



Electrocardiographic Distinction of Left Circumflex and Right Coronary Artery Occlusion in Patients With Inferior Acute Myocardial Infarction

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Previously reported electrocardiographic (ECG) criteria to distinguish left circumflex (LCCA) and right coronary artery (RCA) occlusion in patients with acute inferior ST-segment elevation myocardial infarction (STEMI) afford a modest diagnostic accuracy. We aimed to develop a new algorithm overcoming limitations of previous studies. Clinical, ECG, and coronary angiographic data were analyzed in 230 nonselected patients with acute inferior STEMI who underwent primary percutaneous coronary intervention. A decision-tree analysis was used to develop a new ECG algorithm. The diagnostic accuracy of reported ECG criteria was reviewed. LCCA occlusion occurred in 111 cases and RCA in 119. We developed a 3-step algorithm that identified LCCA and RCA occlusion with a sensitivity of 77%, specificity of 86%, accuracy of 82%, and Youden index of 0.63. The area under the ROC curve was 0.85 and resulted 0.82 after a 10-fold cross validation. The key leads for LCCA occlusion were V3 (ST depression in V3/ST elevation in III >1.2) and V6 (ST elevation ≥ 0.1 mV or greater than III). The key leads for RCA occlusion were I and aVL (ST depression ≥ 0.1 mV). Fifteen of 21 reviewed studies had less than 20 cases of LCCA occlusion, only 48% performed primary percutaneous coronary intervention, and previous infarction or multivessel disease were often excluded. The diagnostic accuracy of reported ECG criteria decreased when applied to our study population. In conclusion, we report a simple and highly discriminative 3-step ECG algorithm to differentiate LCCA and RCA occlusion in an “all comers” population of patients with acute inferior STEMI. The diagnostic key ECG leads were V3 and V6 for LCCA and I and aVL for RCA occlusion. © 2019 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license. (<http://creativecommons.org/licenses/by-nc-nd/4.0/>) (Am J Cardiol 2019;123:1019–1025)

Inferior ST-segment elevation myocardial infarction (STEMI) can result from occlusion of either the left circumflex (LCCA) or the right (RCA) coronary arteries and this may determine the clinical and hemodynamic course. Patients with LCCA occlusion are prone to develop mitral valve regurgitation whereas patients with RCA occlusion may present with right ventricular infarction, bradyarrhythmia, and conduction disturbances.^{1,2} The electrocardiographic (ECG)

distinction between acute LCCA and RCA occlusion remains nowadays a challenge. A large number of studies have reported various ECG criteria to identify the occluded coronary artery.^{3–12} However many of these criteria were extracted from series of selected patients and often an early angiographic documentation of the site of occlusion was lacking.^{13–23} Moreover, the number of patients with LCCA occlusion in these series was small, and furthermore, the measurement of some reported ECG criteria was complex due to their polynomial nature.^{6,10} The aim of this study was to develop a new ECG algorithm to differentiate LCCA and RCA occlusion in a non-selected series of consecutive patients with acute inferior STEMI submitted to primary percutaneous coronary intervention (PPCI). In addition, we extensively reviewed the reported studies and we assessed the diagnostic accuracy of their ECG criteria in our “all comers” population.

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Methods

We conducted a single-center, retrospective, case-control study in patients with acute inferior STEMI. All consecutive patients admitted with LCCA occlusion

from June 2009 to June 2015 were compared with those admitted with RCA occlusion from October 2009 to December 2010. Both groups were identified through our institutional cath-lab registry. The inclusion criteria were: (1) acute myocardial infarction associated with ST-segment elevation of ≥ 0.1 mV in 2 inferior leads (II, III, and/or aVF), (2) referral to PPCI, and (3) index ECG recorded within the 12 hours from the onset of symptoms preceding the PPCI. To allow a better applicability of our algorithm to current clinical practice, we did not exclude patients with previous ischemic heart disease, myocardial infarction, left ventricular hypertrophy, right bundle branch block, or those with multivessel coronary disease. However, we excluded patients with previous coronary bypass graft surgery, left bundle branch block, and ventricular paced rhythm. The study complied with the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Ethics Committee of our institution.

The search of previous publications on ECG criteria for LCCA and RCA occlusion was performed through the Pubmed database using the following terminology (up to June 01, 2018): ("electrocardiogram"[tiab] OR "ECG"[-tiab]) AND ("inferior myocardial infarction"[tiab] OR ("right coronary artery"[tiab] AND "left circumflex"[tiab])). In addition, the reference lists of all selected papers were reviewed to identify missed studies.

We retrieved the following clinical variables from the hospital records: (1) demographic and previous clinical history including co-morbidities; (2) case-history on admission and in-hospital clinical course; and (3) laboratory blood test and echocardiography at admission.

The ECG recordings were coded for anonymity, digitized, and analyzed with electronic calipers (Cardio-Calipers software, Iconico) under appropriate magnification. All ECGs were interpreted by independent investigators blinded to the angiographic data. We evaluated the heart rhythm, heart rate, and the ST-segment deviation at 80 milliseconds after the J point in all leads. We chose this time point to allow a better comparison of our data with those of the previous studies. The TP segment was used as the isoelectric reference line.

Coronary angiographies were analyzed by independent observers who were blinded to the ECG data. The culprit coronary segments were identified by the presence of local intraluminal thrombus and/or by the absence of anterograde coronary blood flow. The location of the occlusion and the coronary branch distribution were determined according to the criteria of the American Heart Association.²⁴ We also analyzed the coronary dominance, the presence of coronary stenosis ($\geq 70\%$) in nonculprit vessels, and the existence of coronary collaterals.

Categorical variables were described by frequencies and percentages and statistical differences were analyzed using the χ^2 test or Fisher exact test when appropriate. The continuous variables were described either by the mean and standard deviation or by the median and interquartile range. The statistical differences in the continuous variables were analyzed using the Student's *t* test for independent samples in case of a normal distribution, or the Mann-Whitney test in case of a non-normal distribution. Sensitivity (Se), specificity (Sp), accuracy (Acc), and Youden index (YI) were

evaluated for each ECG criteria. We performed a decision-tree analysis to construct the new ECG diagnostic algorithm. The best algorithm (the one that maximizes the accuracy in fewer steps) was internally validated with the "cross-validation" method and a logistic regression with resampling validation bootstrapping (500 resamples). Commands "rpart" and "rms" of the R software version 3.3.2 (R Foundation for Statistical Computing) were used for the decision-tree analysis and the validation of the selected algorithm respectively. Thereafter, we conducted a logistic regression analysis to identify the clinical and angiographic variables associated with the algorithm's misclassification of the culprit occluded artery. A backward stepwise method was used to identify independent risk predictors with a $p < 0.05$ for the inclusion or deletion criteria. A p value < 0.05 was considered significant. All analyses were performed using SPSS (IBM SPSS Statistics for Windows, version 20.0) and R software (R Foundation for Statistical Computing, version 3.3.2).

Results

The study population included 230 patients. Occlusion of LCCA was present in 111 cases and that of RCA in 119. The location of the occluded segment in patients in the LCCA group was proximal in 30 cases (27%); distal in 50 (45%); and obtuse marginal in 31 (28%). The distribution of the occluded segment in patients in the RCA groups was proximal in 44 (37%); mid-distal in 69 (58%); posterior descending in 3 (2.5%); and posterolateral branch in 3 (2.5%).

As summarized in Table 1, patients allocated in both groups presented similar clinical and demographic profiles. Patients with LCCA occlusion were more likely to present grade II to IV mitral regurgitation at hospital discharge. Patients with RCA occlusion had lower systolic blood pressure at admission.

Figure 1 illustrates the mean values of the ST-segment deviation measured in all ECG leads in all patients and also shows typical ECG recordings of LCCA and RCA occlusion. As compared with RCA occlusion, patients with LCCA occlusion presented with: (1) Lesser ST-segment elevation in leads III and aVF, (2) a noticeable ST-segment elevation in leads V5 to V6, and (3) less marked reciprocal ST-segment depression in leads I and aVL, but more pronounced reciprocal changes in leads aVR, V1, and V3.

Table 2 summarizes the sensitivity, specificity, diagnostic accuracy, and Youden index of the previously reported 26 criteria and 3 algorithms³⁻²³ differentiating LCCA and RCA occlusion applied to our study population. Based on these data, the most accurate single criteria for LCCA occlusion were ST-segment elevation or isoelectric in lead I and ST-segment elevation in lead V6 \geq lead III. The best single criteria for RCA were ST-segment depression of ≥ 0.1 mV in leads I and aVL, and ST-segment depression of ≥ 0.05 mV in lead I. In addition, Table 2 also lists that in the 3 reported ECG algorithms,^{6,7,11} the most accurate performance was that of Fiol et al. The application of the published ECG criteria and algorithms to our series of patients was followed by a generalized loss of the diagnostic

Table 1

Clinical characteristics of the study population

Variable	Left circumflex coronary artery (n = 111)	Right coronary artery (n = 119)	p value
Men	91 (82%)	98 (82%)	0.94
Age (years), mean (SD)	61.3 (13.5)	62.8 (12.6)	0.41
BMI (kg/m^2), mean (SD)	28.2 (4.9)	27.1 (3.9)	0.07
Smoker	53 (48%)	70 (59%)	0.09
Hypertension*	55 (50%)	62 (52%)	0.70
Dyslipidemia†	60 (54%)	58 (49%)	0.42
Diabetes mellitus	28 (25%)	28 (23%)	0.77
Previous stroke	3 (3%)	3 (3%)	1.00
Peripheral artery disease	6 (5%)	13 (11%)	0.13
Previous myocardial infarction	14 (13%)	16 (13%)	0.85
Heart rate (bpm), mean (SD)	76.3 (18.8)	73.3 (22.7)	0.29
Systolic Blood Pressure (mm Hg), mean (SD)	140 (35)	128 (31)	0.01
Killip class >I	26 (23%)	20 (17%)	0.21
Hemoglobin (g/L), mean (SD)	139 (25.5)	137 (22.0)	0.26
Estimated filtration glomerular rate <60mL/min/1.73m ²	8 (7%)	6 (5%)	0.49
Left ventricular ejection fraction, median (IQR)	52 (14)	55 (11)	0.87
Mitral regurgitation (grade II-IV)	17 (17%)	9 (8%)	0.05
Onset of symptoms-to-PCI (min), median (IQR)	200 (185)	195 (136)	0.61
One-vessel coronary disease	66 (60%)	61 (51%)	0.21
Three-vessel coronary disease	12 (11%)	20 (17%)	0.19
Proximal occlusion	30 (27%)	44 (37%)	0.11
Stent diameter (mm), median (IQR)	3.0 (1.0)	3.0 (0.75)	0.07
In-hospital mortality	4 (4%)	10 (8%)	0.14

BMI = body mass index; bpm = beats per minute; IQR = interquartile range; LCCA = left circumflex coronary artery; n = number; PCI = percutaneous coronary intervention; RCA = right coronary artery; SD = standard deviation.

* Hypertension was defined as a history of diagnosed hypertension or taking antihypertensive medication.

† Dyslipidemia was defined as a history of diagnosed dyslipidemia or taking lipid-lowering medication.

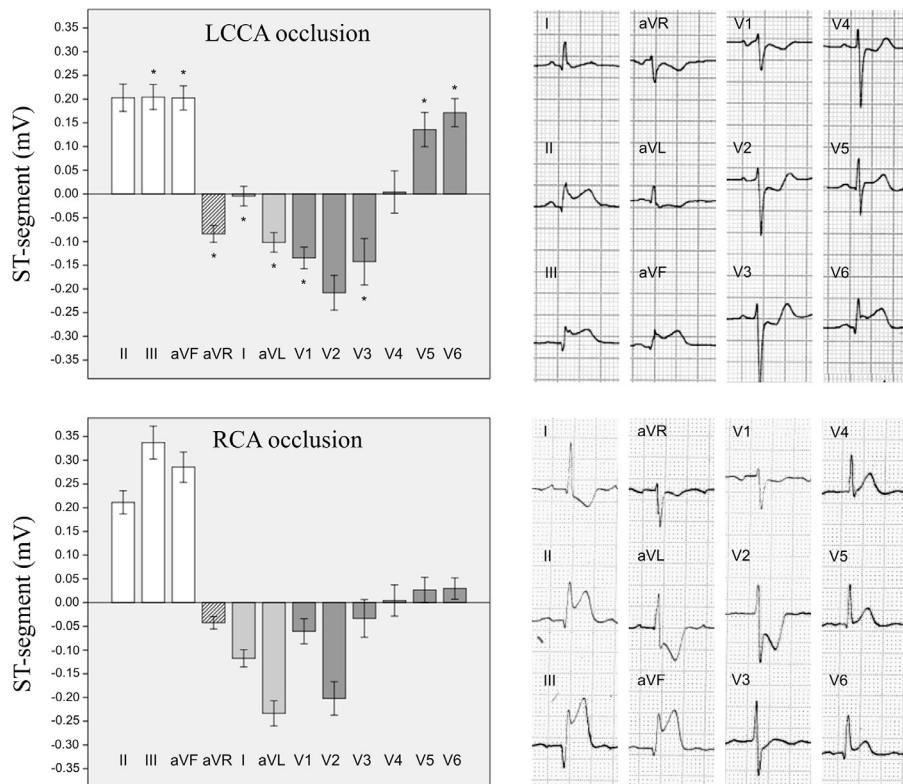


Figure 1. Electrocardiographic findings in 230 patients with acute inferior ST-segment elevation according to the culprit coronary artery.

The 2 panels on the left show graphically (bars) the mean (SE) values of the ST-segment potential in the 12 conventional leads of the patients with inferior ST-segment acute myocardial infarction due to left circumflex occlusion (above) or right coronary occlusion (below). The 2 12-lead ECG on the right correspond to representative cases of both groups. Asterisks indicate a $p < 0.05$ for the t-test comparison of the mean value of each ECG lead between the 2 groups. Abbreviations: (a) LCCA = left circumflex coronary artery; (b) RCA = right coronary artery.

Table 2

Diagnostic yielding of the previously reported ECG criteria for predicting the occluded artery in patients with acute inferior myocardial infarction applied to our study population

ECG criteria	Sensitivity	Specificity	Accuracy	Youden Index
For LCCA occlusion				
STE \geq 0.1 mV in lead I ²²	8%	98%	55%	0.06
STE \geq 0.05 mV in lead I ¹¹	23%	97%	61%	0.19
STE or isoelectric ST-segment in lead I ^{12,13,19,23}	90%	55%	72%	0.45
STE \geq 0.1 mV in leads I, aVL, V4, V5 or V6 ¹⁴	73%	53%	63%	0.26
STE \geq 0.1 mV in leads I, aVL, V5 or V6 ¹⁷	73%	59%	66%	0.32
STE III \leq V6 ⁹	45%	98%	72%	0.43
STE \geq 0.1 mV in V5 ²³	59%	69%	64%	0.28
STE \geq 0.1 mV in V6 ²³	70%	70%	70%	0.40
STE \geq 0.05 mV in lead V5 or V6 ¹³	87%	42%	63%	0.28
STE \geq 0.1 mV in leads V5 and V6 + STE in III \leq V6 ⁹	37%	98%	69%	0.36
STD \geq 0.05 mV in aVR ^{15,23}	66%	60%	63%	0.25
STD \geq 0.1 mV in aVR ^{8,22}	41%	79%	61%	0.20
STD in aVR \geq aVL ⁷	46%	92%	69%	0.37
STD \geq 0.1 mV in V1 ^{17,19}	53%	75%	64%	0.28
STD \geq 0.1 mV in leads V1 or V2 ¹⁹	81%	27%	53%	0.08
STD \geq 0.1 mV in leads V1 and V2 ^{5,22}	55%	71%	63%	0.26
STD / STE ratio: V3 / III $>$ 1.2 ^{3,5,8,10}	35%	95%	66%	0.30
\sum ST-segment in V1-V3 / \sum ST-segment II, III, aVF $>$ 1 ⁶	41%	92%	67%	0.33
ST-segment II-V3/III+V1+I $>$ 1.5 ¹⁰	68%	84%	76%	0.52
For RCA occlusion				
STE in III $>$ II ^{4-6,11,17,18,21-23}	92%	46%	70%	0.38
STD \geq 0.1 mV in lead I ^{8,16,21,23}	55%	90%	72%	0.45
STD \geq 0.05 mV in lead I ^{6,12,19}	81%	65%	73%	0.46
STD \geq 0.1 mV in lead aVL ^{16,18}	89%	51%	70%	0.40
STD \geq 0.1 mV in leads I and aVL ^{5,14,16}	55%	91%	72%	0.46
STD in aVL $>$ I ^{11,12,18}	92%	11%	53%	0.03
STD in V1 $>$ V2 ²³	85%	22%	54%	0.06
Sequential ECG algorithms for LCCA occlusion				
Fiol ⁶	53%	93%	74%	0.47
Tierala ⁷	53%	87%	70%	0.39
Huang ¹¹	44%	92%	69%	0.37

LCCA = left circumflex coronary artery; RCA = right coronary artery; STD = ST-segment depression; STE = ST-segment elevation.

accuracy as compared with that originally reported (Table 3 and Supplementary Table).

Figure 2 shows the new ECG algorithm to differentiate LCCA and RCA occlusion in our series of patients with inferior STEMI using the tree-decision analysis. The algorithm has 3 steps: (1) ST-segment depression \geq 0.1 mV in leads I and aVL; (2) ST-segment elevation \geq 0.1 mV in V6 or greater than III; and (3) ratio ST-segment depression in V3/ST elevation in III $>$ 1.2. This new algorithm afforded a Se of 77%, Sp of 86%, Acc of 82%, and a YI of 0.63 with an area under the curve of 0.85. Of notice, after the 10-fold cross-validation, the area under the curve remained in 0.82. The independent predictors of misclassification of the culprit artery of our algorithm were age (odds ratio [OR] 1.04, 95% confidence interval [CI] 1.01 to 1.07), previous myocardial infarction (OR 2.82, 95% CI 1.7 to 7.09), and left coronary dominance (OR 9.72, 95% CI 3.78 to 26.13).

Discussion

We report a new ECG algorithm to differentiate LCCA and RCA occlusion in patients with acute inferior STEMI. The strength of our algorithm is based on: (1) the inclusion of the largest series of patients with LCCA, (2) the

proximity of our population to the real-life clinical practice since we included patients with previous myocardial infarction, left ventricular hypertrophy, right bundle branch block, or multivessel coronary disease, and (3) the availability in all cases of a coronary angiographic study performed within a median of 200 minutes from the onset of symptoms. Additionally, we extensively reviewed the diagnostic ECG criteria published in the literature and evaluated their diagnostic accuracy when applied to an “all comers” population like that of our study.

Acute occlusion of either the LCCA or RCA can induce ST-segment elevation in leads II, III, and/or aVF, but the distinct anatomic distribution of these 2 coronary arteries and the different spatial location of the perfused myocardial regions will predictively entail specific ECG changes.²⁵ It has been reported that the cardiac ST-segment injury vector is more directed to the left and posteriorly in LCCA occlusion and to the right and downward in RCA occlusion.²⁵ Consistent with this description we found that patients with LCCA occlusion presented lesser ST-segment elevation in leads III and aVF and smaller reciprocal ST-segment depression in leads I and aVL than patients with RCA occlusion. In the precordial plane, the LCCA occlusion induced greater ST-segment elevation in leads V5 to V6

Table 3
Previous studies differentiating acute left circumflex and right coronary artery occlusion in patients with acute inferior ST-segment elevation myocardial infarction submitted to primary percutaneous coronary intervention

Publication	No. patients					Proposed differential diagnostic ECG criteria	Reported diagnostic yielding of the ECG criteria		Diagnostic yielding of the reported ECG criteria applied to our study population		
	LCCA	RCA	Previous infarction	Multivessel disease	ECG analysis		Se	Sp	Se	Sp	Accuracy
Kosuge, 1998 ³	19	133	Excluded	Included	Blinded	STD / STE ratio: $ V3 / III >1.2$	58%	86%	35%	95%	66%
Zimetbaum 1998 ⁴	17	52	Included	Included	Unblinded	STE in lead III > lead II [†]	73%	100%	92%	46%	70%
Baptista 2004 ⁵	15	38	Excluded	LCCA+RCA	Unblinded	STD \geq 0.1mV in I and aVL [†]	76%	67%	55%	91%	72%
						STE in lead III > lead II [†]	89%	40%	92%	46%	70%
				inferior MI		STD / STE ratio: $ V3 / III >1.2$	40%	97%	35%	95%	66%
						STD \geq 0.1mV in leads V1 and V2	60%	87%	55%	71%	63%
Fiol 2004 ⁶	13	50	Excluded	Excluded	Blinded	3-step algorithm including \sum estimates	77%*	100%*	53%	93%	74%
Tierala 2009 ⁷	19	79	Included	Included	Blinded	3-step algorithm	64%	96%	53%	87%	70%
Kanei 2010 ⁸	19	86	Excluded	Included	Blinded	STD / STE ratio: $ V3 / III >1.2$	21%	98%	35%	95%	66%
				LCCA+RCA		STD \geq 0.1mV in lead aVR	53%	86%	41%	79%	61%
						STE in lead III > lead II [†]	94%	58%	92%	46%	70%
				inferior MI		STD \geq 0.1 mV in lead I [†]	86%	63%	55%	90%	72%
Kosuge 2012 ⁹	51	306	Excluded	Included	Blinded	STE \geq 0.1mV in V5 and V6 + STE in III \leq V6	Not reported		37%	98%	69%
Jim 2012 ¹⁰	14	64	Excluded	Excluded	Blinded	ST-segment $ II-V3/III+V1+I >1.5$	79%	94%	68%	84%	76%
				LCCA+RCA		STE in lead II \geq lead III [†]	57%	100%	47%	90%	70%
						STD / STE ratio: $ V3 / III >1.2$	43%	95%	35%	95%	66%
Huang 2016 ¹¹	28	166	Excluded	Included	Blinded	3-step algorithm	89%	100%	44%	92%	69%
Li 2017 ¹²	63	177	Excluded	Excluded	Blinded	STE or isoelectric ST-segment in lead I	97%	73%	90	55%	72%
				inferior MI		STE in lead II \geq lead III [†]	94%	66%	47%	90%	70%
						STD in lead I $>$ aVL [†]	89%	94%	11%	92%	53%

LCCA = left circumflex coronary artery; MI = myocardial infarction; RCA = right coronary artery; Se = sensitivity; Sp = specificity; STD = ST-segment depression; STE = ST-segment elevation.

* Not reported, calculated through the available data in the manuscript.

[†] Criteria for RCA occlusion.

ST-segment elevation in inferior ECG leads

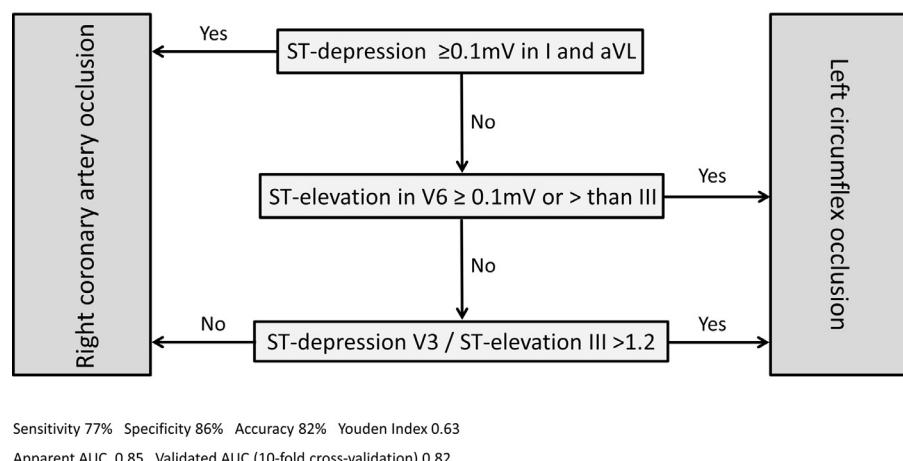


Figure 2. New ECG algorithm for the differential diagnosis of the culprit artery in patients with acute inferior myocardial infarction. Representation of the 3 steps (central panels) and diagnostic decisions (arrows) derived from the result of each ECG criteria.

and deeper ST-segment depression in leads V1 to V3. The decision-tree analysis of our data afforded a 3-step algorithm that identified LCCA and RCA occlusion with a sensitivity of 77%, specificity of 86%, accuracy of 82%, a Youden index of 0.63, and an area under the ROC curve of 0.85. Interestingly, this algorithm highlights the contribution of precordial leads V3 and V6 to identify LCCA occlusion and leads I and aVL to recognize RCA occlusion.

During the last 30 years, a large number of studies have reported ECG criteria to differentiate LCCA and RCA occlusion in patients with inferior STEMI,^{3–23} but the results of these investigations are often heterogeneous and sometimes inconsistent from study to study. Circumstances accounting for this discrepancy may be: (1) the scarce number of patients in the LCCA occlusion group since 15 of 21 (71%) reported studies included less than 20 cases, (2) a reliable angiographic identification of the occluded artery in the context of PPCI was only available in 10 (48%) of the reviewed studies, and (3) conditions that are prevalent in patients with STEMI (i.e., previous myocardial infarction, extended coronary disease, or left ventricular hypertrophy) are often considered as exclusion criteria. Our study contained the largest LCCA series and included 13% of patients with previous infarction and 45% with multivessel disease. Thus, the clinical profile of our patients is close to the daily practice and, interestingly, the diagnostic accuracy of the previously published ECG criteria decreased when was applied to our study population (data summarized in Table 3 and Supplementary Table). In agreement with this observation, an analysis of 266 patients from the DANAMI-2 trial revealed that left coronary dominance, distal occlusions, and multivessel disease were independent predictors of electrocardiographic misidentification of the occluded artery.²⁶ In our study aging was also a misclassification factor, perhaps related to a more frequent extensive coronary disease, left ventricular hypertrophy, and intraventricular conduction disturbances.

The ischemic time elapsed until recording the index ECG will influence the potential accuracy of the ECG

criteria to identify the occluded coronary vessel. Indeed, all criteria are based on the behavior of ST-segment changes (both elevation and depression) and it is well established that the magnitude of the ST-segment deviation induced by a permanent coronary occlusion decreases over time²⁷ due to an increase of the electrical resistance inside the ischemic myocardial region.²⁸ Therefore, the diagnostic yield of our algorithm will likely decrease when applied to patients submitted to PPCI beyond a mean of 200 minutes from the onset of symptoms.

The methodology to measure the ST-segment deviation varies among the studies in the field of electrocardiography. Clinical guidelines recommend measuring the ST-segment at the J point,²⁹ but the studies reviewed in this manuscript measured the ST-segment 60 to 80 milliseconds after the J point. Thus, to allow a better comparison of our data with the previous reports, we measured the ST-segment at 80 milliseconds from the J point. In addition, we performed a duplicate ST-segment sampling at 0 milliseconds and at 80 milliseconds from the J point in the group of patients with LCCA to evaluate to which extent a measure taken at 0 or at 80 milliseconds will affect the results. As illustrated in the Supplementary Figure, both measurements showed a similar trend of ST-segment changes, although their magnitude was higher at 80 milliseconds of the J point. Thus, the ST-segment cut-off values of a given ECG criteria would require a correction for the timing to the J point.

Although the internal validation indicates that our algorithm is robust, a prospective external validation in a cohort of patients with inferior myocardial infarction might be warranted.

Supplementary materials

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.amjcard.2018.12.026>.

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