Image-Based Criteria to Identify the Presence of Epicardial arrhythmogenic Substrate in Patients with Transmural Myocardial Infarction

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ABSTRACT

Background: Patients with transmural myocardial infarction (MI) who undergo endocardial-only substrate ablation are at an increased risk of ventricular tachycardia (VT) recurrence. Late gadolinium-enhanced cardiac magnetic resonance (LGE-CMR) could be used to assess infarct transmurality (IT). However, the degree of IT associated to epicardial arrhythmogenic substrate (AS) has not been determined.

Objective: To determine the degree of IT observed in LGE-CMR and multi-detector computed tomography (MDCT) that predicts the presence of epicardial AS.

Methods: The study included 38 post-myocardial infarction (PMI) patients. Ten patients with a subendocardial infarction underwent endocardial-only mapping and 28 with a "classical transmural MI" (C-TMI), defined as hyperenhancement >75% of myocardial wall thickness (WT), underwent an endo-epicardial mapping. LGE-CMR/MDCT data were registered to high-density endocardial or epicardial maps to be analyzed with respect to the presence of AS.

Results: Of 28 PMI patients with a C-TMI, 18 had epicardial AS (64%) and 10 (36%) did not. An epicardial scar area ≥14 cm² in LGE-CMR identified patients with epicardial AS (sensitivity and specificity of 1). The mean WT in the epicardial scar area in these patients was lower than in patients without epicardial AS (3.14 ± 1.16 mm vs 5.54 ± 1.78 mm; p=0.008). A cut-off value of mean WT ≤3.59 mm identified patients with epicardial AS (sensitivity of 0.91 and specificity of 0.93).

Conclusion: An epicardial scar area ≥14 cm² in the LGE-CMR and a mean CT-WT ≤3.59 mm predict epicardial AS in PMI patients and can be used as criteria to perform an endo-epicardial approach.

Key words: Infarct transmurality, substrate ablation, cardiac magnetic resonance, cardiac computed tomography.

INTRODUCTION

Substrate ablation is an effective treatment for patients that suffer from scar-related ventricular tachycardia (VT) [1]. However, a VT recurrence rate up to 47% has been reported after endocardial-only ablation in large patient population studies [2], which could be related to the presence of arrhythmic substrate (AS) on the epicardium. Recent studies have shown that incomplete AS elimination (i.e., Electrograms with delayed components (E-DCs) not possible to eliminate) was an independent predictor of VT recurrence or sudden cardiac death after substrate ablation [3, 4] and that epicardial access and ablation was also associated to a reduced probability of recurrences [3]. In order to identify and eliminate epicardial AS, a systematic endo-epicardial approach has been proposed in PMI patients [5]. Although this strategy reduced VT recurrences, up to 67% of the patients did not show epicardial AS during epicardial mapping [5]. Therefore, criteria to better identify patients requiring epicardial approach are still needed.

Imaging techniques such as late gadolinium-enhanced cardiac magnetic resonance (LGE-CMR) or multi-detector computed tomography (MDCT) have been shown to be useful in identifying AS prior to VT substrate ablation procedures [3, 6, 7]. Acosta et al. [8] recently reported that complete accessibility to VT substrate, guided by classical cardiac imaging criteria, is associated with better outcomes after VT substrate ablation in PMI patients. Therefore, infarct transmurality (IT) assessed by cardiac imaging could support the appropriate selection of patients that will benefit from a first-line combined endo-epicardial approach. However, the degree of IT observed in imaging techniques that is associated to the presence of epicardial AS has not been fully determined and the classical definition of transmurality may not accurately predict its presence. This could result in an unacceptably high rate of patients undergoing an endo-epicardial access despite not having epicardial AS –reportedly, about 30% (based on LGE-CMR classical transmurality criteria) [8].

The objective of the present study was to determine the minimum scar area in the epicardial layer of post-processed LGE-CMR which is associated with the presence of epicardial AS. In addition, the myocardial wall thickness (WT) associated with the presence of epi-AS was analyzed.

METHODS

Study population

This was a retrospective study in a series of consecutive patients that underwent VT substrate ablation in our institution and that met inclusion criteria. All the substrate ablation procedures were performed after our institution implemented a combined endo-epicardial access for mapping and ablation in cases of transmural infarction [7, 8]. Inclusion criteria were: 1) History of PMI, 2) History of sustained monomorphic ventricular tachycardia (SMVT) or appropriate implantable cardioverter defibrillator shocks, and 3) Cardiac imaging study (LGE-CMR and/or MDCT) obtained before the ablation procedure. The endocardial vs endo-epicardial substrate ablation approach was determined by scar distribution, based in classical transmurality criteria, as previously described [7, 8]. Briefly, in patients with a classical transmural infarction (C-TMI) based on LGE-CMR, a combined endo-epicardial approach was performed (N=28), whereas those with a subendocardial myocardial infarction (MI) underwent an endocardial-only substrate ablation (n=10). The C-TMI definition (hyperenhancement involving ≥ 75% of wall thickness) was used to interpret the LGE-CMR: [9]. Transmurality also was considered in the presence of a MDCT wall thickness < 5mm [10]. When both LGE-CMR and MDCT were available, the VT substrate ablation decision was based on the LGE-CMR information.

Electro-anatomical mapping (EAM) and VT ablation

All patients underwent VT substrate ablation using the "scar dechanneling" technique [3, 11]. Briefly, each E-DC was dichotomously classified as a conducting channel (CC) inner point or a CC entrance, depending on the delayed component precocity. Radiofrequency (RF) was delivered at the CC entrances as previously described [3, 11], using a Navistar catheter (Biosense Webster, Marlton, NJ) controlled by a temperature limit of 45 ºC and a power limit of 40-50 W. The catheter irrigation rate during RF application was 26 mL/min in the endocardium and 17-26 mL/min in the epicardium. During epicardial ablation, coronary arteries were localized by introducing MDCT/LGE-CMR data into the navigation system and their fusion with the EAM; the phrenic nerve course was identified by means of high-output epicardial pacing. A post-ablation remap was always performed to document the elimination of all CC-electrograms and to eliminate the remaining E-DCs by back-up RF applications. Residual inducible VTs after scar dechanneling, if any, were then targeted for ablation. VT isthmus and exit sites were defined by entrainment mapping if the VT was tolerated and by pace mapping if not tolerated.

LGE-CMR acquisition and segmentation

In all patients, a pre-procedural LGE-CMR study was performed in a 3T scanner (Magnetom Trio™-Tim®, Siemens, Erlangen, Germany). Contrast-enhanced images were acquired 10 minutes after bolus injection of 0.2 mmol/kg Gadobutrol (Gadoyist®, Bayer Hispania, Barcelona, Spain) using a commercially available, free-breathing, ECG-gated, navigator-gated, 3D inversion-recovery, gradient-echo technique. Slice thickness was 1.4 mm, with no gap between slices. The field of view was set at 360 mm and matrix size was kept to 256x256 pixels in order to yield an isotropic spatial resolution of 1.4x1.4x1.4 mm.

LGE-CMR images were analyzed using a previously described technique [12]. The 3D left ventricle (LV) was segmented from the whole image volume using ADAS-VT™ software (Galgo Medical, Barcelona, Spain). The LV was automatically divided into 10 layers from the endo- to epicardium, each one representing 10% of the total LV wall thickness (layer 10 and layer 90 for the endocardium and epicardium, respectively). Pixel signal intensity was projected to each layer following a trilinear interpolation algorithm. Myocardial tissue was classified into core zone (CZ), border zone (BZ), and healthy tissue using 60% and 40% of the maximum intensity signal of the scar as thresholds [13]. Finally, different scar areas (core and border zone) were automatically quantified on each myocardial layer.

MDCT acquisition and segmentation

In 25 of the 38 patients, a preprocedural MDCT ECG-gated study was performed on a 128x2-slice computed tomography (CT) scanner (Somatom Definition Flash, Siemens Healthcare, Erlangen, Germany). Images were acquired during an inspiratory breath-hold using retrospective ECG-gaiting technique with tube current modulation set between 50% and 100% of the cardiac cycle. CT angiographic images were acquired during the injection of a 100 mL bolus of Iopromide 370 mg I/mL (Ultravist, Bayer Hispania, Barcelona, Spain) at a rate of 3 mL/s.

MDCT images were retrospectively analyzed using ADAS-VT™ software. The endo- and epicardial surfaces of the LV were segmented using an algorithm based on initial alignment of a cardiac model, followed by manual corrections. The myocardial WT was computed at each point of the segmented endocardial surface as the distance between each point of the endo- and epicardial surfaces of the model.

Integration of LGE-CMR and MDCT data

As LGE-CMR, MDCT, and EAM images from the same patient differ in terms of spatial resolution, contrast, noise, and geometry, integration of multimodal data requires

a standardized system of reference where all the information is mapped. We recently proposed [14] a quasi-conformal mapping technique to fuse information from multiple cardiac imaging modalities into a common reference system, based on a 2D bull's eye plot representation of the LV. The most epicardial layer of the LGE-CMR was used as a 3D reference surface for integrating information on scar tissue characterization from LGE-CMR, WT, voltage and E-DCs. Figure 1 depicts the integration pipeline for LGE-CMR and MDCT.

On the integrated data, the total scar and CZ areas on the epicardial layer were measured and analyzed with respect to the presence of epicardial AS. In addition, the mean WT in areas with epicardial scar (layer 90%) was measured and analyzed with respect to the presence or absence of epicardial AS.

An easy method of computing the mean WT in the MDCT was used. The distance between the endocardial and epicardial surfaces in the area of maximum wall thinning was manually measured ten different times by one expert observer (Figure S1). The mean WT is estimated as the mean of the acquired distances.

Statistical analysis and study groups

Continuous variables are presented as mean value ± standard deviation. Categorical variables are presented as total number and percentages. Populations were compared by the Wilcoxon-Mann-Whitney or Fisher exact test, as appropriate. A p-value ≤ 0.05 was considered for statistical significance. Statistics were obtained using the Matlab statistics toolbox (Matlab R2010a, The Mathworks, Inc., Natick, MA, USA).

RESULTS

The study included 38 PMI patients referred for VT substrate ablation (Table 1). Patient data were analyzed according to the C-TMI definition and subsequent procedural approach (Figure 2), showing that 28 PMI patients (73.68 %) had a C-TMI and underwent a combined endo-epicardial approach. Of them, 18 patients (64.28%) had epicardial AS and 10 patients (35.71%) did not. Ten of the participants (26.32%) had a subendocardial scar and underwent an endocardial substrate ablation approach.

The mean number of acquired points used to build the EAM was 458.79 ± 233.84 on the endocardium and 636.52 ± 305.39 on the epicardium, with an anatomical fill threshold <10 mm in normal voltage tissue and < 8 mm within the scar area (<1.5mV). There were no statistically significant differences in the scar location between transmural and subendocardial infarction patients (Table 1).

LGE-CMR scar area associated with arrhythmogenic substrate

In order to determine the amount of epicardial scar area associated with the presence of epicardial AS, patients with a C-TMI with and without epicardial AS were analyzed. In all cases, AS was found at the endocardium. However, epicardial AS was only found in 18 (64%) patients. The mean scar and CZ areas at each layer are shown in Figure 3. There was a wider mean endocardial scar area in patients with epicardial AS, compared to those without (46.43 ± 14.01 cm^2 vs 26.74 ± 9.45 cm^2, respectively; p = 0.0005), as well as a significantly wider scar area in the 90% epicardial layer (27.14 ± 12.48 cm^2 vs 8.88 ± 4.84 cm^2, respectively; p = 0.0002). There were significant differences in the scar area between patients with and without epicardial AS in all layers (p = 0.0005 at 10%), as illustrated in Figure 3.1A. A scar area ≥ 14 cm^2 in layer 90 was associated with the presence of epicardial AS (Figure 3.1B). This cut-off value correctly identified patients requiring epicardial ablation with sensitivity and specificity of 1. The sensitivity and specificity of the optimal cut-off values per layer are specified in Table 2.

There was a wider mean endocardial CZ area in patients with epicardial AS, compared to those without AS (21.37 ± 10.89 cm^2 vs. 12.93 ± 7.15 cm^2; respectively; p = 0.037). Patients with epicardial AS had wider epicardial CZ (6.74 ± 5.87 cm^2 vs. 0.99 ± 1.27 cm^2; respectively; p = 0.0054). A CZ area ≥ 2.63 cm^2 on the 90% layer identified patients with epicardial AS with a sensitivity = 0.64 and specificity = 0.93. See Table 2 for details on the sensitivity and specificity per layer.

Myocardial wall thickness associated with transmural infarction

Myocardial WT was measured in patients in whom MDCT scan data were available (n=25). In the analysis of LGE-CMR data, 10 of them had subendocaridal scar and 15 had C-TMI. Endocardial AS was found in all of the patients. However, epicardial AS was found in 11 (73.33%) patients with C-TMI. All the patients had at least one point with myocardial wall thickness < 5mm.

The mean WT in areas with hyperenhancement reaching the epicardium, and therefore with epicardial scar on the 90% shell in the LGE-CMR, was 3.14 ± 1.16 mm in patients with epicardial AS vs 5.54 ± 1.78 mm in patients without; p = 0.008. A 3.59 mm mean WT classified PMI patients with and without epicardial AS, with a sensitivity of 0.91 and specificity of 0.93. Figure 4.1 depicts the mean WT within each group and the ROC curve showing the optimal cut-off value that classified patients with and without epicardial AS.

Using 10 random samples from the zone of maximum wall thinning to estimate the mean WT allowed classification of patients with epicardial AS with a sensitivity of 0.87

and specificity of 0.87. The sensitivity and specificity values of the estimated mean with different numbers of samples acquired are specified in Table S1.

Multimodal integration

Of the 25 patients with both LGE-CMR and MDCT imaging techniques, 2 (8%) were misclassified using the proposed cut-off value for the mean WT on MDCT. However, the use of the epicardial scar area cut-off (14 cm^2) on LGE-CMR correctly classified them. On the other hand, the mean WT value on epicardial scar area can be used to clarify the presence of epicardial AS (Figure S2). This shows the value of a multimodal integration for identifying PMI with epicardial AS. Two PMI cases showing the multimodal integration result are shown in Figure 5 (one with and one without epicardial AS); the cut-off values correctly identified the presence or absence of epicardial AS in both cases.

DISCUSSION

The present study identified the optimal IT and WT cut-off values from LGE-CMR and MDCT, respectively, for selection of endocardial or a combined endo-epicardial ablation approach in PMI patients. In the case of LGE-CMR, the presence of scar tissue reaching the epicardial surface does not guarantee the presence of epicardial AS; a minimum epicardial scar area of 14 cm^2 on LGE-CMR is needed to detect patients requiring epicardial ablation. In the case of MDCT, myocardial WT permits estimation of the degree of transmurality on LGE-CMR and accurate identification of patients with epicardial AS (those with a mean WT <3.59 mm).

Identification of epi-AS by LGE-CMR

Previous studies [5] have proposed that a systematic combined endo-epicardial approach reduces VT recurrences after RF ablation in PMI patients. However, up to 67% of patients did not show epicardial AS, suggesting that this approach could result in more complex procedures with no clinical benefit in a substantial proportion of patients [15]. A recent study found that pre-procedure imaging techniques can be used to assess IT and decide when to perform a combined endo-epicardial approach in PMI patients [8]. However, 12.5% of patients selected for endo-epicardial approach using previous definitions of infarct transmurality [9, 10] did not have epicardial AS (30% in patients with a C-TMI based on LGE-CMR criteria). Therefore, more rigorous criteria to define the degree of IT in PMI patients that is associated to the presence of AS in the epicardium are needed for both LGE-CMR and MDCT.

To date, there is no consensus definition of transmural MI based on LGE-CMR, which produces epicardial AS. In the study by Alexandre et al. [9], IT was defined as the presence of hyperenhancement involving ≥ 75% of WT. Recent studies [7, 12] have related the presence of epicardial VT isthmus with epicardial scar. Therefore, defining transmurality as the presence of hyperenhancement ≥ 75% of wall thickness may not be optimal to determine when to perform an epicardial approach. In the present study, 28 PMI patients with C-TMI based on imaging criteria [9] who underwent a combined endo-epi ablation strategy were analyzed. Epicardial AS was found to be absent in 35% of them, which indicates that the previously used criterion (hyperenhancement > 75%) does not guarantee the presence of epicardial AS. This is consistent with a previous study by our group that showed a trend towards less epicardial AS in patients with C-TMI criteria according to LGE-CMR, compared to those patients meeting IT criteria according to MDCT or echocardiogram [8]. These data suggest that more rigorous transmurality criteria for LGE-CMR are required for deciding to perform an epicardial approach. Even the presence of an epicardial scar with an area ≤ 14 cm² identified patients without epicardial AS in the present study.

Epicardial AS was correlated with a higher CZ area in all layers (from endo- to epicardial). However, we did not find a CZ cut-off value for identifying all patients with epicardial AS. Nonetheless, the use of epicardial CZ area to identify PMI patients with epicardial AS had high specificity (0.93) but low sensitivity, which suggests that it should be analyzed together with the epicardial scar area. The scar area was larger in the endocardium than in the epicardium, showing a pyramidal scar distribution in PMI patients, in concordance with previous studies [16]. This could explain how previous studies have related endocardial scar extension with VT recurrences after complete endocardial substrate ablation [17]. However, in our patient population, although the scar area in the endocardial layers was significantly smaller in patients without epicardial AS, there was no optimal cut-off on the endocardial layer to identify patients with epicardial AS (Table 2). Therefore, the extension of the endocardial scar cannot be used to predict the presence of epicardial AS. On the other hand, an epicardial scar area on the LGE-CMR ≥ 14 cm² correctly identified all the patients with epicardial AS.

WT as a criterion for the identification of epi-AS

Ischemic cardiomyopathy induces a loss of cells due to interstitial remodeling on scarred areas, which is reflected as a myocardial wall thinning [18]. MDCT can be used to evaluate LV WT. Myocardial wall thinning has been defined as LV WT <5 mm and

severe wall thinning as < 2 mm [10]. Wall thinning was related with low voltage areas providing a good correlation between endocardial AS and areas with WT <5 mm but found epicardial AS in only 62% of the cases [19]. A recent study [20] has shown that areas of WT < 2 mm identify the presence of epicardial AS in PMI patients with a high sensitivity (0.89) and specificity (1). However, these studies did not use multimodal imaging analysis, i.e. scar area and WT from LGE-CMR and MDCT, respectively. In the present study, we reported the mean WT associated with the presence of epicardial AS in PMI patients. A significant reduction in mean myocardial WT (3.14±1.16 mm) was observed in areas with C-TMI compared with non-transmural infarction patients (5.54±1.78 mm). The cut-off value of 3.59 mm identified patients that could benefit from combined endo-/epicardial ablation (sensitivity 0.91, specificity 0.93). Only 1 patient with >3.59 mm mean WT had epicardial AS and was therefore misclassified based on MDCT images. Nonetheless, this patient had an epicardial scar area of 16.02 cm^2, thus being a good candidate for an endo-/epicardial approach. Combination of complementary information such as myocardial scar distribution in the LGE-CMR and WT analysis in the MDCT could help in some specific cases with borderline values.

All the patients analyzed in this study (with and without epicardial AS) had at least one measurement of WT < 5mm, showing that a simple measurement performed on the MDCT cannot be used to determine the IT. Instead we propose to use the mean WT to classify patients with epicardial AS. However, computing the mean WT using MDCT is not straightforward because it requires specific software. In order to overcome this limitation, we recommend performing a set of 10 different measures directly on the MDCT scan to approximate the mean WT. With the use of 10 random samples at the maximum thinning of the LV, the estimated mean presents a high sensitivity (0.87) and specificity (0.87).

Limitations

The main limitation of the present study is that the proposed cut-off values have been obtained retrospectively in a relatively small number of PMI patients. Prospective studies involving a larger patient population would be needed to confirm the accuracy of the proposed values. The WT measured in the MDCT has been provided as a mean±SD in the location that corresponded to the epicardial scar area in the LGE-CMR of patients with epicardial AS. However, due to the existence of WT variability in this infarct area; it can be recommended to perform a set of measurements to estimate the mean WT in the infarcted area (see example in supplementary material).

CONCLUSION

In PMI patients, the presence of scarred tissue reaching the epicardium identified with LGE-CMR does not guarantee the existence of epicardial AS. An epicardial scar area ≥ 14 cm^2 and/or a CT-WT ≤ 3.59 mm accurately predict the presence of epicardial AS in PMI patients with a high sensitivity and specificity and can be used as criteria to perform a combined endo-/epicardial approach.

DISCLOSURES

None

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Table 1. Baseline clinical characteristics of classical transmural myocardial infarction (C-TMI) with epicardial arrhythmogenic substrate (AS), C-TMI with no epicardial AS and subendocardial myocardial infarction (MI).

	C-TMI with AS (n = 18)	**C-TMI without AS** (n = 10)	**Subendocardial MI** (n = 10)	**P value**
Age, yrs	66.17 ± 11.10	68.20 ± 4.89	73.80 ± 8.51	0.122
Hypertension	13 (72.2%)	10 (100%)	6 (60%)	0.093
LVEF, %	33.06 ± 6.85	31.67 ± 9.72	36.50 ± 12.74	0.519
Time from MI, yrs	17.00 ±6.78	15.25 ±6.27	22.57 ± 8.48	0.143
Scar localization - **Anterior** - **Inferior** - **Lateral**	 - 10(55.5%) - 7(38.88%) - 1(5.55%)	 - 4(40%) - 5(50%) - 1(10%)	 - 3 (30%) - 6 (60%) - 1 (10%)	0.373

LVEF, left ventricular ejection fraction

Table 2. Optimal cut-off values (threshold, sensitivity and specificity) for scar and core zone area per layer.

Layer	Scar area			Core zone area		
	Threshold (cm^2)	**Se**	**Sp**	**Threshold (cm^2)**	**Se**	**Sp**
10%	37.29	0.64	0.93	16.79	0.54	0.8
20%	36.57	0.64	0.93	18.87	0.56	0.92
30%	35.63	0.64	0.93	19.03	0.62	1
40%	35.24	0.62	1	16.44	0.60	0.92
50%	29.78	0.72	0.88	15.28	0.60	0.92
60%	28.8	0.69	0.93	7.4	0.67	0.87
70%	20.7	0.82	0.94	6	0.60	0.92
80%	18.32	0.82	0.94	4.72	0.67	1
90%	14	1	1	2.63	0.64	0.93

Figure 1. Pipeline for multimodal integration (top row, late gadolinium-enhanced cardiac magnetic resonance [LGE-CMR]; bottom row, multi-detector computed tomography [MDCT]): 1) Image segmentation; 2) Left ventricle tissue characterization (based on the percentage of maximum pixel signal intensity [MPI]; see text) and wall thickness (WT) measured in millimeters [mm]; 3) The LV surfaces are mapped on a 2D bull's eye plot (BEP) for integrating LGE-CMR epicardial layer with MDCT myocardial WT; 4) 3D integration of multimodal data showing a sub-endocardial inferior infarction not associated to a significant myocardial wall thinning. Top row: LGE-CMR pixel signal intensity (PSI) classification as core zone (PSI > 60% of the maximum pixel intensity) in red, border zone (40% < PSI < 60% of MPI) in green and healthy tissue (PSI < 40% of MPI) in purple. Bottom row: MDCT WT color-coding.

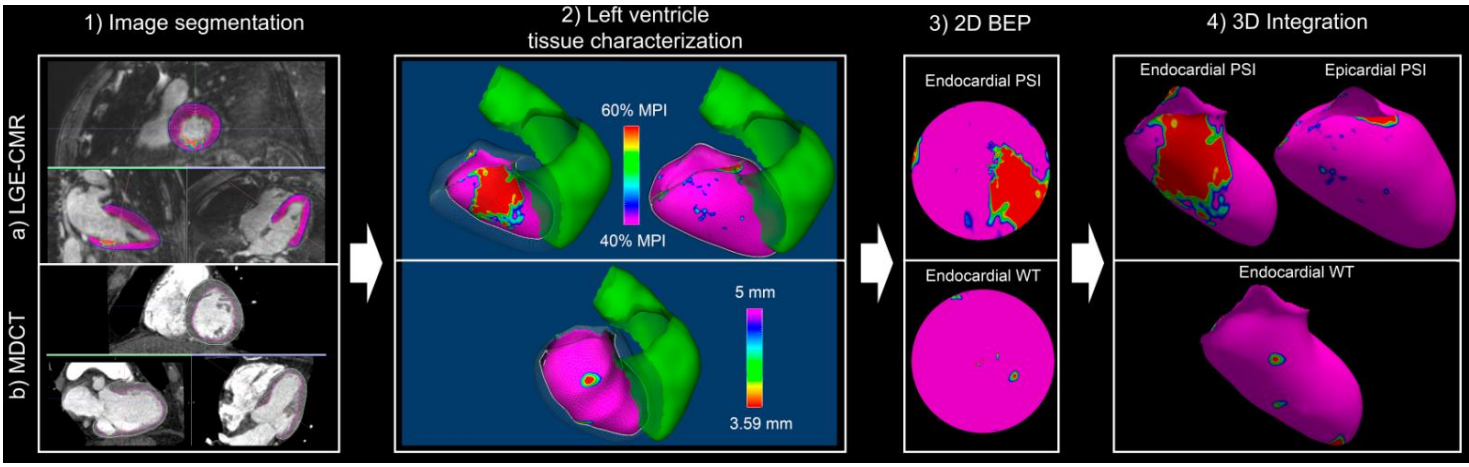


Figure 2. Classification of all post-myocardial infarction patients (n = 38) into groups based on infarct transmurality and procedural approach. All patients underwent late gadolinium-enhanced cardiac magnetic resonance (LGE-CMR). Eighteen patients had a classical transmural scar (defined by LGE-CMR criteria) and a combined endo-epicardial approach with epicardial arrhythmogenic substrate (AS). Seven patients had a transmural scar and a combined endo-epicardial approach but without epicardial AS. Finally, 10 patients had subendocardial scar and only endocardial approach.

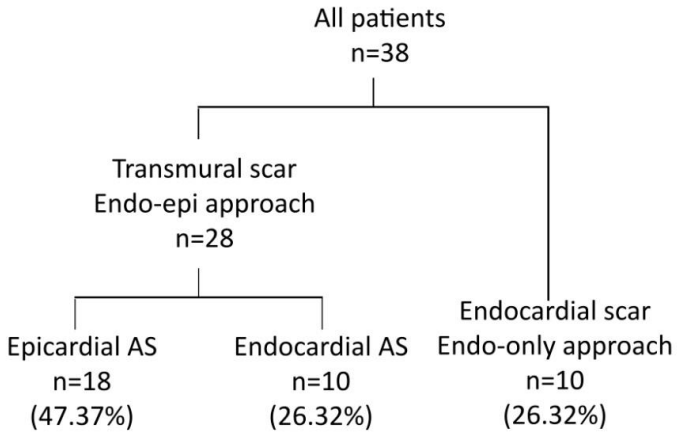


Figure 3. A.) Mean scar (1) and core zone (2) areas of all post-myocardial infarction patients with a classical transmural myocardial infarction, based on late gadolinium-enhanced cardiac magnetic resonance, distributed per layer (Layer 10 and Layer 90 for endocardium and epicardium, respectively) for patients with (dark) and without (light) epicardial arrhythmogenic substrate (AS). B.) Scar and core zone areas on the epicardial layer (90%) for all patients, classified according to the presence or absence of epicardial AS. The horizontal line represents the optimal threshold separating both groups.

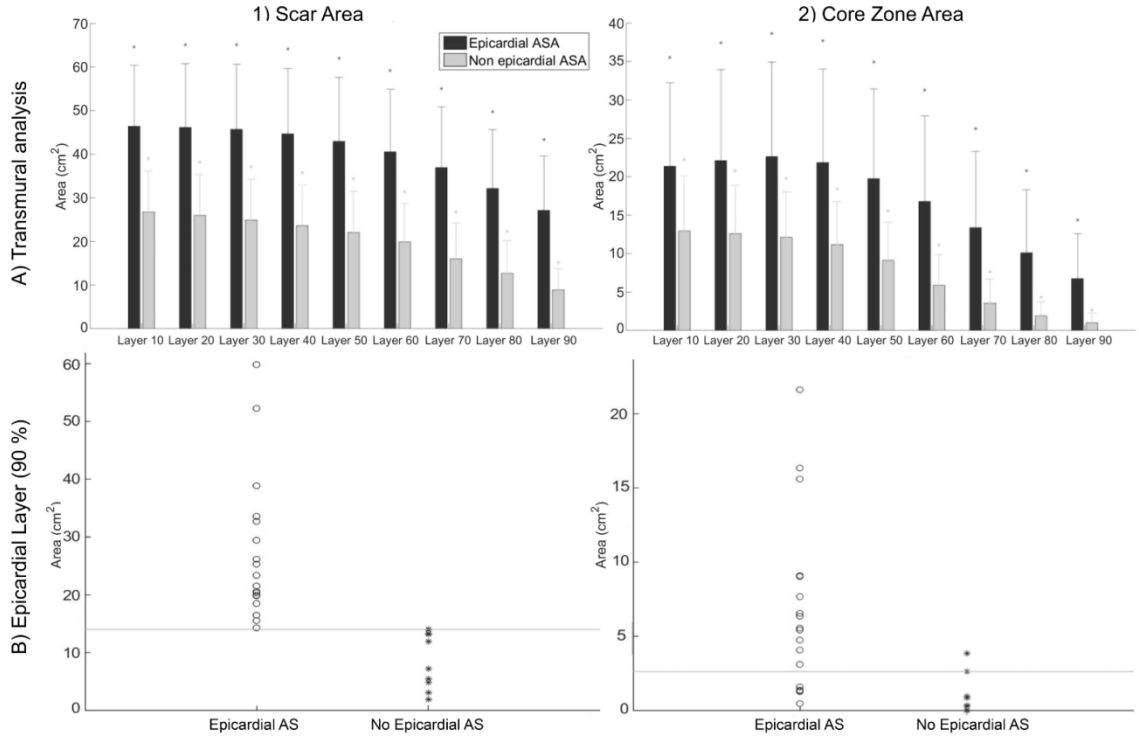


Figure 4. A) Mean myocardial wall thickness (WT) on epicardial scar areas in all post-myocardial infarction (PMI) patients, grouped as follows: i) PMI patients with epicardial arrhythmogenic substrate (AS) and ii) PMI patients without epicardial AS. The horizontal line represents the optimal WT cut-off for classifying PMI patients according to the presence or absence of epicardial AS. B) ROC curve, with sensitivity (Se), specificity (Sp), and area under the curve (AUC) of the optimal cut-off value (3.59 mm) for classifying PMI patients according to the presence or absence of epicardial AS.

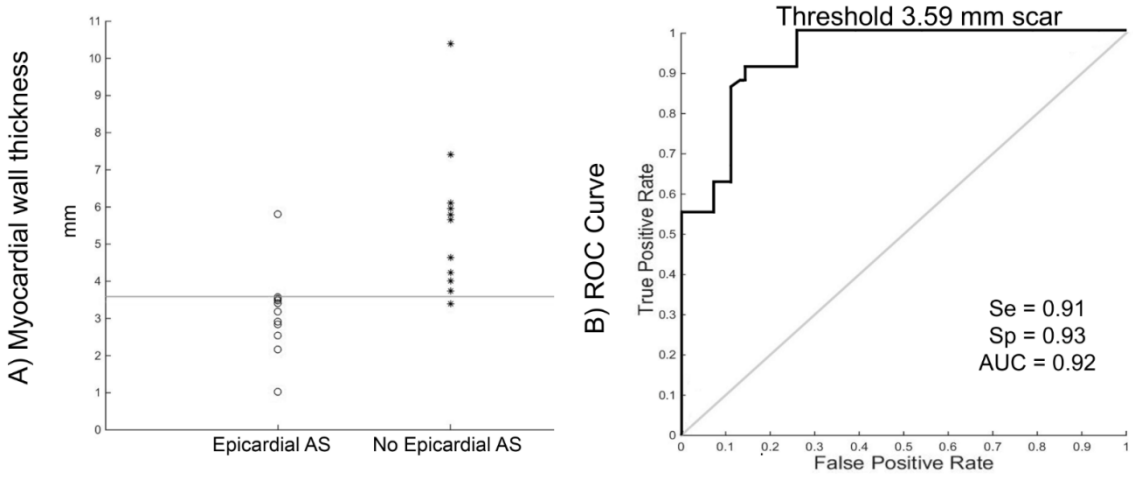
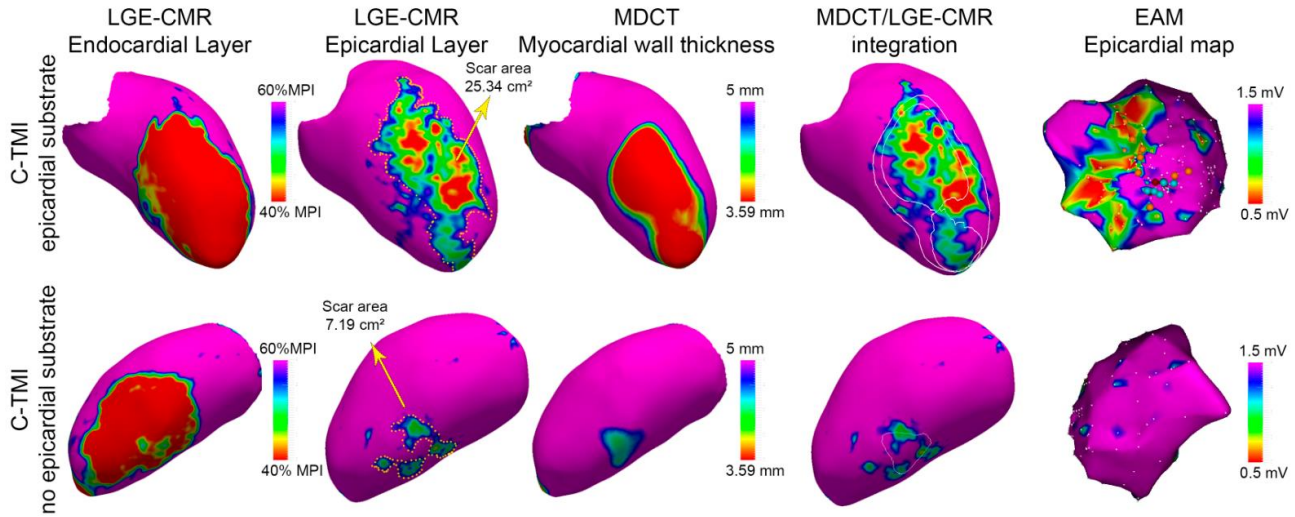


Figure 5. Multimodal integration of late gadolinium-enhanced cardiac magnetic resonance (LGE-CMR), multi-detector computed tomography (MDCT), and electroanatomical mapping data (EAM) showing two PMI patients with a classical transmural infarction (C-TMI) defined by LGE-CMR which had and not epicardial arrhythmogenic substrate (top and bottom rows, respectively). Scar configuration in the endocardial and epicardial layers, obtained from LGE-CMR, is shown in the two left columns (healthy tissue, border zone and core zone in purple, green and red, respectively). Myocardial wall thickness (WT) extracted from MDCT images are mapped onto the epicardial LGE-CMR geometry. Regions with WT < 3.59 mm are colored in red, WT > 5mm in purple, and 3.59 mm < WT <5 mm in green. The EAM (right column) shows the scar identified from standard voltage values (0.5 and 1.5 mV); electrograms with delayed-components are represented as blue dots.



SUPPLEMENTARY MATERIAL

We proposed an easy method for estimating the mean wall thickness (WT) on the multi-detector computed tomography (MDCT). All the patients had at least one point < 5mm, so selecting a sparse measurement of the myocardial wall thickness could misclassify a patient, as shown in Figure S1. In both cases shown, one with epicardial arrhythmogenic substrate and another without, at least one point with WT < 2mm can be found (top row). However, measuring the distance between the endocardial and epicardial surfaces of the ventricle in the area of maximum wall thinning provided a good approximation of the mean WT. We also show the automatically computed WT distribution on the epicardial scar area (bottom row). The patient with epicardial AS has less variability (lower SD) than the one without AS and the mean WT is < 3.59mm. We also provide the sensitivity and specificity of performing different numbers of measurements (from 1 to 10) for estimating the WT (Table S1). Greater sensitivity and specificity is achieved with 10 different measurements.

Figure S1. Easy method for estimating the myocardial wall thickness on MDCT. Two first rows: Two MDCT short axis slices with several wall thickness measurements; Last row: Myocardial wall thickness distribution in all the points within the epicardial scar (green line represents the proposed cut-off value, black lines represent the mean ±SD for each case). 1) One PMI patient without epicardial AS. 2) One PMI patient with epicardial AS.

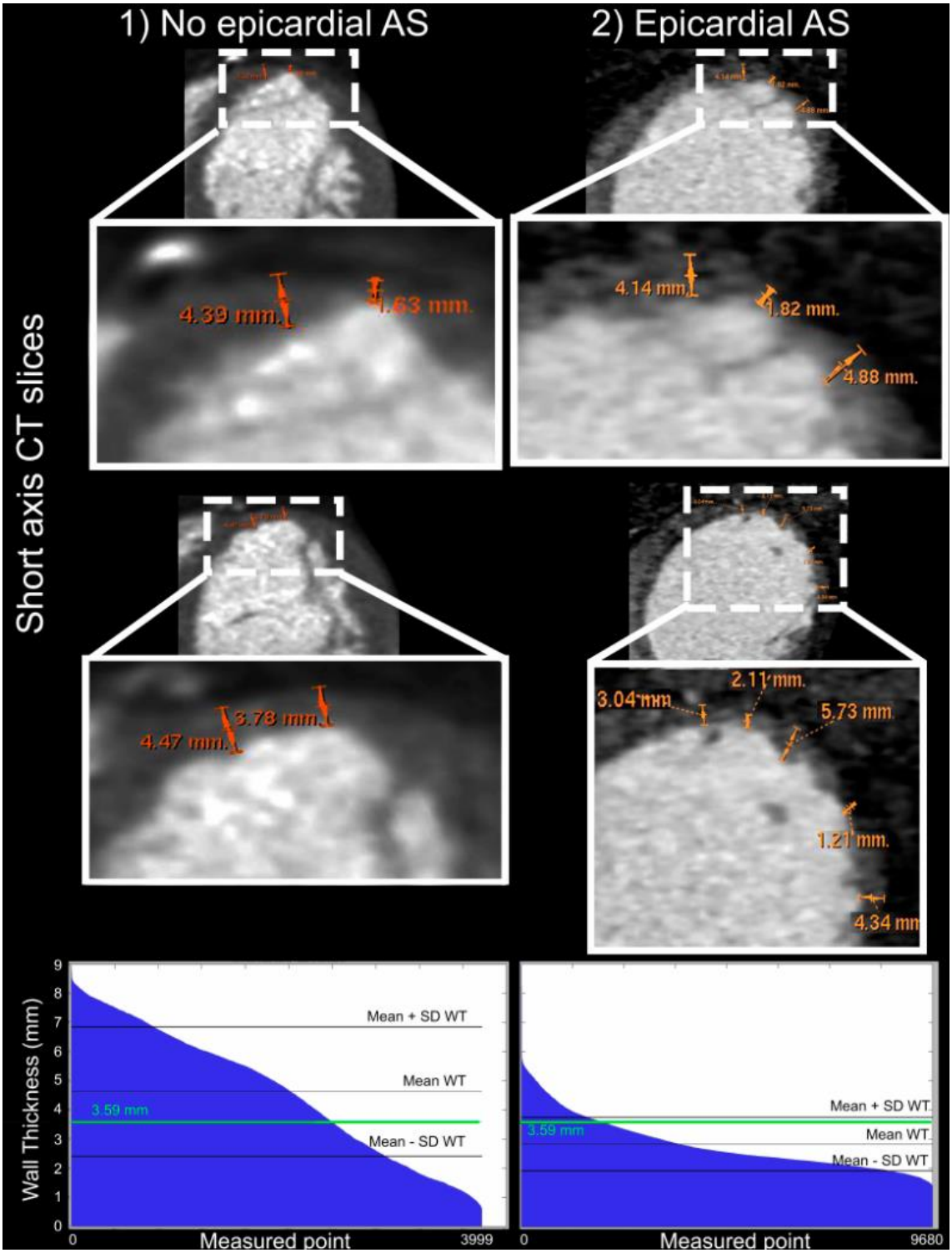


TABLE S1. Sensitivity and specificity of the means estimated with a random number of selected points in the area with lower WT on MDCT.

Number of measurements	Sensitivity	Specificity
1	0.66	0.76
2	0.75	0.84
3	0.75	0.70
4	0.87	0.76
5	0.87	0.76
6	0.80	0.80
7	0.72	0.86
8	0.82	0.78
9	0.90	0.86
10	**0.87**	**0.87**

Figure S2. Multimodal integration of late gadolinium-enhanced cardiac magnetic resonance (LGE-CMR), multi-detector computed tomography (MDCT), and electroanatomical mapping data (EAM) showing two PMI patients with a classical transmural infarction (C-TMI) defined by LGE-CMR which had and not epicardial arrhythmogenic substrate (top and bottom rows, respectively). Scar configuration in the endocardial and epicardial layers, obtained from LGE-CMR, is shown in the two left columns (healthy tissue, border zone and core zone in purple, green and red, respectively). Myocardial wall thickness (WT) extracted from MDCT images are mapped onto the epicardial LGE-CMR geometry. Regions with WT < 3.59 mm are colored in red, WT > 5mm in purple, and 3.59 mm < WT <5 mm in green. The EAM (right column) shows the scar identified from standard voltage values (0.5 and 1.5 mV); electrograms with delayed-components are represented as blue dots.