.7% 69.7–95.2	23.1% 5.0–53.8	68.8% 53.8–81.3	59.5
CEB mean	80.0% 64.4–90.1	12.5% 0.3–52.7	82.1% 66.5–92.5	11.1% 0.3–48.3	68.8% 53.8–81.3	59.5%
CEB max	95.0% 83.1–99.4	12.5% 0.3–52.7	84.4% 70.5–93.5	33.3% 0.8–90.6	81.3% 67.4–91.1	56.2%

CI indicates confidence interval; PPV, positive predictive value; NPV, negative predictive value; AUC, area under receiver operating characteristic curve; CEB, cardiac electrical biomarker; CEB min, minimum measured CEB from one patient's data; CEB median, median value from one patient's data; CEB mean, mean value from one patient's data; CEB max, maximum measured value from one patient's data.

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