Universiteit Leiden
The Netherlands

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NEW MAPPING TECHNIQUES FOR VT

New Adjusted Cutoffs for "Normal" Endocardial Voltages in Patients With Post-Infarct LV Remodeling

Marek Sramko, MD, PhD,[a,b,*] Saif Abdel-Kafi, MD,[a,*] Rob J. van der Geest, MD, PhD,[c] Marta de Riva, MD,[a] Claire A. Glashan, MD,[a] Hildo J. Lamb, MD, PhD,[c] Katja Zeppenfeld, MD, PhD[a]

ABSTRACT

OBJECTIVES This study sought to determine new reference cutoffs for normal unipolar voltage (UV) and bipolar voltage (BV) that would be adjusted for the LV remodeling.

BACKGROUND The definition of "normal" left ventricular (LV) endocardial voltage in patients with post-infarct scar is still lacking. The reference voltage of the noninfarcted myocardium (NIM) may differ between patients depending on LV structural remodeling and the ensuing interstitial fibrosis.

METHODS Electroanatomic voltage mapping was integrated with isotropic late gadolinium–enhanced cardiac magnetic resonance in 15 patients with nonremodeled LV and 12 patients with remodeled LV (end-systolic volume index >50 ml/m^2 with ejection fraction <47% assessed by cardiac magnetic resonance). Reference voltages (fifth percentile values) were determined from pooled NIM segments without late gadolinium enhancement.

RESULTS The cutoffs for normal BV and UV were ≥3.0 and ≥6.7 mV for nonremodeled LV and ≥2.1 and ≥6.4 mV for remodeled LV. Endocardial low-voltage area (LVA) defined by the adjusted cutoffs corresponded better to late gadolinium enhancement–detected scar than did LVA defined by uniform cutoffs. In 15 patients who underwent successful ablation of ventricular tachycardia, the LVA contained >97% of targeted evoked delayed potentials. Insights from whole-heart T1 mapping revealed more fibrotic NIM in patients with remodeled LV compared with nonremodeled LV.

CONCLUSIONS This study found substantial differences in endocardial voltage of NIM in post-infarct patients with remodeled versus nonremodeled LV. The new adjusted cutoffs for "normal" BV and UV enable a patient-tailored approach to electroanatomic voltage mapping of LV. (J Am Coll Cardiol EP 2019;5:1115–26)
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Electroanatomic voltage mapping (EAVM) of the left ventricle (LV) remains a cornerstone of catheter ablation of ventricular tachycardia (VT) in patients with post-infarct scar (1). The main goal of EAVM is to discriminate the scar and its border zone, which almost invariably contain parts of the VT circuit, from relatively healthy noninfarcted myocardium (NIM), which should be spared from ablation

From the [a]Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands; [b]Department of Cardiology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; and the [c]Department of Radiology, Leiden University Medical Center, Leiden, the Netherlands. *Drs. Sramko and Abdel-Kafi contributed equally to the work. The Leiden University Medical Center Department of Cardiology has received unrestricted grant support from Edwards Lifesciences, Medtronic, Biotronik, and Boston Scientific; and has received research grant support from Biosense Webster. Dr. Sramko was supported by the Research Fellowship of the European Society of Cardiology (2017/2018) and by a grant of the Czech Society of Cardiology. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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ABBREVIATIONS AND ACRONYMS

BV = bipolar voltage

CMR = cardiac magnetic resonance

EAVM = electroanatomic voltage mapping

ECV = extracellular volume

EDP = evoked delayed potential

IQR = interquartile range

LGE = late gadolinium enhancement

LV = left ventricle/ventricular

LVA = low-voltage area

NIM = noninfarcted myocardium

RV = right ventricular

UV = unipolar voltage

VT = ventricular tachycardia

injury. This is currently done by applying uniform voltage cutoffs, most commonly 1.5 or 3.0 mV for endocardial bipolar voltage (BV) and 8.3 mV for unipolar voltage (UV). However, these cutoff values were derived either from voltage mapping in people without structural heart disease (2,3) or from a crude comparison of low-voltage areas (LVAs) against dense scar on gross histopathology or nonisotropic imaging (4). None of the cutoffs have been validated to identify NIM in patients with post-infarct scar.

Moreover, the voltage cutoffs are applied uniformly in all patients, not taking into account the interindividual differences in the histopathology of NIM that can affect endocardial voltage. Based on studies in nonischemic cardiomyopathy (5,6), it is conceivable that patients with post-infarct LV remodeling might have substantially lower "normal" LV voltage than patients with nonremodeled LV due to wall thinning and interstitial fibrosis in the NIM, though it is unknown whether adjusting EAVM for LV remodeling would result in clinical benefit.

SEE PAGE 1127

In this study, we investigated the impact of LV structural remodeling on normal voltages of NIM in patients with post-infarct scar. The main study objective was to compare the endocardial voltages of NIM between patients with and without LV structural remodeling, and to determine new reference cutoffs for normal LV endocardial voltages, adjusted for LV remodeling. Subsequently, we evaluated whether LVA defined by the remodeling-adjusted cutoffs would better correspond to tissue characterization by late gadolinium enhancement cardiac magnetic resonance (LGE-CMR) than LVA defined by the currently used uniform cutoffs. At last, we evaluated whether the LVA would contain targeted VT-related sites in patients who underwent successful VT ablation.

METHODS

STUDY POPULATION. The study included 27 of 30 consecutive patients with post-infarct scar who underwent catheter ablation for VT (n = 20) or premature ventricular contraction (n = 7) with real-time integration of 3-dimensional LGE-CMR. To ensure optimal image quality, we included only patients without an implanted cardiac device and excluded 3 patients with imaging artifacts. For the purpose of the study, the patients were divided into 2 groups based on the baseline LV function and geometry assessed by cine CMR: 1) patients with remodeled LV, defined by LV end-systolic volume index of >50 ml/m^2 and ejection fraction of <47% (7); and 2) patients with nonremodeled LV, defined by the absence of these criteria (**Table 1**). Approval by the institutional ethics committee was not required, as all the performed procedures were part of a routine clinical protocol; all patients gave informed consent to the procedures.

CMR AND IMAGE ANALYSIS. CMR was performed on a 3-T Ingenia scanner (Philips Healthcare, Best, the Netherlands) within 1 month before the ablation procedure. Cine images were acquired in standard cardiac views. LGE images were acquired 10 to 15 min after bolus injection of 0.15 mmol/kg of gadoterate meglumine by a whole-heart navigator-gated free-breathing 3-dimensional gradient-echo phase-sensitive inversion recovery sequence (acquired axial-plane resolution of 1.6 × 1.6 mm). In addition to the LGE imaging, the most recent 5 consecutive patients underwent whole-heart pre- and post-contrast T1 mapping using a 3-3-5 modified Look-Locker imaging sequence (10 contiguous short-axis slices with reconstructed voxel resolution of 1.25 × 1.25 × 10 mm). Our hardware setup and parameters of the used sequences have been described in detail elsewhere (8,9).

The images were processed using MASS Research Software version V2018-EXP (Leiden University Medical Centre, Leiden, the Netherlands). LV phasic volumes were measured manually from short-axis image stacks. The short-axis cine images were also used to quantify segmental endocardial circumferential strain by an automated registration-based algorithm implemented in the software (10). Isotropic LGE images were reconstructed to 2-mm-thick short-axis slices and segmented as previously described (11). Scar core and total scar (i.e., scar core + border zone) were defined as signal intensity of ≥50% and ≥35% of the maximum signal intensity within the LV myocardium, respectively (11). NIM was defined as confluent nonenhanced tissue >10 mm away from any scar. Myocardial extracellular volume (ECV) was calculated by a standard formula using the patient's hematocrit and pre- and post-contrast T1 maps. Before generating the T1 maps, the image stacks were registered by an automated algorithm (9).

ELECTROANATOMIC MAPPING AND IDENTIFICATION OF ARRHYTHMOGENIC SUBSTRATE. All patients underwent LV endocardial mapping (CARTO 3, Biosense Webster, Diamond Bar, California) using a 3.5-mm irrigated-tip catheter (NaviStar ThermoCool, Biosense Webster) with a fill threshold of <15 mm.

LGE-derived scar meshes were merged with the voltage maps using the ostium of the left main coronary artery as a registration landmark (11).

In patients undergoing ablation of VT (n = 20), the strategy was to identify and ablate all sites with low voltage potentials with functional conduction delay (evoked delayed potentials [EDPs]), according to our recently described protocol (12). In our experience, such an approach results in limited substrate modification with good long-term outcome (12). In brief, with the catheter in a stable position, voltage and duration of electrograms were systematically measured during sinus rhythm, right ventricular (RV) pacing, and after application of a single RV extrastimulus. Sites exhibiting near-field potentials with a BV <1.5 mV and conduction delay >10 ms or block in response to extrastimulation were tagged as EDPs. Late potentials that did not prolong during an RV extrastimulus were not targeted. If a sustained stable VT was repeatedly induced during the pacing protocol, the VT was terminated by ablation based on entrainment and activation mapping. Radiofrequency energy (45 to 50 W) was applied at all the tagged sites until failure to capture with high-output stimulation (10 mA/2 ms). Although we performed pace mapping at all sites with EDPs to identify exit sites of induced VT, we did not restrict the ablation only to the EDPs related to the induced VT.

Electrical programmed stimulation was performed without pharmacological stimulation before voltage mapping and after the last energy application (basic cycle lengths of 600, 400, and 350 ms with up to 4 extrastimuli from RV and multiple LV sites) (12). If other sustained monomorphic VT remained inducible, additional mapping and ablation was performed until no further substrate could be identified.

Acute success of VT ablation was defined as noninducibility of any VT (complete success) or noninducibility of the clinical VT (partial success) after ablation. Patients were followed 3 months after ablation and every 6 months thereafter. VT recurrence was defined as any VT requiring implantable cardioverter-defibrillator therapy, lasting >30 s on the implantable cardioverter-defibrillator monitor or documented on 12-lead electrocardiogram.

REVERSE INTEGRATION OF EAVM AND CMR DATA TO DETERMINE THE REFERENCE VOLTAGE. Exported voltage maps were analyzed by an independent examiner to remove signal artifacts and ectopic beats. Next, the maps were projected back on the segmented short-axis CMR images, using the CARTO registration matrix obtained during real-time image integration (**Figure 1**). Each EAVM point was matched with local image characteristics (presence of scar, wall thickness, and circumferential strain) using 100 transmural chords (11). EAVM points located in NIM, defined as myocardium located >10 mm from LGE-defined scar, were extracted and carefully reviewed. Points that were displaced >5 mm toward the LV cavity and had apparently lower voltage than 2 to 3 adjacent points were excluded (6 ± 3 per patient) because of assumed inadequate catheter contact. To overcome unequal spatial distribution of the acquired EAVM points in the LV, the voltage and imaging characteristics were averaged over 18 cardiac segments (6 segments at basal, mid, and apical levels) (**Figure 1**). Reference BV and UV were calculated from the average voltages of NIM segments pooled from all patients in the group. The cutoffs for "normal" BV/UV were defined as the fifth percentile values (2,3).

TABLE 1 Baseline Characteristics

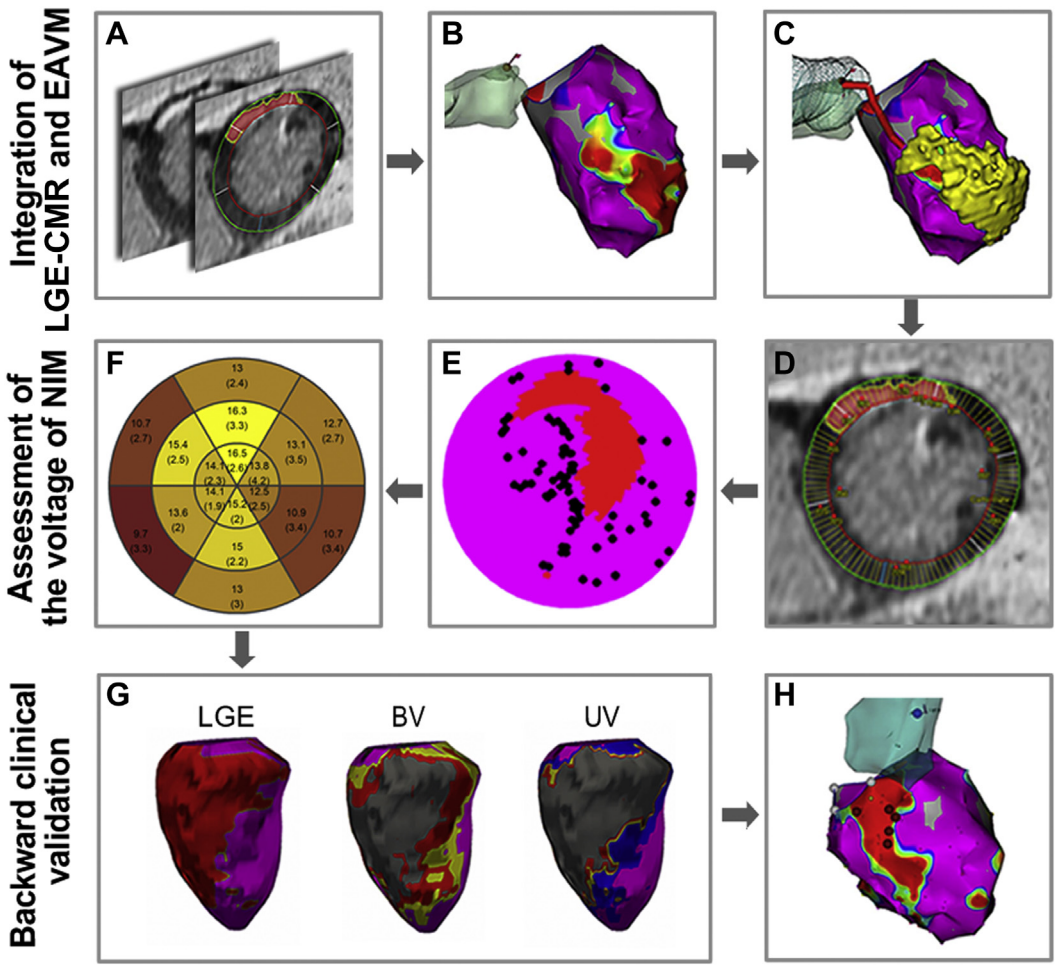
	Nonremodeled LV (n = 15)	Remodeled LV (n = 12)	p Value
Age, yrs	65 ± 6	63 ± 10	0.50
Male	15 (100)	11 (92)	0.40
Body surface area, m^2	2.1 ± 0.1	2.1 ± 0.2	0.80
Arterial hypertension	13 (87)	7 (58)	0.20
Diabetes mellitus	4 (27)	2 (17)	0.70
ACE inhibitor/ARB	15 (100)	11 (92)	0.40
Beta blockers	14 (93)	10 (83)	0.83
Class III antiarrhythmics	0 (0)	3 (25)	0.075
Anterior or anterolateral scar	2 (13)	3 (25)	0.60
Time since the first MI, yrs	15 (7–21)	12 (5–17)	0.30
LVEF, %	55 ± 8	27 ± 4	<0.001
LV circumferential strain, %*	26 ± 6	16 ± 2	<0.000
LV EDVI, ml/m^2	87 ± 19	132 ± 34	<0.001
LV ESVI, ml/m^2	42 ± 14	96 ± 27	<0.001
LV wall thickness, mm*	8.6 ± 0.9	7.8 ± 0.9	0.043
LV mass, g	130 ± 33	167 ± 34	0.009
Total scar relative extent, %	16 ± 6	22 ± 6	0.022
Scar core relative extent, %	11 ± 4	16 ± 7	0.048

Values are mean ± SD, n (%), or median (interquartile range). *Calculated for segments of noninfarcted myocardium.

ACE = angiotensin-converting-enzyme; ARB = angiotensin receptor blocker; EDVI = end-diastolic volume index; ESVI = end-systolic volume index; LV = left ventricular; LVEF = left ventricular ejection fraction; MI = myocardial infarction.

BACKWARD VALIDATION OF THE DETERMINED VOLTAGE CUTOFF VALUES. Using ParaView 3D visualization software version 5.5 (Kitware Inc., Clifton Park, New York) and the registration matrix obtained during real-time image integration, the voltage map of each patient was projected onto the LV endocardial shell derived from LGE-CMR (**Figure 1**). This enabled a direct comparison of the endocardial surface area of LGE-detected scar with LVA defined by the remodeling-adjusted voltage cutoffs and by the currently used uniform cutoffs (BV <1.5 and

FIGURE 1 Workflow of Image Processing



(A) Segmentation of scar on short-axis late gadolinium enhancement (LGE) images, **(B)** electroanatomic voltage mapping (EAVM) with tagged ostium of left main coronary artery, **(C)** registration of EAVM and LGE-detected scar using the left main coronary artery tag, **(D)** pairing EAVM points with image characteristics using 100 radial chords, **(E)** reviewing and extracting EAVM points in noninfarcted myocardium (NIM), **(F)** calculation of the average voltage of NIM segments, **(G)** comparison of low-voltage area with LGE-detected scar projected on the same LV shell, and **(H)** successfully ablated evoked delayed potentials within low-voltage area. BV = bipolar voltage; CMR = cardiac magnetic resonance; LV = left ventricle; UV = unipolar voltage.

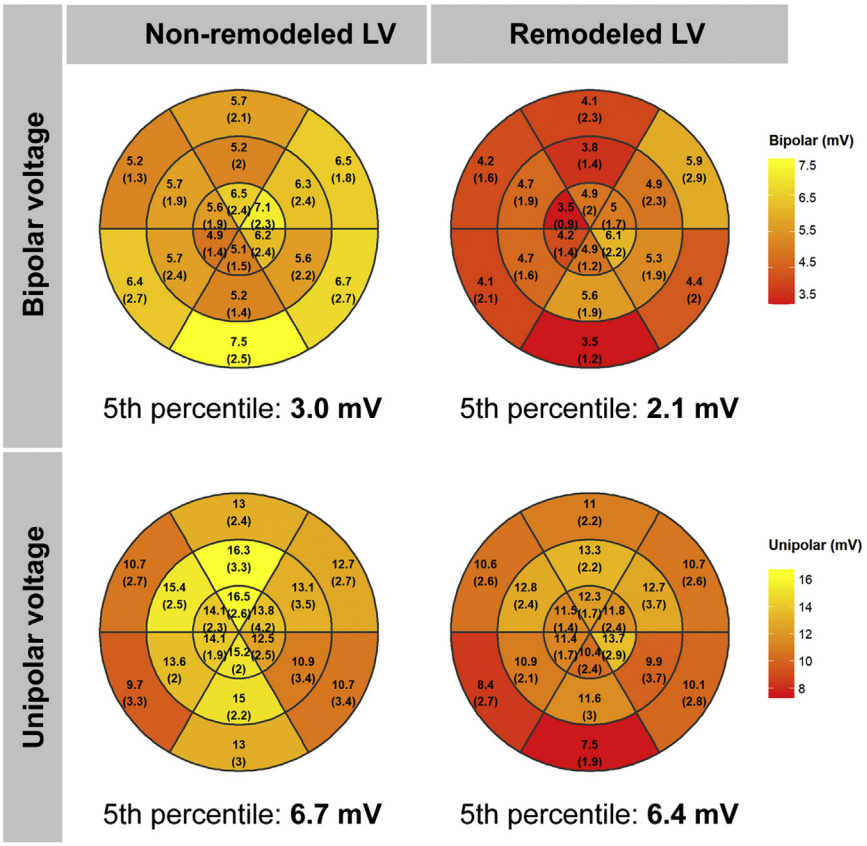
3.0 mV, and UV <8.3 mV). Last, the voltage maps were reviewed in the CARTO environment to evaluate the proportion of the sites with ablated EDPs within the LVA (Figure 1).

STATISTICAL ANALYSIS. Continuous variables are reported as mean ± SD or median (interquartile range [IQR]), according to the normality of the distribution. They were compared by the Student's *t*-test and Mann-Whitney *U*-test. Categorical variables were compared by chi-square test or Fisher exact test. Factors associated with endocardial voltage were identified by linear regression and Pearson's correlation. Paired Wilcoxon signed rank test was used to compare LVA with endocardial surface of LGE-detected scar. All analyses were performed in R software version 3.2 (R Foundation for Statistical Computing, Vienna, Austria). A p value < 0.05 was considered significant.

RESULTS

STUDY POPULATION. At the time of EAVM, 15 patients had a nonremodeled LV (all men; age 65 ± 6 years) and 12 patients had a remodeled LV

FIGURE 2 The Mean and Fifth Percentile BV and UV Values of NIM



Polar-plot representation of mean ± SD values of BV and UV of the segment of NIM. The values were calculated by pooling the average segment values from all patients in each groups. The fifth percentile values shown beneath each graph were regarded as the lower cutoff for normal endocardial voltage. NIM = noninfarcted myocardium; other abbreviations as in Figure 1.

(11 men; age 63 ± 10 years). Besides the default given LV dilation, relative wall thinning, and impaired contractility, the patients with remodeled LV had larger LV mass and larger relative scar size. Other baseline characteristics did not differ between the groups (Table 1).

REFERENCE LV VOLTAGE. On average, 88 ± 44 EAVM points per patient were obtained in NIM, and a median of 6 (IQR: 3 to 8) points were used to calculate the average voltage of 1 NIM segment. An overview of all the EAVM points is depicted in Online Figure 1. The number of NIM segments with paired voltage or imaging data used for calculation of the reference LV voltage was 197 in patients with nonremodeled LV and 153 in patients with remodeled LV.

The average BV of NIM was 5.9 ± 2.5 mV in patients with nonremodeled LV and 4.6 ± 2.0 mV in patients with remodeled LV ($p < 0.001$); the average UV of NIM was 13.4 ± 4.1 mV and 11.3 ± 7.2 mV, respectively ($p < 0.001$). The cutoffs for reference BV and UV (fifth percentile values) were ≥3.0 mV and ≥6.7 mV in patients with nonremodeled LV and ≥2.1 mV and ≥6.4 mV in patients with remodeled LV.

In both groups, UV of NIM was relatively lower at the LV base compared with nonbasal segments (14 ± 4 mV vs. 12 ± 4 mV in preserved LV and 12 ± 4 mV vs. 10 ± 3 mV in remodeled LV; both $p < 0.001$) (Figure 2), but it did not differ between septal and free-wall NIV segments. No difference in BV was observed in either group between basal versus nonbasal or septal versus free-wall NIV segments.

FACTORS RELATED TO THE VOLTAGE OF NIM. Both BV and UV of NIM were negatively associated with LV remodeling and related CMR characteristics: LV ejection fraction, volume, and circumferential strain (Table 2, Figure 3). There was a weak positive

TABLE 2 Factors Associated With Endocardial Voltage of NIM

	Bipolar Voltage	Unipolar Voltage
Per-patient analysis (n = 27)		
Presence of LV remodeling	-1.170 (-2.050 to -0.300)*	-1.990 (-3.750 to -0.230)*
LVEF	0.030 (0.003 to 0.060)†	0.060 (0.030 to 0.090)†
LV EDVI	-0.020 (-0.003 to -0.030)†	-0.020 (-0.010 to -0.030)†
LV ESVI	-0.020 (-0.005 to -0.030)†	-0.030 (-0.040 to -0.020)†
Circumferential strain‡	0.090 (0.010 to 0.200)*	0.150 (0.001 to 0.300)
Wall thickness‡	0.300 (-0.200 to 0.800)	0.500 (-0.800 to 1.200)
Analysis of NIM segments (n = 350)		
Circumferential strain	0.060 (0.020 to 0.090)†	0.140 (0.080 to 0.200)†
Wall thickness	0.170 (0.040 to 0.310)*	-0.140 (-0.410 to 0.120)

Values are β (95% confidence interval). *p < 0.05 by analysis of variance for the presence of LV remodeling and by F statistics for the continuous variables. †p < 0.001 by F statistics for the continuous variables. ‡Average of NIM segments within a patient.

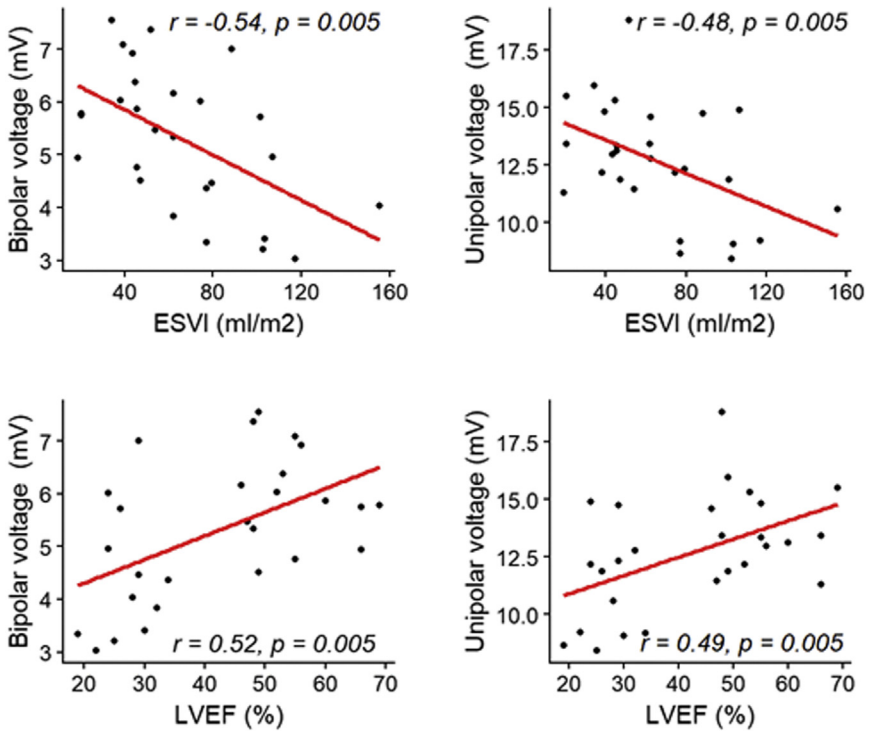
NIM = noninfarcted myocardium; other abbreviations as in Table 1.

association between LV wall thickness and BV (r = 0.1), but no association was observed between wall thickness and UV (Figure 4). No association was found between BV or UV and any of the clinical variables listed in Table 1.

Whole-heart T1 mapping was available in 2 patients with nonremodeled LV and 3 patients with remodeled LV. Compared with the patients with nonremodeled LV, the patients with remodeled LV had increased ECV and decreased BV and UV of the NIM segments, whereas ECV and voltage of the segments with LGE-detected compact scar were comparable (Figure 5, Online Table 1).

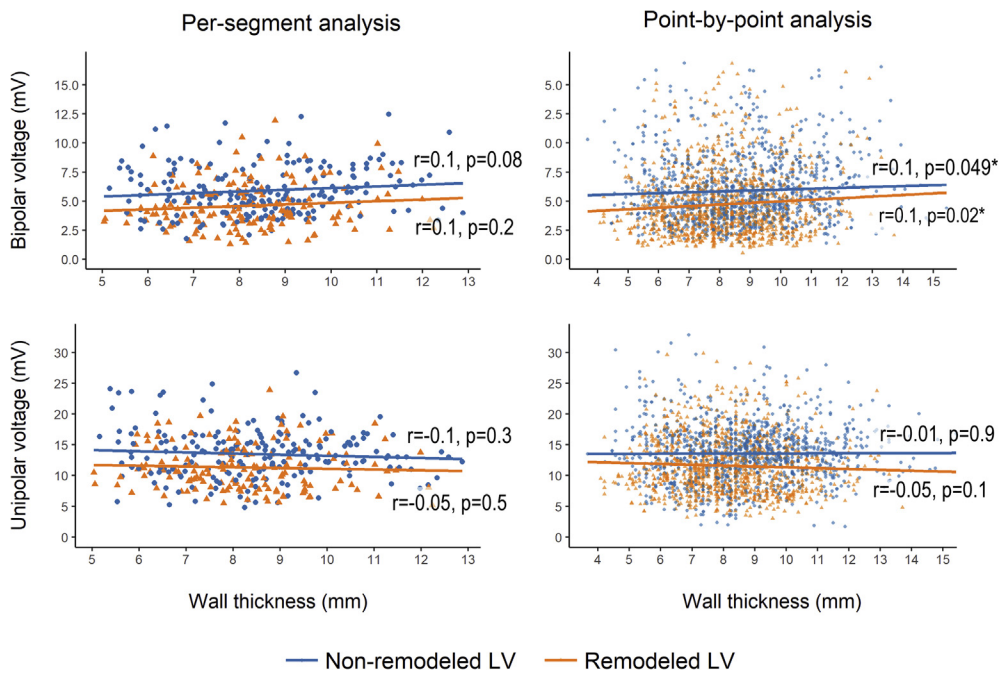
COMPARISON OF LGE-DETECTED SCAR AND LVA. A direct comparison between endocardial surface areas of LGE-detected scar versus LVA defined by the remodeling-adjusted and previously proposed uniform cutoffs is shown in Figure 6. LVA defined by a uniform cutoff of BV <1.5 mV evidently underestimated total scar and scar core in both patient groups. LVA defined by BV <3.0 mV corresponded well with total scar and scar core in patients with nonremodeled LV, but significantly overestimated total scar and scar core in patients with remodeled LV. In contrast, LVA defined by UV <8.3 mV largely overestimated total scar and scar core in both patient groups. The best match between LVA and total scar was achieved by applying the adjusted cutoffs of

FIGURE 3 Correlation of Voltages and LV Remodeling



The graphs show good correlation between patient-specific mean BV and UV of NIM and LV ejection fraction (LVEF) and end-systolic volume index (ESVI). Abbreviations as in Figure 1.

FIGURE 4 Correlation of Voltage and Wall Thickness of NIM



A total of 197 and 153 segments and 1,061 and 1,161 points for nonremodeled and remodeled LVs, respectively. In the measured range of wall thickness, there was a weak positive correlation between the LV wall thickness and BV, but only when the groups were analyzed point by point **(upper right panel)**. Abbreviations as in Figures 1 and 2.

BV <3.0 and 2.1 mV or UV <6.7 and 6.4 mV for nonremodeled and remodeled LVs, respectively.

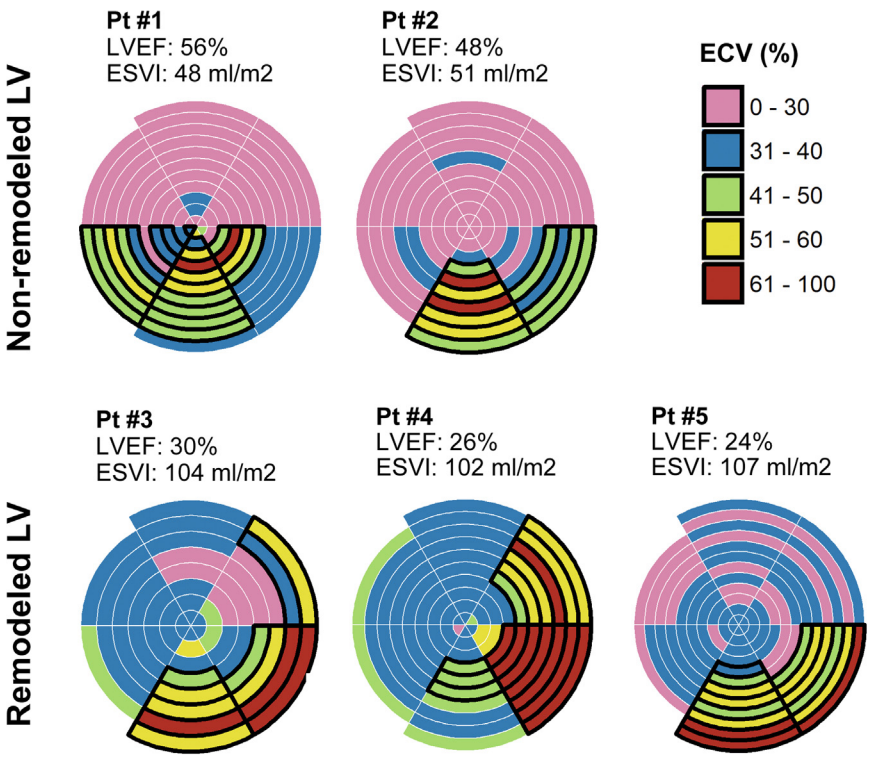
LOCATION OF EDPS IN LVA. EDPs, as a surrogate for VT substrate, were identified in 15 of 20 patients undergoing VT ablation (median 9 [IQR: 3 to 18] distinct sites per patient). Ablation at these sites (mean procedural time 190 ± 51 min, ablation time 10 ± 7 min) resulted in noninducibility of clinical VTs in all 15 patients (8 complete success, 7 partial success). During a median follow-up of 13 (IQR: 3 to 24) months, only 2 (13%) patients experienced VT recurrence (after 10 and 37 months, respectively).

LVA defined by the remodeling-adjusted cutoffs of BV <3.0 and 2.1 mV and UV <6.7 and 6.4 mV contained 99 ± 4% and 97 ± 6% of all the EDPs in the nonremodeled and remodeled LVs, respectively. In contrast, LVA defined by BV <1.5 mV contained only 59 ± 27% of the EDPs (Figure 7). In addition, the remodeling-adjusted LVA covered significantly smaller LV endocardial surface compared with the LVA defined by uniform cutoffs: 23 ± 8% versus 28 ± 8% of the LV for BV <3.0 and 2.1 mV versus <3.0 mV ($p = 0.02$); and 21 ± 8% versus 29 ± 10% of the LV for UV <6.7 and 6.4 mV versus <8.3 mV ($p < 0.001$).

DISCUSSION

MAIN FINDINGS. This study used direct integration of EAVM with isotropic LGE-CMR to determine reference cutoffs for normal endocardial voltage in patients with post-infarct scar according to LV structural remodeling. The key novel findings were as follows. First, endocardial voltages of NIM were markedly decreased in patients with remodeled compared with nonremodeled LV. Consequently, different cutoff values for "normal" voltage were generated for remodeled and nonremodeled NIM: BV ≥2.1 mV versus ≥3.0 mV and UV ≥6.4 mV versus ≥6.7 mV, respectively. Second, LVA defined by remodeling-adjusted cutoffs corresponded accurately and significantly better with the endocardial surface of LGE-CMR compared with currently used uniform voltage cutoffs. Third, in patients who underwent successful VT ablation, the remodeling-adjusted LVA contained virtually all targeted VT related sites (EDPs) (Central Illustration). Altogether, these novel

FIGURE 5 Regional Distribution of Myocardial ECV Assessed by T1 Mapping



Polar plots showing assessment of extracellular volume (ECV) in 5 patients who underwent whole-heart T1 mapping. The **black border lines** outline segments with scar on corresponding LGE images. The 3 patients with remodeled LV (Patients #3, #4, and #5) had diffusely increased ECV of the NIM (segments outlined in **gray**). Pt = patient; other abbreviations as in Figures 1 and 3.

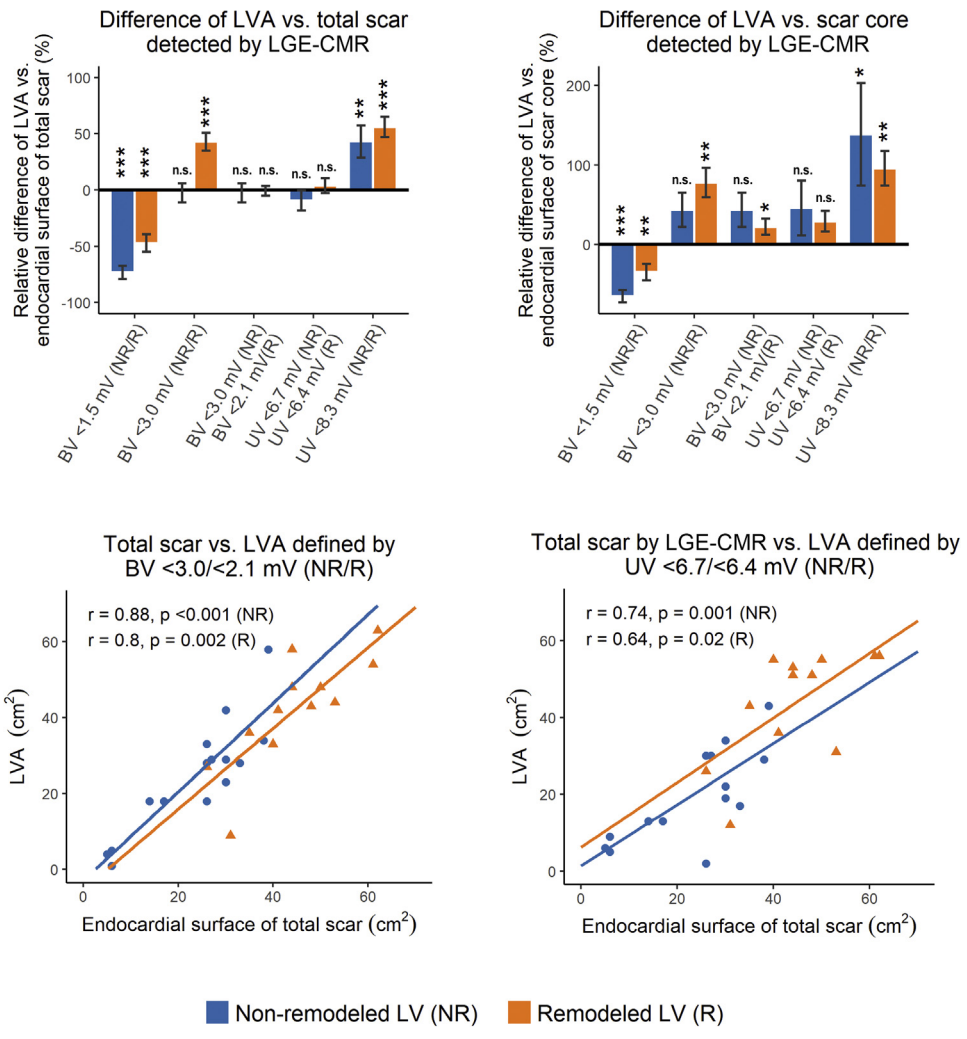
findings highlight the importance of tailoring EAVM depending on LV remodeling.

DEFINITION OF NORMAL ENDOCARDIAL VOLTAGE IN PATIENTS WITH POST-INFARCT SCAR. Despite routine clinical use of EAVM to characterize LV myocardial tissue, there is a lack of consensus on the definition of normal LV endocardial voltage in patients with post-infarct scar. Currently, most centers use a uniform cutoff of BV ≥1.5 mV. However, this cutoff was validated merely to detect dense scar core assessed by gross pathology or nonisotropic LGE-CMR, not to discern healthy NIM (4). This explains the observations from 2 previous studies, as well as this one, that EAVM guided by the 1.5-mV cutoff tends to largely underestimate LGE-detected scar, particularly if the definition of the LGE-detected scar includes the scar border zone (13,14).

Some authors consider BV ≥3.0 mV as normal LV endocardial voltage. This cutoff value was determined by voltage mapping in 15 healthy people (2) and was corroborated by a histological study in pigs with healed myocardial infarction (15). Interestingly, we found the same cutoff value for normal BV also in our patients with nonremodeled LV. But in patients with remodeled LV, who had diffusely decreased BV in NIM, the ≥3.0-mV cutoff incorrectly classified a significant portion of NIM as scar. We showed that the distinction between NIM and scar could be improved in patients with LV remodeling by adjusting the cutoff to ≥2.1 mV.

There is even less consensus on the definition of normal UV. Several centers have adopted a cutoff value of UV ≥8.3 mV, which was derived from voltage mapping in 6 patients without structural heart disease (3). We found that application of such relatively high cutoff in ischemic patients significantly overestimated the extent of scar tissue as compared with LGE-CMR, both in remodeled and nonremodeled LV. Our data support using substantially lower UV cutoffs to distinguish between post-infarct scar and NIM: ≥6.7 mV for nonremodeled LV and ≥6.4 mV for

FIGURE 6 **Overlap of LVA Defined by Various Cutoffs and Scar Detected by LGE**



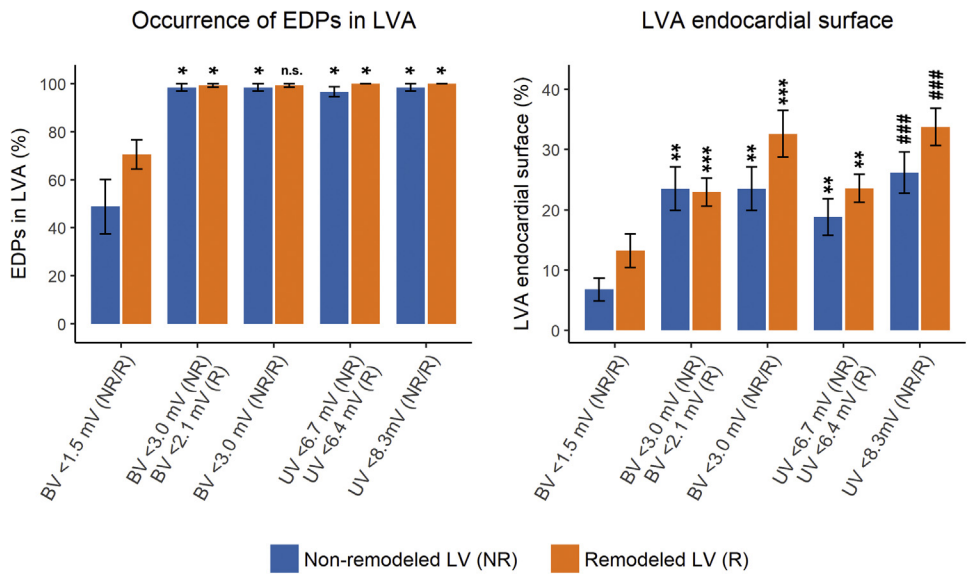
The **bars in the upper row** show mean ± SE relative difference (from the zero line) between low-voltage area (LVA) and endocardial surface of scar detected by LGE. Scatter plots in the **bottom row** show Pearson's correlation of endocardial surface of total scar and LVA defined by the remodeling-adjusted BV and UV cutoffs. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ by a paired Wilcoxon test. n.s. = not significant; NR = nonremodeled; R = remodeled; other abbreviations as in Figure 1.

remodeled LV. These values are comparable to those suggested by a histological study in pigs (UV ≥6.2 mV) or by a study in ischemic patients (UV ≥6.5 mV) (14,15). Further research is needed to explore potential implications of the observed difference of UV between base and nonbasal segments, and whether UV cutoffs should also be adjusted for particular LV regions.

This study showed that the voltage-remodeling relationship was actually continuous. Thus, it seems futile to use a single cutoff value in all patients. Using 2 sets of voltage cutoffs based on the binary presence of LV remodeling may be imperfect; however, we could demonstrate that such an approach already significantly improved EAVM of LV compared with the current single cutoffs. Future studies should search for even more sophisticated approaches to individualized EAVM. Perhaps, T1 mapping could be used to "calibrate" a patient-specific normal voltage based on the fibrosis of NIM.

LV voltages can be affected not only by patient-related factors, but also by characteristics of the

FIGURE 7 Occurrence of Targeted EDPs in LVA



(Left panel) Proportion (mean ± SE) of targeted evoked delayed potential (EDPs) in the LVA in patients with successful ablation for ventricular tachycardia. **(Right panel)** Corresponding LV endocardial surface according to the definition of LVA. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ by a paired Wilcoxon test against BV of <1.5 mV; ### $p < 0.001$ against BV <1.5 mV and UV <6.7 and 6.4 mV. NR = 8 patients; R =7 patients. Abbreviations as in Figures 1 and 6.

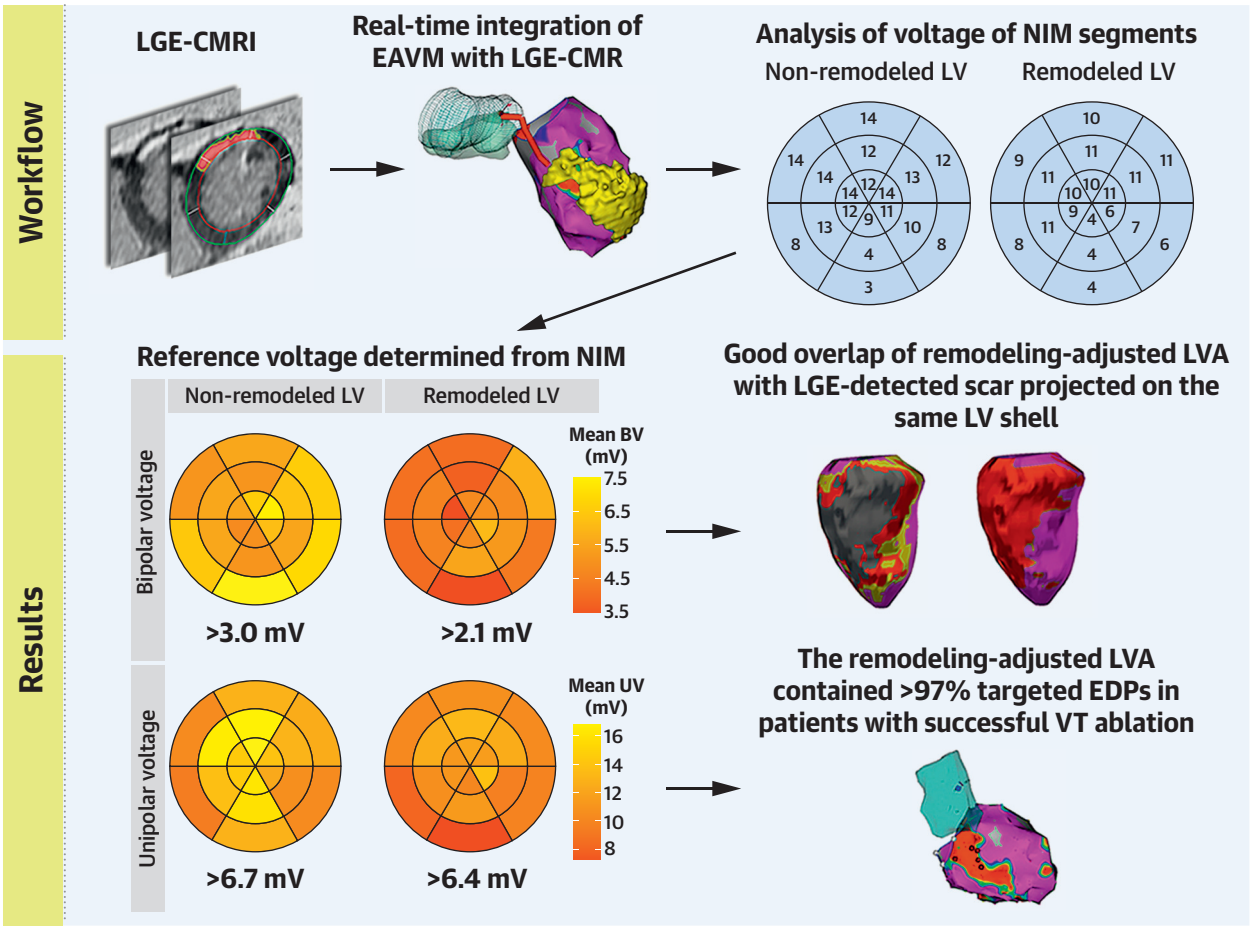
mapping catheter, such as the electrode size and spacing (1). The findings of this study are applicable only for 3.5-mm-tip catheters, which are currently most widely used for EAVM of LV in clinical practice. We believe that it is prudent to establish different voltage cutoffs, following the same concept, for newer high-resolution catheters with multiple smaller-tip electrodes and narrower spacing.

RELATIONSHIP BETWEEN ENDOCARDIAL VOLTAGE AND LV STRUCTURAL REMODELING. Post-infarct LV remodeling is a complex process that involves interstitial fibrosis of the NIM (16). One of the electrophysiological consequences of fibrosis is reduction of the amplitude of endocardial electrograms due to loss of viable myocytes (5,6). Based on this premise, we can hypothesize that the decrease of the voltage of NIM in the patients with remodeled LV was mainly due to more extensive interstitial fibrosis. In fact, this hypothesis was supported by the findings from whole-heart T1 mapping showing greater ECV and lower voltages of NIM in patients with remodeled LV. These findings corroborate our recent histological study in nonischemic patients (5). Although post-infarct LV remodeling also involves wall thinning of the NIM (16), our results indicate that the wall thinning alone had a minimal impact on the voltage of NIM. It is possible that the weak wall thickness-voltage relationship found in our patient sample could have been related to the relatively small range of the observed wall thickness (5 to 14 mm).

CLINICAL IMPLICATIONS. The fact that EAVM guided by our proposed cutoffs reliably delineated LGE-CMR-detected scar means that these cutoffs may be used for substrate VT ablation in patients in whom CMR integration is unavailable. More importantly, in patients who underwent successful VT ablation based on targeting EDPs, the remodeling-adjusted LVA contained 97% to 99% of the ablated sites. Thus, the operator may limit the search for VT-related sites to within the LVA, thereby reducing the procedural time or increasing the map density in relevant regions. Empirical ablation of the entire LVA defined by the adjusted cutoffs would theoretically cover all relevant targets without causing ablation injury to tissue without scar. Whether EAVM guided by the new adjusted cutoffs would also improve clinical outcome of the ablation needs to be confirmed by further research.

STUDY LIMITATIONS. It should be highlighted that the proposed voltage cutoffs apply only for ischemic patients. As the study included mostly patients with

CENTRAL ILLUSTRATION **Real-Time Integration of EAM With LGE-CMR**



Sramko, M. et al. J Am Coll Cardiol EP. 2019;5(10):1115–26.

EAVM = electroanatomic voltage mapping; EDP = evoked delayed potential; LGE = late gadolinium enhancement; LV = left ventricular; LVA = low-voltage area; CMR = cardiac magnetic resonance; NIM = noninfarcted myocardium; VT = ventricular tachycardia.

inferior or inferolateral scar, NIM segments from these regions are relatively underrepresented. The cutoffs were derived and validated on the same dataset, which might have biased the comparison of LVA and scar detected by LGE-CMR. However, the main purpose of the analysis was to demonstrate the importance of adjusting the criteria for LVA depending on the LV remodeling.

CONCLUSIONS

This study demonstrated the importance of interpreting LV endocardial voltage in patients with post-infarct scar in the context of LV structural remodeling, and accordingly proposed new reference cutoffs for "normal" LV endocardial voltage that are adjusted for LV remodeling. The findings of this study provide an important step toward a more tailored approach to LV EAVM.

ADDRESS FOR CORRESPONDENCE: Dr. Katja Zeppenfeld, Department of Cardiology, Leiden University Medical Center, P.O. Box 9600, 2300 RC Leiden, the Netherlands. E-mail: k.zeppenfeld@lumc.nl.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: LV endocardial voltage in patients with ischemic scar should be interpreted in the context of the LV structural remodeling. Lower cutoffs for "normal" voltage should be applied in patients with remodeled LV, because they may have reduced voltage of the NIM due to more extensive interstitial fibrosis.

TRANSLATIONAL OUTLOOK 1: Future trials should evaluate whether EAVM guided by the new remodeling-adjusted cutoffs would translate to improved efficacy of substrate-guided ablation of ventricular arrhythmias, especially if image integration cannot be performed.

TRANSLATIONAL OUTLOOK 2: Future studies should investigate whether assessment of fibrosis of NIM by T1-mapping could be used to determine patient-specific reference voltage cutoffs.

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KEY WORDS electroanatomic mapping, endocardial voltage, fibrosis, scar, ventricular remodeling

APPENDIX For a supplemental figure and table, please see the online version of this paper.