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JOURNAL OF Electrocardiology

Journal of Electrocardiology 50 (2017) 82-89

www.jecgonline.com

Position of ST-deviation measurements relative to the J-point: Impact for ischemia detection

Sumche Man, MD, PhD, C. Cato ter Haar, MD, Marjolein C. de Jongh, BSc, Arie C. Maan, PhD, Martin J. Schalij, MD, PhD, Cees A. Swenne, PhD*

Cardiology Department, Leiden University Medical Center, Leiden, The Netherlands

Abstract	has to be measured for detection of acute ischemia in the ECG. Methods: We analyzed 53 ECGs, recorded preceding emergency catheterization of acute coronary syndrome patients with a completely occluded culprit artery (cases), and 88 control ECGs recorded in the cardiology outpatient clinic. ECG-amplitude measurements were made every 10 ms, between 20 ms before till 80 ms after the J point. STEMI-detection algorithms varied from the traditional STEMI criterion (elevations in at least two adjacent ECG leads), via the STEMI equivalent criterion (depressions in V2 and V3), to the most liberal STEMI-detection algorithm in which elevations as well as depressions in two adjacent leads were considered as signs of ischemia. Results: Diagnostic accuracy was highest (93.6%) for the most liberal STEMI-detection algorithm at 10 ms after the J point; sensitivity was 94.3% and specificity was 93.2%. Conclusion: The results of our study suggest that STEMI detection close to the J point is optimal. © 2016 Elsevier Inc. This is an open access article under the CC BY license
Kevwords:	(http://creativecommons.org/licenses/by/4.0/). Acute coronary syndrome: Myocardial ischemia: STEMI classification: ST-deviation measurement: Electrocardiography

Introduction

Chest pain at rest can be caused by many conditions other than an acute coronary syndrome (ACS). When chest pain triggers an emergency call, the electrocardiogram (ECG) made at first medical contact is the only objective diagnostic tool available (serum biomarkers increase only after necrosis has occurred [1] to corroborate the decision to accept or reject the working diagnosis of ACS). ACS ECGs are classified as either ST-elevation/ST-elevation equivalent myocardial infarction (STEMI) or as non-ST-elevation myocardial infarction (NSTEMI). This classification is important because it largely determines what the initial therapy will be. STEMI patients are triaged for emergency coronary angiography with a view on revascularization (primary percutaneous coronary intervention, pPCI). NSTEMI patients are triaged for anti-thrombotic therapy.

STEMI is diagnosed by applying a set of criteria to the ST deviations as measured in the 12 leads at the J point or at a fixed distance in time thereafter [2–6]. The J point marks the end of the QRS complex. In a 12-lead ECG, theoretically, 12 different lead-dependent J points can be identified; the

global J point is the latest of the lead-dependent J points. In practice, determination of the J point is difficult in standard 12-lead ECG view, because this does not facilitate easy visual determination of the latest of lead-dependent J points. But even with an aligned display of the ECG leads it can be difficult to determine the J point, due to preexisting or ischemia-induced conduction disturbances or early repolarization, including a preexisting or newly-formed J wave [7-9]. In addition to ST-deviation measurements at the J point [2,3], ST-deviation measurements at a fixed time-interval (40, 60 or 80 ms) after the J point have been applied in several studies [4-6], and the Multidisciplinary Standardized Reporting Criteria Task Force of the Society for Academic Emergency Medicine (SAEM), the American College of Emergency Physicians (ACEP), the American Heart Association (AHA), the American College of Cardiology (ACC), and the Emergency Medicine Cardiac Research and Education Group - International (EMCREG-I) indicate that ST amplitudes for ischemia detection should be measured between 40 and 80 ms after the J point [10]. Partly, a time-shifted measurement could resolve the problem of an uncertain J point, because the ST segment is smoothly behaving in contrast to the vicinity of the J point. On the other hand, ST segments are not always horizontal, and this will cause systematic differences in STEMI diagnosis. An initial exploratory study,

^{*} Corresponding author at: Cardiology Department, Leiden University Medical Center, POBox 9600, 2300 RC, Leiden, The Netherlands. *E-mail address:* c.a.swenne@lumc.nl

restricted to precordial leads, in 37 patients who underwent primary PCI and were angiographically diagnosed with an LAD occlusion, showed an increased sensitivity for delayed ST amplitude measurements [11]. The full impact of time-shifted ST-deviation measurement with a complete 12-lead ECG analysis for STEMI classification in a group of patients in whom the ischemia location is not restricted to occlusions in one specific coronary artery is, however, not known. This prompted us to do the here-described study, in which we investigated the consequences of time-shifted ST-deviation measurement on the sensitivity and specificity of STEMI classification.

Methods

We studied ECGs of two patient groups, cases and controls. Cases were 53 ACS patients scheduled for pPCI, and described in an earlier study [12]. This was a consecutive subgroup of pPCI patients who were selected because they had a completely occluded culprit artery during coronary angiography. Patients with a documented prior myocardial infarction were excluded. All ECGs preceded PCI. When more than one ECG preceding PCI was available, the ECG closest in time with respect to PCI was selected.

Controls were a group of 88 patients in whom we earlier studied ECG changes over 25 years [13]. Only electively made ECGs, made in the outpatient clinic were selected; ECGs made during a hospital admission or at the emergency department were excluded. Only ECGs with regular sinus rhythm were included. The 88 initial ECGs of this patient group were used for our current study.

ECGs were analyzed by using our LEADS (Leiden ECG Analysis and Decomposition Software) program [14]. In short, LEADS performs baseline correction, calculates an averaged beat and computes global onset-Q, J-point, and end-of-T landmarks, to be reviewed and when necessary edited by the LEADS analyst. Correction of the global J point is done in a screen that visualizes the predominant, averaged beat with all 12 ECG leads in superimposition mode. In this display, the LEADS analyst can adjust the global J point by positioning a crosshair cursor at the latest of the lead-dependent J points. In case of the current study, final global J points were determined by a panel of observers consisting of 2 cardiologist experts and 2 researchers during an interactive LEADS session with online screen sharing [12]. Consensus was reached, with ample discussion if necessary. After establishment of the global J point, ST deviations were measured in all leads, every 10 ms, between 20 ms before until 80 ms after the global J point.

The following decision logic was used to characterize the ST deviations (see Kamphuis et al. [12]; see also Fig. 1). An ECG amplitude was classified as elevation when ≥ 0.1 mV in any lead, except for leads V2 and V3, in which the threshold for elevation was 0.2 mV. An ECG amplitude was classified as depression when ≤ -0.1 mV in any lead, except for leads V2 and V3, in which the threshold for depression was -0.05 mV. Four STEMI subgroups were used:

- "STEMI strict": two adjacent limb or precordial leads show ST elevation;
- "STEMI equivalent": leads V2 and V3 show ST depression;

- "STEMI extended": two adjacent limb leads, including the inverted leads III and aVL (-III and -aVL), or two adjacent precordial leads, show ST elevation;
- "STEMI equivalent extended": two adjacent limb leads, including the inverted leads III and aVL (-III and -aVL), or two adjacent precordial leads, including the inverted leads V1 and V6 (-V1 and -V6), show ST depression.

It has to be noted that the above criteria are not mutually exclusive; it is possible that one particular patient belongs to more than one of these subgroups.

For the purpose of this study we have extended the STEMI strict and STEMI equivalent criteria, in order to detect ischemia at all locations in the heart that give rise to a minimal amount of ST deviation, irrespective of the sign of this deviation [15]. Hence, supra-threshold ST elevation as well as depression contributed to the STEMI diagnosis. In conventional diagnostics, ECGs fulfilling the STEMI extended criteria (when either lead aVL and the inverted lead III, or lead III and the inverted lead aVL show ST elevation) or the STEMI equivalent extended criteria would be characterized as NSTEMI ECGs.

Subsequently, these four STEMI subgroups were combined to four cumulative STEMI groups:

- 1. STEMI strict
- 2. STEMI strict + STEMI equivalent
- 3. STEMI equivalent + STEMI extended
- 4. STEMI extended + STEMI equivalent extended.

In this cumulative grouping system, in which each higher group includes all ECGs of the lower group, the STEMI strict group is the most restrictive and the STEMI extended + STEMI equivalent extended is the most liberal. Subsequently, for each ST-deviation measurement relative to the J point, each ECG was classified into the appropriate STEMI subgroup(s) and cumulative group/groups. Sensitivity was computed as the percentage correct-negative controls and diagnostic accuracy was computed as the sum of the numbers of correct-positive cases and correct-negative controls divided by the sum of the total numbers of cases and controls.

Results

Cases were 53 ACS patients, female/male ratio was 13:40, mean \pm SD age was 40.0 \pm 12.4 years, mean \pm SD BMI 28.1 \pm 7.4 kg·m⁻², mean \pm SD time lapse between the ECG and angiography was 37 \pm 23 min. The mean \pm SD estimated time lag between onset of symptoms and PCI was 4.0 \pm 5.4 h, range 0.8–34 h. Angiographically-determined culprit sites were in the LAD in 20 patients, in the LCX in 9 patients and in the RCA in 24 patients. Preliminary results for the case patients have been described elsewhere [16].

Controls were 88 patients, female/male ratio was 30:58, mean \pm SD age was 40.0 \pm 12.4 years, mean \pm SD BMI 24.2 \pm 3.4 kg·m⁻². The control patients had various and sometimes



Fig. 1. Pictorial representation of the various STEMI criteria. The left panel of the figure shows the four STEMI subgroups in which a given ECG can be classified. The right panel shows the four cumulative STEMI groups. Each next cumulative STEMI group includes the previous one plus a new STEMI subgroup. The red-colored radial amplitudes illustrate the voltage thresholds in the various leads. Concentric circles indicate amplitude of 0.5, 1.0, 1.5 and 2.0 µV, respectively.

combined pathology; an overview is given in Table 1. According to the Glasgow ECG interpretation program [17], 38/88 (43%) of the ECGs were abnormal or borderline abnormal. An overview of the ECG diagnoses in this patient group is given in Table 2. ST abnormalities were present in 24/88 (27%) control ECGs. A breakdown of these abnormalities is included in Table 2.

The results of the study have been summarized graphically in Figs. 2 and 3. Fig. 2 depicts the percentages of STEMI detections in the cases and in the controls, for the four cumulative STEMI groups, and for the various ST-measurement instants relative to the J point. Fig. 3 depicts the diagnostic performance as a trade-off between the true-positive rate (percentage of cases identified by the algorithm) and the false-positive rate (percentage of controls incorrectly identified as cases by the algorithm) for the four cumulative STEMI groups. The axes of this figure are similar to those of a receiver-operating characteristic (ROC). Usually, an ROC represents the performance of a detector

as a function of the detection threshold. In the current study, the threshold values for elevation and depression were fixed, as described in the Methods section, and Fig. 3 shows the performance as a result of the variation of the ST-deviation measurement instant relative to the J point. Numerically, the results of the study have been listed in Table 3 in the form of sensitivity, specificity and diagnostic accuracy for all eleven ST-measurement positions and for all four cumulative STEMI groups.

To illustrate the ST-deviation classification algorithm, we describe here the results of the ST-deviation measurements at J+10 ms in more detail. As illustrated in Fig. 2 and numerically represented in Table 4, at the J+10 ms measurement instant, 44 cases were detected by the STEMI strict criterion, 3 additional cases were detected by the STEMI equivalent criterion, another 2 additional cases were detected by the STEMI equivalent criterion, and 1 more additional case was detected by the STEMI equivalent extended criterion. Three cases were not detected by any of

Table 1Clinical diagnoses in the control group.

Clinical diagnosis	Ν	%
Congenital	31	35.2
Valvular heart disease	16	18.2
Systemic hypertension	29	33.0
Pulmonary hypertension	0	0
Non-ischemic myopathy	4	4.5
Stable angina	8	9.1
Myocardial infarction	14	15.9
Heart failure	0	0
Conduction disorders	19	21.6
Arrhythmia/Channelopathy	4	4.5
Diabetes mellitus	12	13.6
Total	137	

The total number of diagnoses in this group (137) is larger than the number of patients (88) because some of the patients had multiple diagnoses.

the criteria. The criteria for the four STEMI subgroups are associated with typical patterns of ST deviations. Partly, these patterns can be explained by the culprit location; the associated culprit locations have been listed in Table 4. Fig. 4 gives examples of each of these typical patterns. Panel A shows a typical STEMI pattern as seen in one of the 44 patients that were detected by the STEMI strict criterion. Panel B shows an STEMI equivalent pattern (suprathreshold depressions in leads V2 and V3) as seen in one of the patients who did not comply with the STEMI strict criterion. Panel C shows an STEMI extended pattern (here, elevation in aVL and in the inverted lead III) as seen in one of the patients who did not comply with either the STEMI strict or the STEMI equivalent criteria. Panel D shows an STEMI equivalent extended pattern (here, depressions in leads V5 and V6) as

Table 2

ECG abnormalities in the control group.

ECG abnormality	Ν	%
Sinus tachycardia/bradycardia	21	23.9
Abnormal P wave	7	8.0
Abnormal AV conduction	2	2.3
Abnormal frontal QRS axis	12	13.6
Prolonged QRS duration	14	15.9
High QRS amplitude	9	10.2
Abnormal ST segment	24	27.3
Lateral ST-T changes	9	
Inferior ST-T changes	8	
Septal ST-T changes	2	
LVH w ST-T changes	4	
BVH w ST-T changes	1	
ST elevation	8	
ST junctional depression	4	
Abnormal T wave	21	23.9
Long QT	2	2.3
Other	38	43.2

The total number of ECG abnormalities in this group (150) is larger than the number of patients (88) because some of the patients had multiple abnormalities. Because ST abnormalities are especially important in the setting of this study, a breakdown of this category has been incorporated in the table (several patients had more than one ST abnormality). Bundle branch blocks were not excluded. The study group included 9 patients with a form of bundle branch block: 2 with left anterior fascicular block, and 7 with right bundle branch block (2 incomplete, 1 combined with left anterior fascicular block).



Fig. 2. Diagnostic performance of the four cumulative STEMI groups STEMI strict (red), STEMI strict + STEMI equivalent (green), STEMI equivalent + STEMI extended (blue), STEMI extended + STEMI equivalent extended (black), expressed as the percentage of STEMI-classified cases (solid lines) and as the percentage of STEMI-classified controls (dashed lines) as a function of the ST measurement instant relative to the J point.

seen in one of the patients who did not comply with either the STEMI strict, STEMI equivalent or STEMI extended criteria. Panel E, finally, shows an ECG of one of the 3 patients that did not comply with either criterion, in this case because of subthreshold ST deviations.

Overviewing the results as displayed in Fig. 2, it appears that, with early (10 or 20 ms before the J point, hence, within the QRS complex) ST measurements, STEMI criteria are still very well met in the case patients, but many false-positive STEMI detections occur in the control patients. For any given measurement instant at 10 ms or later after the J point, the false-positive detections increase only slightly when the STEMI equivalent subgroup is added to the STEMI strict group. Adding the STEMI extended and the STEMI equivalent extended subgroups did not lead to any further false-positive detections. However, addition of each of these criteria gave an increase in true-positive detections. Furthermore, considering the full of measurement delays, increasing measurement delays after the J point gave rise to a global trend of increasing false-positive and true-positive detections; the increase in the false-positive detections was stronger than the increase in the true-positive detections.

The performance curves of all four cumulative STEMI groups in Fig. 3 show the relation between sensitivity and specificity. Measurements done within the QRS complex (at J–10 ms and at J–20 ms) had a low specificity. Measurements done at J+10 ms had the best specificity, and later measurements showed an increase in sensitivity, at the cost of loss of specificity (increase in false positives). Much of the performance depends on the STEMI algorithm: going from the "STEMI strict" curve via the "STEMI strict" plus STEMI equivalent strict" and "STEMI extended plus STEMI equivalent strict" curves, the performance improved considerably, notably by an increase in sensitivity.



Fig. 3. Diagnostic performance curves of the four cumulative STEMI groups: STEMI strict (red), STEMI strict + STEMI equivalent (green), STEMI equivalent + STEMI extended (blue), STEMI extended + STEMI equivalent extended (black). The curves were created, like in receiver operating characteristics, by plotting the true-positive rate (sensitivity) against the false-positive rate (1-specificity). Measurement positions of the ST deviations (time shifts with respect to the J point from -20 to +80 ms, in steps of 10 ms) were varied along the curves.

The results in Table 3 show that for any of the cumulative STEMI groups the maximal diagnostic accuracy (92–94%) was attained at the J+10 ms measurement instant and the highest diagnostic accuracy (94%) was attained for the most-extensive STEMI classification criterion: STEMI extended + STEMI equivalent extended.

Discussion

Our study describes how the performance of an STEMI detection algorithm varies when the ST deviations are measured at various distances in time with respect to the J point. The results can be summarized as follows: a) early measurements are not recommendable, because they have a very low specificity; b) a slight delay of 10 ms after the J point gives about the same sensitivity as a measurement at

the J point, but with a better specificity; c) longer delays (measurements in the ST segment or even in the T wave) give an even better sensitivity but at the cost of a remarkable decrease in specificity; d) the best diagnostic performance is attained with the most-comprehensive STEMI criterion: STEMI extended + STEMI equivalent extended. In clinical practice, this would mean that ST amplitudes should preferably be measured just after the J point, but not earlier or later.

In the past years, it was increasingly recognized that the original STEMI criteria (in this paper called "STEMI strict" criteria) are not completely covering the ECG manifestations seen with an occlusion of an epicardial artery that places a significant portion of the myocardium in jeopardy and can result in a poor outcome if not recognized and treated appropriately. An initial step to widen the STEMI strict criteria was the definition of the STEMI-equivalent criterion,

Table 3

Overview of the performance of the cumulative STEMI algorithms at the various measurement instants relative to the J point, expressed as sensitivity (sens, in %), specificity (spec, in %) and diagnostic accuracy (acc, in %).

Measurement instant relative to the J point (ms)	Cumulative STEMI groups											
	Strict			Strict + Equivalent		Equivalent + Extended			Extended + Equivalent extended			
	sens	spec	acc	sens	spec	acc	sens	spec	acc	sens	spec	acc
-20	67.9	55.7	60.3	88.7	4.5	36.2	92.5	3.4	36.9	100.0	1.1	38.3
-10	66.0	81.8	75.9	75.5	25.0	44.0	84.9	22.7	46.1	88.7	18.2	44.7
0	79.2	96.6	90.1	84.9	84.1	84.4	92.5	83.0	86.5	96.2	77.3	84.4
+10	83.0	96.6	91.5	88.7	93.2	91.5	92.5	93.2	92.9	94.3	93.2	93.6
+20	83.0	93.2	89.4	86.8	89.8	88.7	90.6	89.8	90.1	92.5	89.8	90.8
+30	84.9	83.0	83.7	88.7	79.5	83.0	94.3	79.5	85.1	96.2	79.5	85.8
+40	84.9	78.4	80.9	88.7	75.0	80.1	94.3	75.0	82.3	96.2	75.0	83.0
+50	88.7	76.1	80.9	92.5	73.9	80.9	94.3	73.9	81.6	96.2	73.9	82.3
+60	90.6	69.3	77.3	94.3	67.0	77.3	96.2	67.0	78.0	98.1	67.0	78.7
+70	90.6	65.9	75.2	92.5	64.8	75.2	98.1	64.8	77.3	100.0	64.8	78.0
+80	98.1	58.0	73.0	98.1	56.8	72.3	100.0	56.8	73.0	100.0	56.8	73.0

In each of the four cumulative STEMI groups, the highest diagnostic accuracy was attained at 10 ms after the J point.

Table 4 Distribution of the cases detected by the STEMI algorithms at the J+10 ms measurement instant, including information about the culprit artery location.

	Ν	LAD	LCX	RCA
Cases detected by "STEMI strict"	44	18	8	18
Additional cases detected by "STEMI equivalent"	3	0	0	3
Additional cases detected by "STEMI extended"	2	1	0	1
Additional cases detected by "STEMI equivalent extended"	1	0	1	0
Cases missed	3	1	0	2
Totals	53	20	9	24

consisting of depressions in leads V2 and V3 and seen with posterior ischemia [18]. More recently, several others of such ECG manifestations were described: in a recent review [19], five of these ECG patterns are discussed, among which are the De Winter sign [20], a new ECG sign of proximal LAD occlusion [20] and the Wellens syndrome [21]. Some authors have proposed to call all these patterns "STEMI equivalents". Here we have, analogous to a previous study by our group [12], restricted the use of the term "STEMI equivalent" to depressions in leads V2 and V3. Additionally, we have generalized the STEMI strict and STEMI equivalent patterns by extending them in all directions of the frontal and transverse planes (see Fig. 1, bottom of the right panel).

Most importantly, ischemia detection performance increased considerably when the most liberal STEMI detection algorithm was used, i.e., STEMI extended plus STEMI equivalent extended. This finding prompts a reconsideration of the current STEMI criteria. This implies that the direction of the ischemia-induced ST deviation is not relevant; instead, elevation as well as depression should be taken as signs of ischemia. All patients of the case group had an angiographically demonstrated completely occluded culprit artery and hence, in retrospect, deserved PCI as initial therapy. Obviously, our group of 53 patients with a completely occluded culprit artery cannot reflect all possible ECG manifestations seen with acute ischemia. E.g., ST depression when widely present in the ECG leads can be a manifestation of acute left main stenosis, and often has an unfavorable outcome [22,23]. Although we had no such patient in our study group, the STEMI extended + STEMI equivalent extended criteria should detect such a case.

Our study demonstrates that it is worthwhile to put effort into reliable determination of the J point, instead of quasi-solving the problem by measuring, *e.g.*, 40 ms after the J point. First, if the J point has not been established with sufficient accuracy, the timing of a measurement later in the ST segment will be equally inaccurate. Second, for delayed measurements, the diagnostic performance will be much lower, because of a considerable increase of false-positive results. This increase of false-positive detections is the logical consequence of ST-segment sloping that produces increased amplitudes the further the measurement is from the J point.

Another advantage of an accurate J point determination is that it decreases the risk connected with an erroneous early J-point setting. By definition, the global J point is the latest of the lead-dependent J points. When the latest lead-dependent J point is missed, the resulting global J point will be too early. Less careful or less precise J-point assessment implies the risk of a strong increase in false-positive STEMI detections that is already manifested when the J point is set 10 ms early (see Figs. 2 and 3, and Table 3).

Although we have not investigated this, it is likely that in routine clinical practice when 25 mm/s paper output is used, and the J point and ST amplitudes are manually determined/ measured, it is not possible to attain similar results as those in this study, in which computer-assisted ECG processing was utilized. Without the help of a superimposed display of all leads, or a synchronous marker in all leads, it is very difficult to determine the J point and to do the ECG amplitude measurements at that J point or at a given interval thereafter. Likely, in the near future, most ECGs will be processed and stored digitally. At this point in time, this is already available in multiple clinics and ambulances. When digital ECG processing is available, automated J-point identification and ST-deviation measurements are feasible. Ischemia detection criteria like the ones used in this study can then being implemented to assist the cardiologist's decision, then the cardiologist can concentrate on expert over-reading of the automatically determined J point.

Limitations

Principal limitations of our study are the selection of the cases and the controls. We selected case patients with complete occlusions, but it is known that part of the STEMI patients (about 30%) have incomplete occlusions before PCI [24]. Patients with incomplete occlusions may have different ECG manifestations of their ischemia, and have not been included in our study. Possibly, because of a bias toward the more serious cases, this had exaggerated our sensitivity results. The second principal limitation is to be found in the selection of the control patients. Ideally, control ECGs should be obtained under similar conditions (patients with chest pain at rest who have called the ambulance) but in whom it has convincingly been demonstrated that there was no ischemia at the time at which the triage ECG was made. We have no access to such a database. Instead we have taken non-ischemic ECGs of a mixed patient group as control data; in the light of this choice, we ignored the usual sex and age matching of the control and case group; indeed, the properties of the ST amplitudes in the control group are more determined by the gamut of pathology in this group than by age or sex. Notably, a considerable number of patients (24/88) in the control group, who presented with ST abnormalities (see Table 2) were potential candidates for false-positive ischemia detections. Should a more appropriate control group become available in the future, the current study could be redone and the results (i.e., specificity) would become more representative for the initial triage in ACS. If such a study yields similar results, adaptation of the guidelines regarding STEMI detection could be considered.

Conclusions

Our study suggests that: a) the optimal time instant to measure ST deviations is 10 ms after the J point, and b) the



Fig. 4. ECG examples of ST-deviation classifications at the J+10 ms measurement instant. Panel A: ECG of case #29 (male, 54 years, culprit artery LAD) showing a typical STEMI pattern (ST elevations in leads I, aVL, V1-V5) detected by the STEMI strict criterion. Panel B: ECG of case #6 (male, 80 year, culprit artery RCA), not compliant with the STEMI strict criterion, but manifesting an STEMI equivalent pattern (suprathreshold depressions in leads V2 and V3). Panel C: ECG of case #33 (male, 54 years, culprit artery LAD; nota bene: by chance this patient has the same sex, rounded age and culprit artery as case #29), not compliant with either the STEMI strict or the STEMI equivalent criteria, but showing an STEMI extended pattern (elevation in aVL and in the inverted lead III). Panel D: ECG of case #45 (male, 44 years, culprit artery LCX), not compliant with either the STEMI equivalent or STEMI extended criteria, but showing an STEMI equivalent extended pattern (depressions in leads V5 and V6). Panel E: ECG of case #27 (female, 81 years, culprit artery LAD), not compliant with any of the STEMI criteria because of subthreshold ST deviations, hence missed by the STEMI-detection algorithm (false negative).

most liberal STEMI algorithm, STEMI extended plus STEMI equivalent extended, yields the largest sensitivity without decreasing specificity. These findings should be corroborated by including a control group of patients with chest pain at rest, but with a negative diagnostic ACS workup.

Acknowledgement

We thank Dr. Nicolas Davidenko, University of California Santa Cruz, for critically reading our paper.

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