Validation of the Vessel-specific Leads (VSLs) for Acute Ischemia Detection on a Dataset with Non-ischemic ST-segment Deviation

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Abstract

Existing criteria recommended by ACC/ESC for identifying patients with ST-elevation myocardial infarction (STEMI) from the 12-lead ECG perform with high specificity (*SP*), but low sensitivity (*SE*). In our previous study, we found that the *SE* of acute ischemia detection can be markedly improved without any loss of *SP* by calculating, from the 12-lead ECG, ST elevation in 3 vessel-specific leads (VSLs). To further validate the method, we evaluated the *SP* using a dataset with non-ischemic ST-segment changes, consisting of 12-lead ECGs of 100 patients. These ECGs were chosen to represent five causes of pathological ST deviation, other than acute coronary occlusion: ventricular pre-excitation, acute pericarditis, early-repolarization syndrome, left ventricular hypertrophy, and left bundle branch block. Both STEMI and VSL criteria were tested by calculating *SP* as the performance measure. We found that *SP* of the STEMI criteria was 100%, 4%, 29%, 100%, and 64%, respectively, for the five subgroups. The corresponding values of *SP* for the VSLs were 92%, 88%, 100%, 77%, and 68%. For the entire group, *SP* was 57% for the STEMI criteria and significantly higher for the VSLs at 83%. Thus, the VSLs not only are more sensitive in detecting acute ischemia, but also significantly more specific in rejecting patients with non-ischemic ST deviation than the existing STEMI criteria.

1. Introduction

In patients presenting with symptoms suggesting acute coronary syndromes (ACS), currently used clinical diagnostic criteria [1, 2] based on ST-segment elevation in the 12-lead ECG identify patients suffering from ST elevation myocardial infarction (STEMI) with high specificity, but low sensitivity [3, 4]. Consequently, many false-negative patients may not receive the emergent reperfusion therapy (whether primary PCI or thrombolytic therapy) and its potential benefit. In a previous study [5], we have shown that the 3 vessel-specific leads (VSLs) derived from conventional 12-lead ECG can improve acute myocardial ischemia detection sensitivity (*SE*) without any loss of specificity (*SP*). However, the two test datasets, the *STAFF* III dataset [6] captured during controlled acute ischemia and the *Glasgow* dataset [7] collected from patients who were hospitalized for chest pain, contain few ECGs with non-ischemic ST deviation that are known to cause false-positive STEMI detection [8]. The aim of the present study was to further evaluate the *SP* performance of the modified VSLs, using a dataset with non-ischemic ST-segment changes.

2. Methods

2.1. Patient population

Patient population consisted of 100 patients (75 males, age range 12–83 yrs, average age 52 yrs), for whom 12-lead ECGs were retrieved from a centralized ECG management system at Skåne University Hospital, Lund, Sweden [9]. Patients were chosen to represent five subgroups with various causes of pathological ST deviation, other than acute coronary occlusion: a) ventricular pre-excitation (n = 12), b) acute pericarditis (n = 26), c) "early repolarization syndrome" (ERS) (n = 14), d) left ventricular hypertrophy (LVH) with "strain" (n = 26), and e) left bundle branch block (LBBB) (n = 22). Exclusion criteria were: ECGs with inadequate signal quality, heart rate exceeding 120 bpm, and atrial flutter.

2.2. Derivation of VSLs

The method of improved acute ischemia detection based on 12-lead-derived VSLs has been described elsewhere [5]. Brief description of the method follows.

To determine the locations on the body surface with the largest ST elevation and depression during occlusion of each of the three main coronary arteries—i.e., left anterior descending coronary artery (LAD), left circumflex coronary artery (LCx), and right coronary artery (RCA)— the 120-lead BSPM dataset recorded at Dalhousie University during episodes of acute ischemia induced by elective balloon-inflation PCI of LAD (n = 32), RCA (n = 36),

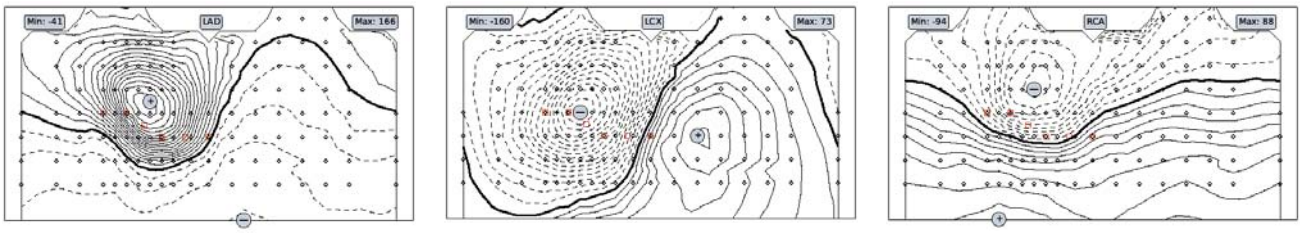

Figure 1. Mean BSPM at J point, at peak ischemia: (Left) for patients (n = 15) with LAD occlusion, (Middle) for patients (n = 15) with LCx occlusion, and (Right) for patients (n = 15) with RCA occlusion. The map was constructed from 120 leads, on an unrolled cylindrical projection of the chest, with sites of 6 precordial leads indicated by red squares. Max/min potential values are marked by +/– sign and their amplitudes (in microvolts) are in right/left corner of the panel; isopotential lines are linearly spaced at 10-μV increments.

and LCx (n = 23) arteries [10] was used. The leads with the most elevated/depressed ST potentials for LAD, LCx, and RCA occlusions are denoted as V_{LAD+}, V_{LAD-}, V_{RCA+}, V_{RCA-}, V_{LCX+}, V_{LCX-}. The mean peak-inflation map at the J-point for each artery occlusion was obtained by averaging BSPMs of 15 patients from each group with the largest ST changes. From these three ST maps, the torso sites with the maximal ST changes were determined as shown in Fig. 1.

Using a linear transformation, the unipolar potentials of the VSLs are computed from the 8 independent leads (II, III, V1, … , V6) of the 12-lead ECG. The coefficients C_{ij} are shown as a 6 × 8 transformation matrix **C**.

$$\begin{bmatrix} V_{LAD+} \\ V_{LAD-} \\ V_{LCX+} \\ V_{LCX-} \\ V_{RCA+} \\ V_{RCA-} \end{bmatrix} = \begin{bmatrix} C_{11} & C_{12} & C_{13} & C_{14} & C_{15} & C_{16} & C_{17} & C_{18} \\ C_{21} & C_{22} & C_{23} & C_{24} & C_{25} & C_{26} & C_{27} & C_{28} \\ C_{31} & C_{32} & C_{33} & C_{34} & C_{35} & C_{36} & C_{37} & C_{38} \\ C_{41} & C_{42} & C_{43} & C_{44} & C_{45} & C_{46} & C_{47} & C_{48} \\ C_{51} & C_{52} & C_{53} & C_{54} & C_{55} & C_{56} & C_{57} & C_{58} \\ C_{61} & C_{62} & C_{63} & C_{64} & C_{65} & C_{66} & C_{67} & C_{68} \end{bmatrix} \times \begin{bmatrix} I \\ II \\ V1 \\ V2 \\ V3 \\ V4 \\ V5 \\ V6 \end{bmatrix}$$

The transformation coefficients of matrix **C** were derived from the Dalhousie 120-lead BSPM Superset (n = 892) by means of standard least-square regression method [11]. The estimates of C_{ij} were chosen to minimize the error sum of squares over all available data samples of the QT interval for all subjects of the Superset.

The three vessel-specific bipolar leads for LAD, LCx, and RCA can then be calculated as the difference between the respective positive and negative terminals. Alternatively, they can be calculated directly:

$$\begin{bmatrix} L_{LAD} \\ L_{LCX} \\ L_{RCA} \end{bmatrix} = \begin{bmatrix} T_{11} & T_{12} & T_{13} & T_{14} & T_{15} & T_{16} & T_{17} & T_{18} \\ T_{21} & T_{22} & T_{23} & T_{24} & T_{25} & T_{26} & T_{27} & T_{28} \\ T_{31} & T_{32} & T_{33} & T_{34} & T_{35} & T_{36} & T_{37} & T_{38} \end{bmatrix} \times \begin{bmatrix} I \\ II \\ V1 \\ V2 \\ V3 \\ V4 \\ V5 \\ V6 \end{bmatrix}$$

The same transformation equations can be used to calculate both the ECG waveforms for the input ECG samples and/or the ST values for the VSLs from the ST values measured from the 8 input ECG leads.

Table 1. Detection thresholds for VSLs

Detection Criteria	Threshold (μV)		
	LAD (M/F)	LCX (M/F)	RCA (M/F)
VSLs	210/160	105/100	105/100

To maintain the same high detection specificity of the STEMI criteria currently used in clinical practice, gender- and lead-specific thresholds for the VSLs, have been determined empirically [5] and listed in Table 1. The STEMI criteria implemented are ST elevation measured at the J-point in two contiguous leads ≥ 0.2 mV (or 200 μV) in men or ≥ 0.15 mV (or 150 μV) in women in leads V2 and V3 and/or ≥ 0.1 mV (or 100 μV) in other leads [1]. The VSLs can be scaled so that the same threshold values (200, 150, and 100 μV) used for the STEMI criteria can also be used for the scaled VSLs.

2.3. VSLs performance testing

The *Lund* dataset was used to test both STEMI and VSL criteria by calculating *SP* as the performance measure. Using a bootstrap method with replacement [12], *SP* values for 1,000 bootstrap trials and the mean values and ±95% confidence limits were generated. In the performance comparison of STEMI *vs* VSL criteria, pairwise *t*-test was used to obtain the *p*-value. Statistically significant differences were considered those with $p < 0.05$.

3. Results

The performance results are shown graphically in Fig. 2. For each ECG record the maximum ST value from the three VSLs is plotted as a data point according to the ST

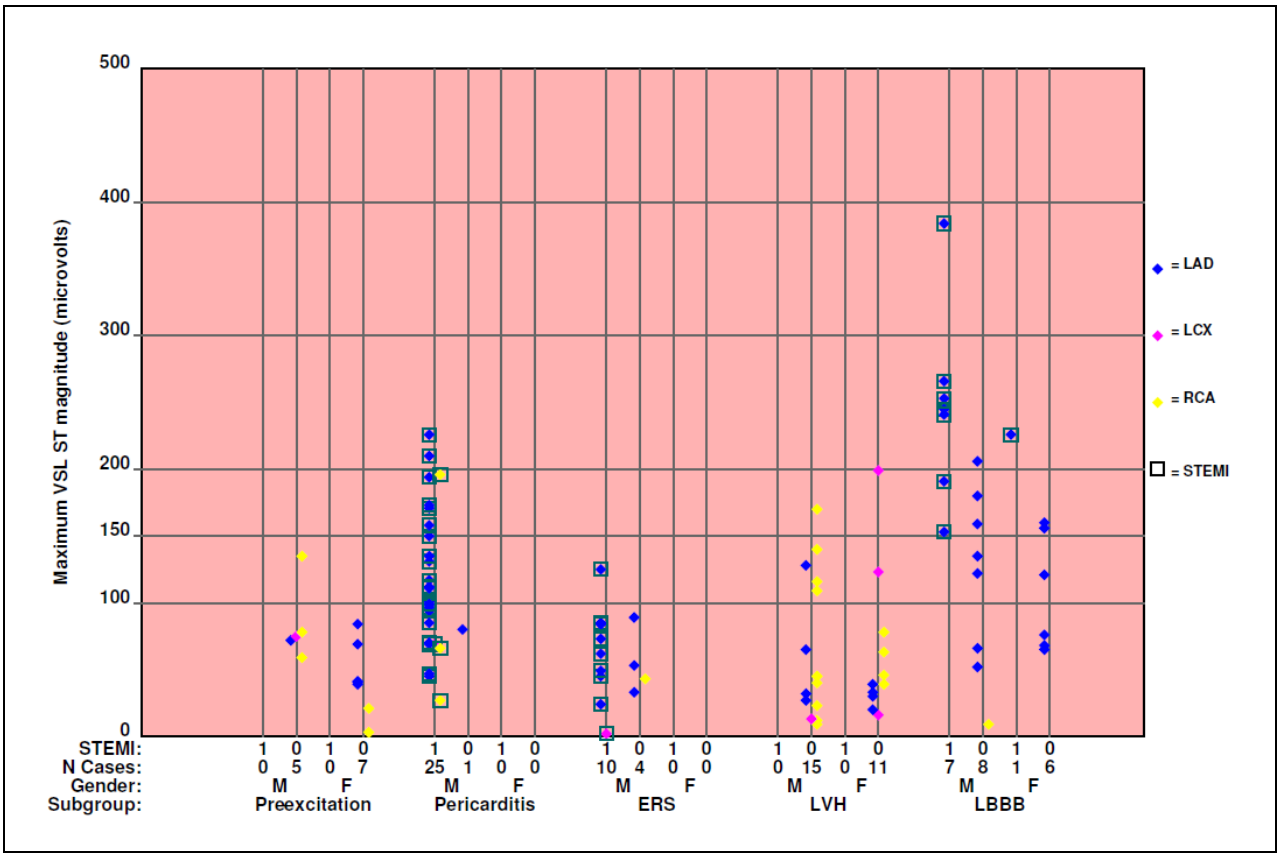

Figure 2. Summary performance plot for the *Lund* dataset. For each ECG record the maximum ST value (in uV) from the three VSLs is plotted as a data point (LAD in blue, LCX in pink, and RCA in yellow). Data point with a square box indicates the record met the STEMI criteria.

magnitude in uV as indicated on the y-axis. For each non-ischemic ST deviation subgroup, the data points are plotted in four groups: 1) STEMI positive and Male, 2) STEMI negative and Male, 3) STEMI positive and Female, and 4) STEMI negative and Female. For data that met the current STEMI criteria a square box is added to the data point for better visualization. Within each group, LAD (in blue) is plotted first and followed by LCX (in pink) and RCA (in yellow).

Data points above the thresholds (210 uV for LAD Male, 160 uV for LAD Female, 105 uV for LCX and RCA Male, and 100 uV for LCX and RCA Female) are counted as false positive (*FP*) and data points below the thresholds are counted as true negative (*TN*). *SP* is then calculated as $TN/(FP + TN)$. The *SP* results are summarized in Table 2.

4. Discussion

The standard ECG serves as the primary test to support the decision for emergency reperfusion therapy for patients with the wide range of symptoms suggesting potentially reversible acute coronary thrombosis [13]. The currently accepted criteria for STEMI are routinely used,

Table 2. Performance summary of STEMI *vs* VSLs

Lund Dataset	Detection Specificity Percent (95% Confidence Interval)		
	STEMI	VSLs	*p*-value
Preexcitation ($n = 12$)	100 (100–100)	92 (76–100)	0.339
Pericarditis ($n = 26$)	4 (0–11)	88 (76–100)	< 0.001
ERS ($n = 14$)	29 (5–52)	100 (100–100)	< 0.001
LVH ($n = 26$)	100 (100–100)	77 (61–93)	0.011
LBBB ($n = 22$)	64 (44–84)	68 (49–88)	0.576
All cases ($n = 100$)	57 (47–67)	83 (76–90)	< 0.001

but their limited sensitivity delays definitive treatment in many patients [14]; and their limited specificity causes inappropriate activation of the cardiac catheterization laboratory in some patients [15]. This study focuses on the investigation of specificity of vessel-specific leads (VSLs) in distinguishing between patients with ST-segment deviation associated with acute coronary occlusion and those not associated with occlusion [8]. The specificity of VSLs is compared to that achieved by the currently-used STEMI criteria.

The variation of the level of the ST deviation is known to be increased in pathological conditions such as those included in the "non-ischemic" patient population in this study. In general, the ST segments representing the "post-depolarization" condition are altered by the abnormal ventricular depolarization in cardiac abnormalities such as pre-excitation, hypertrophy, and pericarditis.

Indeed, ST segment deviation from TP segment baseline is the key ECG abnormality in the "early-repolarization syndrome". For pericarditis and ERS patients in this study, VSLs performed much better than STEMI criteria. In patients with LVH, the specificity was slightly higher for STEMI criteria. For pre-excitation and LBBB patients both STEMI criteria and VSLs performed similarly. For the entire group, *SP* was 57% for the STEMI criteria and significantly higher for the VSLs at 83%.

5. Conclusion

The results of this study show that our proposed three vessel-specific leads (VSLs) derived from the standard 12-lead ECG can identify acute ischemia not only with higher sensitivity (as we have shown previously), but also with higher specificity in comparison with the existing ACC/ESC STEMI criteria applied to the same 12 standard leads. In clinical practice, the increased sensitivity and specificity should allow more patients to be accurately identified as candidates for the acute therapy. This finding needs to be further corroborated on a larger patient population with AMI prevalence typical of the population presenting to the emergency room.

Acknowledgements

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