Lateral MI Explains the Presence of Prominent R Wave ($R \geq S$) in V_1

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Aims: It is necessary to clarify if the presence of a prominent R wave in V_1 , in post-myocardial infarction (MI) patients, is due to the involvement of the posterior wall (currently inferobasal segment) or the lateral wall (as has been demonstrated recently by electrocardiographic contrast-enhanced cardiac magnetic resonance [ECG-CE-CMR] correlations studies).

Methods: In 155 patients with inferolateral zone MI, as detected by CE-CMR, the following ECG parameters were evaluated and correlated with MI location according to CE-CMR: R/S ratio in $V_1 \geq 1$ (classic criteria for posterior MI), R/S ratio in $V_1 \geq 0.5$, and R in $V_1 \geq 3$ mm.

Results: R/S ≥ 1 criterion: Present in 20 cases: 3 of lateral MI, 17 of inferolateral MI, 0 of inferior MI. Absent in 135 cases, 81 of lateral/inferolateral MI (28/53), 54 of inferior MI (SE 19.8%, SP 100%). R/S ≥ 0.5 criterion: Present in 47 cases: 6 of lateral MI, 39 of inferolateral MI, 2 of inferior MI. Absent in 108 cases, 56 of lateral/inferolateral MI (25/31), 52 of inferior MI (SE 44.6%, SP 96.4%). R ≥ 3 mm criterion: Present in 30 cases: 5 of IM lateral, 23 of inferolateral MI, 2 of inferior MI. Absent in 125 cases, 73 lateral/inferolateral MI (26/47), 52 inferior MI (SE 27.7%, SP 96.4%).

Conclusions: The presence of prominent the R wave in V_1 is due to the lateral MI and not to the involvement of inferobasal segment of inferior wall (old posterior wall).

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In 1964, Perloff¹ reported that the $R/S \geq 1$ pattern in V_1 in post myocardial infarction (MI) patients was a diagnostic criterion for MI located in the posterior wall, an area that according to this author corresponds to the basal part of the inferior wall that bends upward in a cranial direction. This terminology² has persisted, despite pathologic³ evidence that the prominent R wave in V_1 is due to MI in the lateral, not the posterior wall.

In recent years, contrast enhancement cardiac magnetic resonance (CE-CMR) has been shown to

provide a highly accurate diagnosis of myocardial infarction, even in the setting of non-Q wave MI.^{4–10} As a result, a number of different groups^{11–17} has been able to compare ECG findings with CE-CMR to demonstrate the fallacy of the dogma that a prominent R wave in V_1 is due to posterior MI. Instead, it has become evident that MI located predominantly between the two papillary muscles in the left ventricular (LV) lateral free wall—secondary to occlusion of the left circumflex (LCX) coronary artery—is the origin of

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Figure 1. Schematic representation of the heart inside the thorax in oblique position. The necrosis vector produced by inferobasal MI (previously named posterior MI) (right) is directed toward V₃–V₄, while the necrosis vector generated by lateral MI (left) is directed toward V₁.

the prominent R wave in V₁ because the necrosis vector faces V₁ (Fig. 1). This ECG criterion is very specific but relatively insensitive for the detection of lateral wall MI especially because infarction in this zone preferentially involves the basal lateral wall, which is often electrocardiographically silent (e.g., often is not reflected in a mirror equivalent of the Q wave, which would be an R wave in V₁).^{18,19}

Moreover, the ECG investigations with CE-CMR have demonstrated that MI involving the inferobasal region (segment 4 in the standard myocardial 17 segment model) does not give rise to a prominent R wave in V₁. Although contrary to the original Perloff report,¹ it has been demonstrated that a prominent R wave in V₁ is not present in isolated inferior MI, even in rare cases in which the basal portion of this wall bends upward in a superior direction away from the rest of the inferior wall. As a possible explanation of this finding, CMR images of individuals in whom the basal portion of the inferior wall does not lie on the diaphragm and hence could potentially form the “posterior” wall, have shown instead that the direction of the longitudinal axis of the heart in the transaxial plane is oriented obliquely in a lateral direction rather than posteroanteriorly. Consequently, in all cases of infarction of the basal inferior wall that will give rise to a necrosis vector it will faces V₃–V₄, rather than V₁.^{9,12} (Fig. 1).

Despite these studies,^{11–17} expert panels involved in writing scientific guidelines appear unconvinced^{20,21} and have suggested that additional studies are necessary before this alternative interpretation is accepted. Accordingly, the goal of the present study was to validate the findings of prior reports from the Barcelona,¹⁴ Pisa,¹⁵ and Maastricht¹⁶ groups in the largest ECG-CMR

investigation to date, involving 26 centers in Europe, the United States, and South America.

METHODS

Study Population

Patients were enrolled in an international, multicenter, double-blinded, randomized trial²² between 2003 and 2004. In this study, 566 patients with a first-time MI were studied in 26 centers around the world (13 in the United States, 8 in Europe, and 5 in South America) (Fig. 2). The protocol was approved by the institutional review board at each center. Written informed consent was obtained from all patients.

The inclusion criteria consisted of clinical stability, age over 18 years, first-time MI, and coronary angiography identifying the infarct-related artery (IRA). Patients with prior revascularization, multivessel coronary artery disease, end-stage renal disease, and those with magnetic resonance imaging (MRI) contraindications were excluded.

Patients were classified as acute (≤ 16 days post-MI; $n = 282$) or chronic MI (17 days to 6 months post-MI; $n = 284$) depending on the elapsed time between hospital admission and CMR imaging. Patient characteristics are shown in Table 1.

Of the patients initially enrolled, those who were identified as having inferolateral involvement on CE-MRI (inferior, lateral, or inferolateral MI) were selected for the present study (details below). Patients with ECGs presenting with confounding diagnoses such as bundle branch block, ventricular preexcitation, and ventricular hypertrophy were excluded.

CE-CMR Performance and Analysis

Standard delayed CE-CMR was performed before contrast (control) and at 10 and 30 minutes after gadoversetamide administration at doses of 0.05, 0.1, 0.2, or 0.3 mmol/kg body weight. Participating centers used commercially available scanners (1.5 T) and sequences from all major US/European vendors (12 from Siemens [Malvern, PA, USA], 6 from General Electric [Milwaukee, WI, USA], and 8 from Philips [Andover, MA, USA]). A segmented inversion-recovery gradient-echo sequence was used. Short-axis views were obtained every 10 mm throughout the entire LV myocardium. Two- and four-chamber long-axis views also were obtained. Slice thickness was 6

Figure 2. Flow diagram of the methodology implemented in the study. Five hundred sixty-six patients were included in an international, multicenter, double-blinded, randomized trial.²² Those who presented inferolateral involvement were evaluated. The variables $R/S > 1$, $R/S > 0.5$, and $R > 0.3$ mV were studied in the cases of inferior, lateral, and inferolateral MI and in cases of isolated inferior MI.

Table 1. Study Population Characteristics

Characteristic	Acute MI (282)	Chronic MI (284)
Age $\pm$ SD, y	54.0 $\pm$ 11.4	53.6 $\pm$ 11.3
Male gender, n (%)	215 (76)	218 (77)
Risk factors, n (%)		
Diabetes mellitus	51 (18)	45 (16)
Hypertension	130 (46)	149 (52)
Cigarette smoker	93 (33)	103 (36)
Hypercholesterolemia	162 (57)	178 (63)

mm; typical in-plane resolution was 1.9×1.4 mm. The inversion time was adjusted to null normal myocardium for each acquisition.

CE-CMR images were scored at a core laboratory for the presence and location of infarction blinded to patient identity and any associated clinical information using the standard 17-segment model.²³ The x-ray coronary angiograms were analyzed for the perfusion territory of the IRA also using the 17-segment model at a separate core facility blinded to patient identity and to the CMR findings. The location of infarction by CE-CMR was validated on the basis of a match with the x-ray coronary angiogram data.²²

For the purpose of the current investigation, only scans performed 10 minutes postcontrast administration, and showing a "match" in MI

location with the IRA perfusion territory by x-ray coronary angiography, were included in the study. First, MI location was categorized into four groups (Fig. 3):

- (1) "Lateral MI" involving the lateral wall (segments 5,6,11,12, and 16);
- (2) "Inferior MI" involving the inferior wall (segments 4,10,15) and the inferior part of the septal wall (segments 3 and 9);
- (3) "Inferolateral MI" involving segments of both walls;
- (4) No inferolateral involvement.

Due to the small number of isolated lateral MI cases, we decided to combine the lateral and

Figure 3. The standard model of 17 myocardial segments of the left ventricle adapted from Cerqueira et al.²³

inferolateral groups and compare with isolated inferior MI group.

Then, patients were further classified into those with lateral/inferolateral involvement or those with exclusively inferior involvement.

ECG Analysis

Twelve-lead ECGs were performed at the time of CMR. Two independent cardiologists with expertise in ECG interpretation analyzed the ECG records blinded to CE-CMR results. The measurements were made with the aid of a magnifying glass. Intra- and interobserver variability, assessed by the intraclass correlation coefficient, was higher than 0.95. The following variables were measured in lead V₁ to the nearest 0.5-mm amplitude and 20-ms duration.

We applied the classical criteria for posterior MI (R/S ratio > 1)¹⁶ and new criteria proposed by Bayés de Luna et al.¹⁴: R-wave amplitude > 3 mm, R/S ratio > 0.5 in the two groups: the lateral/inferolateral group and the isolated inferior MI group.

Statistical Analysis

Diagnostic accuracy of the different criteria was assessed by calculating different indicators: sensitivity, specificity, and positive and negative predictive values. The 95% confidence intervals

of all these indicators were calculated using confidence interval analysis for Windows software (CIA for Windows v 2.1.2, Southampton, United Kingdom).

RESULTS

From the total of 566 patients enrolled in the original gadoversetamide, multicenter investigation,²² 155 patients demonstrated infarction involving the lateral, inferior, or inferolateral zone by CE-MRI. Of these 155, we found inferolateral involvement (lateral or inferolateral) in 101 patients, and isolated inferior involvement in 54 patients. Figures 5, 6, and 7 show typical examples of lateral, inferolateral, and inferior MI, respectively.

R/S ratio ≥ 1 (Classic Criteria for Posterior MI)

This criterion was present in 20 of the 155 patients. All patients with this criterion had lateral or inferolateral infarction (see Fig. 4A) and none had an isolated inferior MI (sensitivity = 19.8; specificity = 100; positive predictive value [PPV] = 100%; negative predictive value [NPV] = 40).

R Wave ≥ 3 mm

This criterion was present in 30 of the 155 patients. Twenty-eight with this criterion had lateral or inferolateral infarction (see Fig. 4B) and two had an isolated inferior MI (sensitivity = 27.7%; specificity = 96.3%; PPV = 93.3%; NPV = 41.6%).

R/S Ratio ≥ 0.5

This criterion was present in 47 of the 155 patients. Forty-five with this criterion had lateral or inferolateral infarction (see Fig. 4C) and two had an isolated inferior MI (sensitivity = 44.6%; specificity = 96.3%; PPV = 95.7%; NPV = 48.1%).

DISCUSSION

The study of Perloff¹ was based on 20 cases of MI in the posterior wall diagnosed by vectorcardiography criteria and only four cases had anatomopathologic verification. It should be noted that the author himself expressed some doubt about the location of MI and its placement in the posterior

Figure 4. Results of different variables evaluated with sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). (A) R/S > 1 criterion, (B) R/S < 0.5 criterion; and (C) R > 0.3 mV criterion.

wall: "it is recognized that the anatomic names given to the areas of infarction do not necessarily indicate the region of the heart that has been infarcted." He goes on to state, "this dorsal or infra-atrial position of the left ventricle represents an area that is most likely oriented posteriorly in the living subject."

Nevertheless, despite this uncertainty, these criteria have been used for decades as a gold standard in the diagnosis of posterior MI.

In as early as 1956, Dunn³ used pathological correlations to demonstrate that the R wave in

V₁ should be attributed to lateral rather than posterior infarctions. In addition, modern imaging techniques using radionuclide imaging,²⁴ and CE-CMR by the Bayés de Luna group,¹⁴ demonstrated that the location of infarction that gives rise to a tall R wave in V₁ is lateral and not posterior (currently also known as the inferobasal region). Other recent studies¹⁵⁻¹⁷ corroborate these results, yet in the majority of guidelines and textbooks that make reference to electrocardiographic localization of MI according to the presence of a Q wave or

Figure 5. Example of lateral MI. CE-CMR (above): left, short-axis view showing lateral involvement (bright myocardium, arrow); right, long-axis view showing that the inferior wall is not involved. ECG (below) with R/S > 1 in V₁.

Figure 6. Example of inferolateral MI. CE-CMR (above): left, short-axis view showing inferolateral involvement (bright myocardium, arrow); right, chamber view showing lateral involvement (bright myocardium, arrow). ECG (below) with pathological Q wave inferior leads and R/S > 1 in V₁.

its equivalent, Perloff's findings remain unfettered nearly 50 years later, despite all the limitations described above.

In hindsight, Perloff's initial study appears to have three important misconceptions: (1) the long axis of the left ventricle was considered to be

Figure 7. Example of isolated inferior MI. CE-CMR (above): left, short-axis view showing inferior involvement (bright myocardium, arrow); right, long-axis view showing the inferior basal involvement (bright myocardium, arrow). ECG (below) with pathological Q waves in inferior leads. Note the rS morphology in V₁ despite the inferobasal wall (previously named posterior wall) involvement.

located in a completely posteroanterior direction (in reality it points in a leftward oblique direction), (2) the inferobasal segment of the left ventricle, what Perloff described as the true posterior wall, was assumed to bend upward in a superior direction away from the rest of the inferior wall (in fact this occurs only in $\approx 20\%$ of the population²⁵), and (3) the inferobasal segment was thought to depolarize early (in reality it depolarizes ≈ 40 ms after the onset of heart activation). Since a Q wave starts with the beginning of the QRS complex, a Q wave—or its mirror image, an R wave in V₁—cannot be generated by the lack of activation of the basal inferior segment that occurs late after the beginning of the QRS.

In the current study, we confirm that a prominent R wave in V₁ ($R \geq S$) is due to lateral MI, as previously suggested.^{14–17} However, it is important to note that the sample size was far larger, and the population was based on a multicenter, international enrollment in comparison with previous investigations that were single-center cohorts.

Identifying the location of MI in the lateral rather than the inferior wall has more than just academic value. Properly localizing the MI may help risk stratify whether certain complications

of acute MI are more likely. For example, mitral regurgitation and atrioventricular block occur more frequently in the setting of inferior MI. In addition, it has been demonstrated recently that the risk of malignant ventricular arrhythmia, in the absence of residual ischemia, is higher after inferior MI than anterolateral MI.²⁶ This may be due to regional differences in the concentration of vagal receptors and the protective effect of the vagal response.

CONCLUSIONS

- The criterion R/S in V₁ ≥ 1 is nearly 100% specific for the diagnosis of lateral MI, although sensitivity is low.
- The criteria R/S ≥ 0.5 and R ≥ 3 mm in V₁ are more sensitive for the diagnosis of lateral infarction without significant modifications in specificity.
- The prominent R wave in V₁ according to the outlined criteria (including the classic criteria of posterior infarction) is due to involvement of the lateral wall and not the basal part of inferior wall including segment 4 (posterior wall). This confirms four prior reports, but in a multicenter, international investigation.
- Scientific societies should now have enough evidence to replace outdated interpretations of the electrocardiogram, and its localization of posterior MI.

LIMITATIONS

The exposed results are limited to patients with first MI, no prior revascularization and without any ECG confounders. The accuracy of these findings should be further tested in "real-world" consecutive patients.

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