Noninducibility and Late Potential Abolition

A Novel Combined Prognostic Procedural End Point for Catheter Ablation of Postinfarction Ventricular Tachycardia

John Silberbauer, MA, MD (Res), MRCP; Teresa Oloriz, MD; Giuseppe Maccabelli, MD; Dimitris Tsiachris, MD, PhD; Francesca Baratto, MD; Pasquale Vergara, MD, PhD; Hiroya Mizuno, MD, PhD; Caterina Bisceglia, MD, PhD; Alessandra Marzi, MD; Nicoleta Sora, MD; Fabrizio Guarracini, MD; Andrea Radinovic, MD; Manuela Cireddu, MD; Simone Sala, MD; Simone Gulletta, MD; Gabriele Paglino, MD; Patrizio Mazzone, MD; Nicola Trevisi, MD; Paolo Della Bella, MD

Background—Successful late potential (LP) abolition and postprocedural ventricular tachycardia (VT) noninducibility constitute significant end points after catheter ablation for VT. We investigated the prognostic impact of a combined procedural end point of VT noninducibility and LP abolition in a large series of post–myocardial infarction patients with VT.

Methods and Results—A total of 160 (154 men, 94% with implantable cardioverter defibrillators) consecutive post–myocardial infarction patients undergoing first-time ablation procedures from 2010 to 2012 were included. Of the 159 patients surviving the procedure, 137 (86%) were either inducible or in VT at baseline and 103 (65%) had baseline LP presence, of which 79 (77%) underwent successful LP abolition. The combined end point was assessable in 155 (97%) patients. There were 50 (32%) patients with VT recurrences and 17 (11%) cardiac deaths during follow-up. Patients who fulfilled the combined end point of VT noninducibility and LP abolition compared with inducible patients exhibited a significantly lower incidence of VT recurrence (16.4% versus 47.4%; log-rank $P<0.001$) and cardiac death (4.1% versus 42.1%; log-rank $P<0.001$). Among noninducible patients, those with additional LP abolition also had a lower incidence of VT recurrence (16.4% versus 46.0%; log-rank $P<0.001$). After multivariate analysis, the combined end point of VT noninducibility and LP abolition (hazard ratio, 0.205, $P<0.001$) was independently associated with VT recurrence and cardiac death (hazard ratio, 0.106; $P=0.001$).

Conclusions—Achieving a combined catheter ablation procedural end point of VT noninducibility and LP abolition reduces VT recurrence rates to low levels (16%). The overall strategy was associated with a significant impact on cardiac survival. **(*Circ Arrhythm Electrophysiol*. 2014;7:424-435.)**

Key Words: cardiomyopathies ■ catheter ablation ■ myocardial infarction ■ tachycardia, ventricular

The implantable cardioverter defibrillator (ICD) is indicated for primary and secondary prevention of sudden cardiac death because of ventricular arrhythmias in patients with a prior myocardial infarction (MI) and reduced left ventricular (LV) function.[1,2] In patients implanted with ICDs for primary prevention, regardless of cause, the risk of death is significantly increased by both appropriate and inappropriate shock therapy.[3] ICD-unresponsive sudden cardiac death remains in ≈5% of recipients.[4] Pre-emptive substrate-based ablation has been shown to reduce the risk of ventricular tachycardia (VT) recurrence and ICD therapy, including shocks, without affecting mortality in patients with documented VT undergoing ICD implantation.[5,6] We recently reported that successful late potential (LP) abolition reduces the risk of VT recurrence and that achieving postprocedural VT noninducibility reduces both VT recurrence and cardiac death in patients undergoing catheter ablation for VT because of multiple causes in the setting of a dedicated VT unit (VTU).[7,8] Despite the prognostic value of programmed ventricular stimulation (PVS), limitations for its use as a sole procedural end point include deficient baseline inducibility, poor reproducibility, and a low negative predictive value for VT recurrence (26%–44%) among noninducible patients.[8–11] In a large series of patients with post-MI VT, we assessed the benefit of a strategy based on both VT and sinus rhythm (SR) electrogram-guided mapping and ablation, specifically targeting LPs, and whether achieving the novel combined procedural end point of VT noninducibility and LP abolition could further reduce VT recurrence and cardiac mortality.

Clinical Perspective on p 435

Received September 2, 2013; accepted April 9, 2014.

From the Arrhythmia Unit and Electrophysiology Laboratories, Ospedale San Raffaele, Milan, Italy.

Correspondence to Paolo Della Bella, MD, Arrhythmia Unit and Electrophysiology Laboratories, Ospedale San Raffaele, Via Olgettina 60, Milan, Italy. E-mail dellabella.paolo@hsr.it

Circ Arrhythm Electrophysiol **is available at http://circep.ahajournals.org** **DOI: 10.1161/CIRCEP.113.001239**

Methods

One hundred sixty consecutive post-MI patients with drug-refractory (≥1 antiarrhythmic) VT were referred for catheter ablation at the San Raffaele Hospital VTU, Milan, Italy, between January 2010 and December 2012 and constituted the study population. The study period started when the VTU was established at this institution and ended to allow ≥6 months of follow-up (until June 2013). The study was approved by the institutional review committee, and all patients gave written informed consent. Thirty-six had a prior ablation procedure at a referring center. Prospective data collection comprised medication history, cardiovascular disease type and investigations, and presence of other comorbidities including cerebrovascular, respiratory, chronic renal, and thyroid disease. Patients were all receiving optimal medical therapy.

Arrhythmia presentation was classified as electrical storm, incessant, or recurrent VT as previously described.[8] A VT ablation was scheduled either as an emergency, with circulatory support if necessary, or electively in low-risk stable patients.[8] Antiarrhythmic therapy was withdrawn 5 half-lives before the procedure, apart from amiodarone, which was stopped 48 hours before. The decision to obtain subxiphoid epicardial access was based on clinical and prior procedural data or as part of research protocol and undertaken using a posterior approach. Double-LV access (retrograde aortic and transseptal) was standard. Procedures were performed under general anesthesia with inotropic support (epinephrine±norepinephrine). Inotropes were uptitrated to maintain a mean arterial blood pressure >65 mm Hg during SR and poorly tolerated VT (aiming for at least short-duration (≤1 minute) ablation if feasible). Poorly tolerated VT was defined as unmappable if no ablation could be undertaken despite these measures. Hypotension despite high-dose inotropes triggered the implementation of invasive hemodynamic support using an intra-aortic balloon pump or extracorporeal membrane oxygenation.

VT Ablation Strategy and Procedure

Patients underwent high-density electroanatomic mapping (EAM; defined as a 5-mm EAM interpolation fill threshold in areas with a bipolar voltage <1.5 mV and 10 mm elsewhere) with the CARTO 3 (Biosense Webster, Diamond Bar, CA) or NavX Ensite Velocity (St. Jude Medical Inc, Milwaukee, WI) systems. Substrate mapping was performed during SR or ventricular pacing. Scar and border zone were defined as areas with a bipolar voltage of <0.5 mV and 0.5 to 1.5 mV, respectively. Electrogram-guided ablation was based principally on LPs, considered to have a high likelihood of relating to putative VT isthmuses. LPs were defined as local ventricular potentials occurring after the terminal portion of the surface QRS, whereas early potentials (EPs) were defined as those inscribed within the QRS. The LP definition included either continuous fragmented activity, bridging from the main component within the QRS to the latest signal recorded, or isolated potentials recorded after the QRS offset, without a definite voltage cutoff. The electrogram was always marked at the latest recorded activity. Abnormal EPs were defined as fragmented electrograms, typically recorded at the scar border (in the range between 0.5 and 1.5 mV); pacing was systematically attempted at these sites looking for morphology match with any induced VT and for latency between the stimulus and the QRS (>40 ms). Pacing was performed at increasing strengths, from twice the diastolic threshold ≤10 mA using a 2-ms pulse width (Figure 1). LPs were a primary target in all patients and EPs secondary or adjunctive. Three-dimensional color-coded voltage and LP maps were made using the above EAM systems. For LP maps, the terminal portion of every local electrogram was manually marked during the mapping procedure allowing the generation of a high-density color-coded map with the lower time threshold set to the difference between the reference and end of the surface QRS complex.[7] This defined the baseline location and size of LP areas for comparison with remaps undertaken postablation. EPs were manually tagged as points on the 3-dimensional EAM maps (Figure 2).

After substrate mapping, PVS with ≤4 extrastimuli from the right ventricular apex and multiple LV sites was performed. End points for PVS were sustained VT or ventricular fibrillation (VF), ventricular refractoriness, or a minimum coupling interval of 200 ms with the final extrastimulus. Inducibility was categorized according to narrow (VT, excluding VF) and broad (VT, including VF) definitions.[11] A summary of our VT ablation strategies (divided into groups) are outlined (Figure 3):

1. In patients with tolerated or hemodynamically supportable VT, VT was ablated using activation and entrainment mapping. After VT termination, ablation continued in SR aiming at the complete abolition of LPs (1A) when present or EPs when absent (1B).
2. In patients with noninducible or hemodynamically unsupportable VT, ablation was performed during SR, targeting LP areas when present (2A) and EPs when absent (2B).
3. In patients without inducible VT and without electrogram-guided targets (as previously defined), ablation was undertaken using pace mapping (assessing for 12/12 match with a clinical VT if available or with anatomic and scar-based lines [3]).

Radiofrequency current was delivered with a 3.5- or a 4-mm open-irrigated catheter with power settings of 30 to 60 W and a temperature limit of 43°C. Catheter preference included contact force assessment since available, which as we have shown improves LP identification.[12] By study design, we aimed to achieve the combined procedural end point of VT noninducibility (narrow definition of VT inducibility, excluding VF) and LP abolition (endocardial and epicardial when assessed) in all cases. Patients who were baseline inducible but who did not have PVS at the end of the procedure, either because they were in VT or because clinical deterioration prevented this, were considered inducible for the analysis. Patients were grouped into 3 based on their final postablation status for the primary analysis: group A, noninducible with LP abolition; group B, noninducible without LP abolition; and group C, inducible.

Follow-Up

Patients underwent 5 days of 12-lead ECG telemetry in the VTU to monitor for early VT recurrence postoperatively with amiodarone therapy reinstituted if necessary. In cases of drug-refractory VT recurrence, catheter ablation was repeated. Regular outpatient follow-up visits were scheduled at 3-monthly intervals or whenever any symptoms recurred.

Primary end points of the study were the recurrence of sustained mono- or polymorphic VT/VF triggering ICD intervention as well as the occurrence of cardiac death and sudden cardiac death (defined as death resulting from malignant ventricular arrhythmias occurring within 1 hour of the onset of symptoms). For secondary analyses, early VT recurrence was defined as that occurring within 3 months of ablation.

Statistical Analysis

Continuous variables are presented as means (±SD) or medians (interquartile range or range if specified) and categorical variables as numbers and percentages. Comparisons between groups were undertaken using the *t* test or nonparametric tests for continuous variables and Fisher exact test or χ^2 test for proportions as indicated. Agreement was assessed using Cohen κ coefficient. Event-free survival was estimated by the Kaplan–Meier method using the log-rank test. Univariate Cox proportional hazard analyses were used to assess the relationship between background characteristics and procedural end points with respect to time to VT recurrence and cardiac death. Baseline variables that were significantly ($P \leq 0.05$) related to the primary end points in the univariate analyses were entered into a forward stepwise logistic regression analysis. The resulting model was confirmed with backward analysis. Differences were considered statistically significant at the 2-sided $P<0.05$ level. All analyses were undertaken using IBM SPSS Statistics version 21 (IBM Corporation).

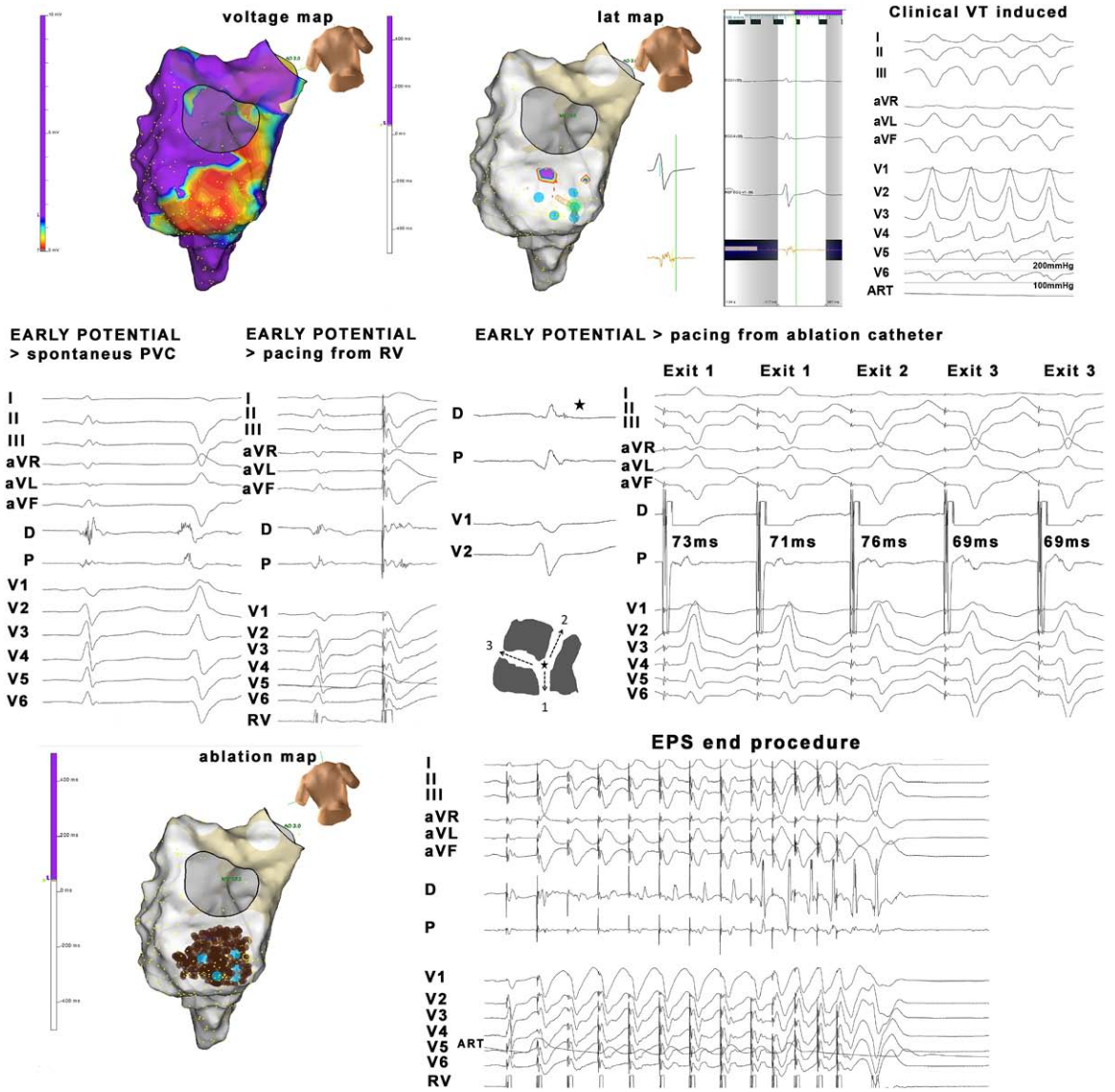

Figure 1. Case illustrating early potential (EP) assessment in a patient with an inferior myocardial infarction and no late potentials. **Top** (**left** to **right**), Bipolar voltage map showing an inferior infarct, and activation map showing lack of late potentials and induced clinical ventricular tachycardia (VT) morphology. The VT was not tolerated and therefore not mappable using either activation or entrainment mapping. **Middle** (**left** to **right**), A spontaneous ventricular ectopic with a similar morphology to the clinical VT dissociates the sharp near-field and far-field electrograms with the near-field electrogram becoming early with respect to the QRS complex, and remote pacing from the right ventricle (RV) also dissociates the component electrograms with the near-field now later than the far-field and pacing from the ablation catheter (amplitude, 10 mV; pulse width, 2 ms) showing a long stimulus to QRS >40 ms. The stimulus to QRS interval reflects the conduction time from the stimulus site to the edge of the scar (see theoretical circuit). The QRS configuration differs from that of ventricular tachycardia in exit 1 and exit 3; however exit 2 is close to the exit site of the clinical VT. **Bottom** (**left** to **right**), After substrate ablation targeting EPs, the electrophysiological study with 4 extrastimuli was negative. EPS indicates electrophysiological study; and PVC, premature ventricular contraction.

Results

One hundred sixty patients (154 [96%] male; aged 70.0±8.1 years) underwent VT ablation for post-MI VT during the study period. Five were excluded from the combined end point analysis because they could not be assigned to any procedural end point group (1 death, 1 contraindication to PVS, and 3 noninducible after VT mapping/ablation but without baseline LP mapping). The background characteristics of the 155 patients, according to group, are shown in Table 1. Patients in group A more frequently had a prior catheter ablation than those in group B (P=0.04); otherwise there were no significant differences. Compared with group A, group C patients had a lower LV ejection fraction (P=0.01) and increased New York Heart Association class IV association (P≤0.01). No patients were lost to follow-up with a median follow-up time of 563 (365–870) days.

VT Ablation Procedure

Procedural characteristics and findings are shown in Table 2. Twelve patients required invasive hemodynamic support (9 intra-aortic balloon pump, 3 extracorporeal membrane oxygenation) and a combined endo-epicardial approach was used in 32

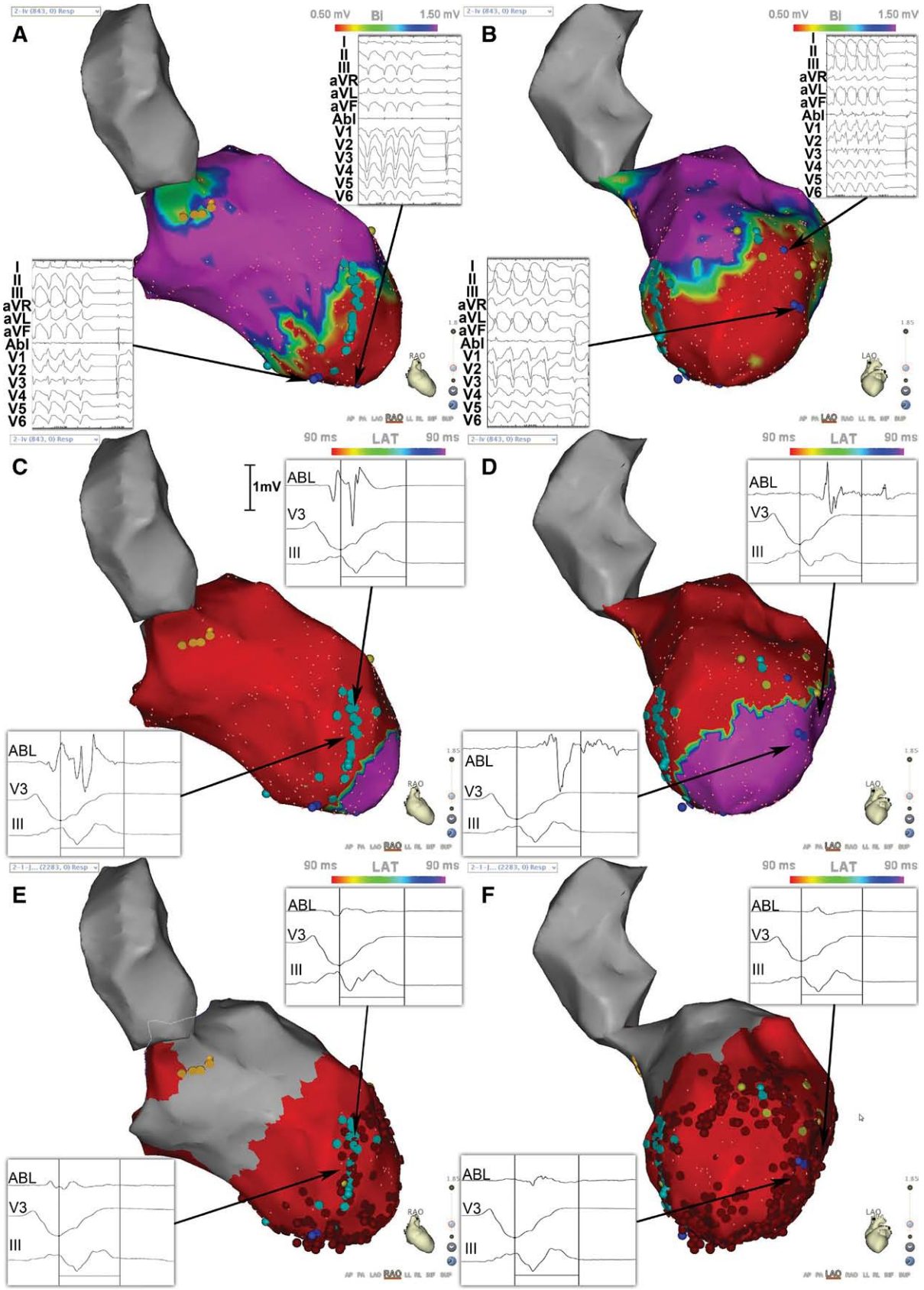

Figure 2. A (right anterior oblique [RAO] view) and **B** (left anterior oblique [LAO] view), Bipolar findings of a large apical myocardial infarction (MI) with 2 septal and 2 lateral ventricular tachycardia (VT) termination sites. **C** (RAO), A line (blue dots) of septal early potentials (fractionated and isolated insets), unidentified by the late potential (LP) map. **D** (LAO), Lateral LPs (fractionated and isolated insets). **E** and **F**, The remap, with ablation points, verifying successful LP abolition with the anteroapical portion of the LP area being isolated by proximal entry site ablation. ABL indicates ablation distal electrogram; and LAT, local activation time.

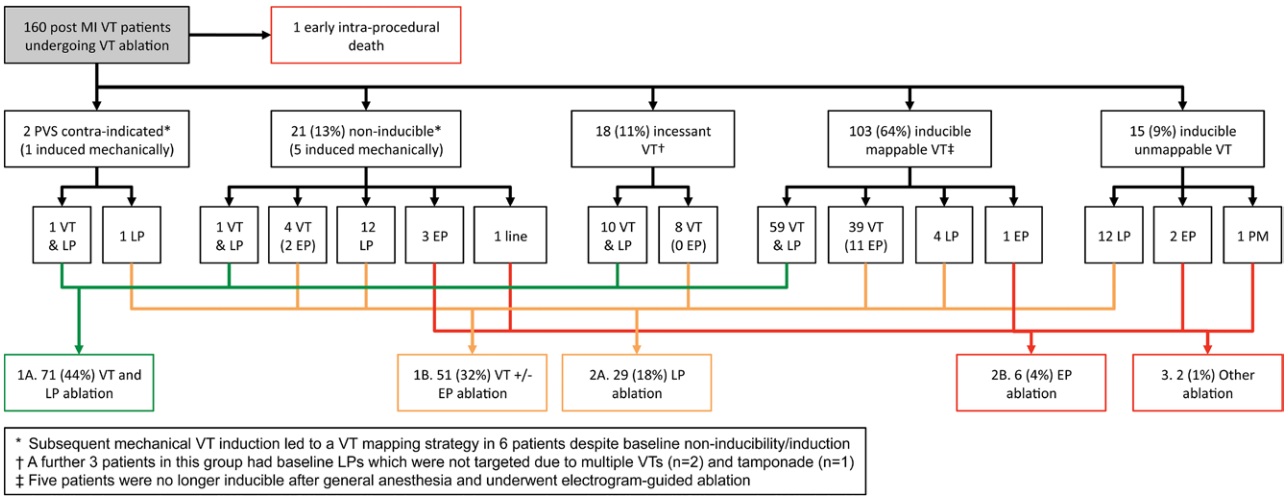

Figure 3. Flowchart for ventricular tachycardia (VT) ablation in 160 post–myocardial infarction (MI) patients indicating the primary ablation strategy used (see text). In the absence of a primary strategy based on VT inducibility and late potentials (LPs) a secondary strategy based on early potentials (EPs) was undertaken. PM indicates pace mapping; PVC, premature ventricular contraction; and PVS, programmed ventricular stimulation.

(21%) procedures. Figure 4 provides a study flowchart describing VT inducibility and LP mapping pre-/postablation and combined procedural end point data and grouping. Of the 160 patients, 137 (86%) were either inducible or in VT at baseline with 21 (13%) noninducible and 2 with a relative contraindication to PVS (left atrial appendage thrombus) and 103 (65%) had baseline LP presence, of which 79 (77%) underwent successful LP abolition. Postablation, 19 either remained inducible or in VT or had clinically deteriorated prohibiting further PVS and were considered inducible for the combined end point analysis (group C), of which, 5 underwent apparently successful LP abolition, 5 had LP abolition failure, 6 had no identifiable LPs, and 3 did not undergo baseline LP mapping. Sixty-three (41%) were noninducible with either failed LP abolition or no baseline LP presence (group B), and 73 (47%) were noninducible with successful LP abolition (group A). Five were excluded as described.

Complications

Of the 160 patients, 4 (2.5%) died in hospital. Causes were heart failure, pneumonia, hepatorenal failure, and intraprocedural refractory VF. One patient had cardiac tamponade needing emergency surgery. One patient had a postoperative acute coronary syndrome, and 1 patient developed a tracheal hematoma, both needing intervention. One patient developed a subdiaphragmatic hematoma after epicardial puncture treated conservatively. Two patients with ICDs developed complete atrioventricular block, and there were 5 femoral vascular complications, treated conservatively. These accounted for an overall 7% nonfatal complication rate with 4% not requiring intervention.

Postprocedural Management

Eighteen in-hospital VT recurrences occurred, 6 treated medically and 12 with redo ablation procedures. Of the 81 (52%) currently on amiodarone therapy (65% excluding those with prior amiodarone-related side effects), 38 (25%) were discharged on this (P<0.01) with 133 (86%) on a conventional β-blocker. Of the 10 patients without a pre-existing ICD, 3 underwent ICD implantation postablation. The remaining 7 had preserved LV function and underwent predischarge negative PVS. Nine patients underwent upgrading to a biventricular defibrillator (4 in group A, 5 in group B).

VT Recurrence

Fifty patients (32%) had a VT recurrence during the follow-up period with a median recurrence time of 82 (16–192) days. Patients who fulfilled the combined end point of VT noninducibility and LP abolition exhibited a significantly lower incidence of VT recurrence compared with noninducible patients at the end of the procedure without additional LP abolition (16.4% versus 46.0%; log-rank P<0.01) and those with VT inducibility (16.4% versus 47.4%; log-rank P<0.01), whereas no difference occurred between noninducible patients without LP abolition and inducible ones (46.0% versus 47.4%; log-rank P=0.44; Figure 5A). Including only patients with baseline LP presence (n=102), the agreement between LP abolition and noninducibility was fair (κ=0.24±0.21; P≤0.01). Considering those with baseline LP presence and final noninducibility, achieving LP abolition was associated with a lower incidence of VT recurrence compared with those with failed LP abolition (16.4% versus 57.9%; log-rank P<0.01; Figure 5B).

Significant univariate predictors of VT recurrence were LV ejection fraction (hazard ratio [HR], 0.97; P=0.03), endocardial LP presence (HR, 0.53; P=0.01), endocardial or epicardial LP presence (HR, 0.55; P=0.04), LP abolition (HR, 0.40; P<0.01), increased number of procedural VTs (HR, 1.29; P=0.05), postprocedural VT inducibility (narrow, not broad definition; HR, 2.35; P=0.02), and the combined end point of VT noninducibility and LP abolition (HR, 0.21; P<0.01; Table 3). After multivariate analysis, only the combined end point of VT noninducibility and LP abolition (HR, 0.21; P<0.01) remained significant predictors of VT recurrence (Table 4).

Subanalysis examined the predictors of early VT recurrence (27/50 recurrences). Univariate predictors were

Table 1. Presentation Characteristics of the Study Population (n=155)

	Noninducible With LP Abolition (n=73)	Noninducible Without LP Abolition (n=63)	1 vs 2 *P* Value	Inducible (n=19)	1 vs 3 *P* Value
Male sex	70 (96%)	63 (100%)	0.25	16 (84%)	0.10
Age	70.2±7.8	69.2±8.7	0.48	70.6±7.2	0.83
Clinical history					
LVEF, %	34.1±9.2	31.2±9.6	0.07	27.9±9.5	0.01
Prior ablation	20 (27%)	8 (13%)	0.04	5 (26%)	0.93
Prior amiodarone	49 (67%)	42 (67%)	0.96	12 (63%)	0.75
Discharge amiodarone	14 (19%)	15 (24%)	0.47	9 (47%)	0.01
ES/incessant VT	27 (37%)	21 (33%)	0.66	8 (42%)	0.68
Revascularization					
None	18 (25%)	16 (25%)	0.24	6 (32%)	0.23
CABG	22 (30%)	11 (18%)		3 (16%)	
PCI	21 (29%)	27 (43%)		9 (47%)	
CABG and PCI	12 (16%)	9 (14%)		1 (5%)	
NYHA class					
I	14 (19%)	11 (18%)	0.30	2 (11%)	<0.01
II	37 (51%)	28 (44%)		5 (26%)	
III	21 (29%)	19 (30%)		7 (37%)	
IV	1 (1%)	5 (8%)		5 (26%)	
Coronary disease					
Single vessel	21 (29%)	17 (27%)	1.00	10 (53%)	0.22
Double vessel	18 (25%)	16 (25%)		5 (26%)	
Triple vessel	34 (47%)	30 (48%)		4 (21%)	
MI territory					
Anterior	20 (27%)	24 (38%)	0.08	9 (47%)	0.25
Inferior	48 (66%)	30 (48%)		9 (47%)	
Anterior and inferior	5 (7%)	9 (14%)		1 (5%)	
ICD					
None	4 (6%)	3 (5%)	0.98	2 (11%)	0.48
Single chamber	17 (23%)	16 (25%)		2 (11%)	
Dual chamber	33 (45%)	29 (46%)		8 (42%)	
Biventricular	19 (26%)	15 (24%)		7 (37%)	

CABG indicates coronary artery bypass surgery; ES, electrical storm; ICD, implantable cardioverter defibrillator; LP, late potential; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; and VT, ventricular tachycardia.

endocardial LP presence (HR, 0.43; *P*=0.01), endocardial or epicardial LP presence (HR, 0.44; *P*=0.04), LP abolition (HR, 0.20; *P*<0.01), discharge amiodarone (HR, 3.02; *P*≤0.01), and the combined end point of VT noninducibility and LP abolition (HR, 0.21; *P*=0.01) in contrast to postprocedural VT inducibility (either narrow or broad definition) and ejection fraction. All of the above variables remained statistically significant in successive multivariate models.

Beyond the 12 patients who underwent redo procedures before discharge, redo VT ablation was performed in an additional 14 patients. Of these, only 1 of 26 remained inducible, 14 (53.8%) were noninducible with either failed LP abolition or no baseline LP (12%) presence, and 11 (42.3%) were noninducible with successful LP abolition. Patients who fulfilled the combined end point of VT noninducibility and LP abolition had a lower incidence of VT recurrence after the last procedure compared with noninducible patients with failed LP abolition (9.1% versus 50%; log-rank *P*<0.01). In fact, LP abolition turned out to be the only predictor of VT recurrence in these patients with a redo procedure (HR, 0.10; *P*=0.03).

Cardiac Death

Nine patients (6%) died from noncardiac and 17 (11%) from cardiac causes during the study period (15 because of cardiac decompensation and 2 sudden deaths). In those who died from cardiac causes, median time to death from the first procedure was 63 (15–418) days.

Early VT recurrence was associated with a marked increased incidence of cardiac death (22.2% versus 8.6%; log-rank *P*=0.02). Patients who fulfilled the combined end point of VT

Table 2. Procedural Data

	Noninducible With LP Abolition (n=73)	Noninducible Without LP Abolition (n=63)	1 vs 2 *P* Value	VT Inducible (n=19)	1 vs 3 *P* Value
Hospital stay					
Inpatient stay, d	8 (7–13)	9 (7–14)	0.25	14 (9–17)	<0.01
Procedural parameters					
Procedure time, min	220 (180–255)	210 (180–240)	0.52	270 (180–330)	0.05
Endo-epicardial access, %	15 (21%)	11 (18%)	0.65	6 (32%)	0.38
Endocardial RF time, min	25.5 (18–38.5)	23.5 (16.2–32)	0.31	25.5 (17.7–32.2)	0.66
Epicardial RF time, min	6 (2–20)	8 (2–22.5)	0.94	5 (0–8.7)	0.35
Baseline VT inducibility					
Monomorphic VT inducibility	56 (77%)	46 (73%)	0.62	14 (74%)	0.77
VF inducible	0 (0%)	1 (2%)	0.46	0 (0%)	0.46
Incessant VT	6 (8%)	7 (11%)	0.57	4 (21%)	0.21
VT noninducible	11 (15%)	9 (14%)	0.90	0 (0%)	0.11
VT characteristics					
VT in procedure (≠)	1 (1–2)	2 (1–2)	0.34	2 (1–3)	0.01
VT ablated in procedure (≠)	1 (0–1)	1 (0–2)	0.07	1 (0–1)	0.25
Nontolerated VT	30 (41%)	27 (43%)	1.00	7 (37%)	0.95
Clinical VT ablated/documented	24/44 (55%)	31/49 (63%)	0.39	7/14 (50%)	0.77
Final VT inducibility					
VT noninducibility (broad)	66 (90%)	55 (87%)	0.56	0 (0%)	<0.01
VT noninducibility (narrow)	73 (100%)	63 (100%)	0.56	0 (0%)	<0.01
Electrogram-based parameters					
Endocardial LP presence	72/73 (99%)	18/63 (29%)	<0.01	10/16 (62.5%)	<0.01
Epicardial LP presence	10/15 (67%)	6/11 (55%)	0.74	3/6 (50%)	0.43
Endo- or Epicardial LP presence	73 (100%)	19/63 (30%)	<0.01	10/16 (62.5%)	<0.01
Endocardial LP abolition	72/72 (100%)	2/18 (11%)	<0.01	5/10 (50%)	<0.01
Epicardial LP abolition	10/10 (100%)	2/6 (33%)	<0.01	0/3 (0%)	<0.01
LP abolition	73 (100%)	0 (0%)	<0.01	4/16 (25%)	<0.01
EP ablation	9/73 (12%)	18/63 (29%)	0.02	4/19 (21%)	0.46
Outcome					
Follow-up time, d	590 (422–885)	556 (364–858.5)	0.91	255 (44–500)	0.02
Time to VT recurrence, d	112 (64.7–336.5)	70 (6–197.5)	0.17	72 (17–246.5)	0.38
VT recurrence	12 (16%)	29 (47%)	<0.01	9 (47%)	<0.01
Cardiac death	3 (4%)	6 (10%)	0.25	8 (42%)	<0.01
Noncardiac death	3 (4%)	5 (8%)	0.47	1 (5%)	1.00

EP indicates early potential; LP, late potential; RF, radiofrequency; VF, ventricular fibrillation; and VT, ventricular tachycardia.

noninducibility and LP abolition compared with those with VT inducibility exhibited a significantly lower incidence of cardiac death (4.1% versus 42.1%; log-rank $P<0.01$). Moreover, noninducible patients at the end of the procedure (without additional LP abolition) also had a lower incidence of cardiac death compared with VT inducible patients (9.5% versus 42.1%; log-rank $P<0.01$), whereas the difference between noninducible patients with and without LP abolition was not significant (4.1% versus 9.5%; log-rank $P=0.25$; Figure 5C). Cardiac death was highly related to final VT inducibility status in the overall population (6.6% versus 42.1%; log-rank $P<0.01$).

Univariate predictors of cardiac death were female sex (HR, 4.80; $P=0.04$), New York Heart Association class (HR, 2.69; $P<0.01$), atrial fibrillation (HR, 2.73; $P=0.05$), endocardial LP presence (HR, 0.35; $P=0.01$), LP abolition (HR, 0.32; $P=0.05$), VT inducibility (narrow [HR, 8.71; $P<0.01$] and broad [HR, 3.70; $P=0.01$] definitions), and the combined end point, both in noninducible patients with LP abolition (HR, 0.08; $P<0.01$) and those without LP abolition (HR, 0.17; $P<0.01$), and are shown in Table 3.

After multivariate analysis, New York Heart Association class (HR, 2.03; $P=0.02$) and the combined end point remained significant predictors of cardiac death (Table 4). For the combined end point, VT noninducibility and LP abolition (HR, 0.11; $P\leq0.01$) and VT noninducibility without LP abolition (HR, 0.21; $P<0.01$) were significant as compared with inducible patients.

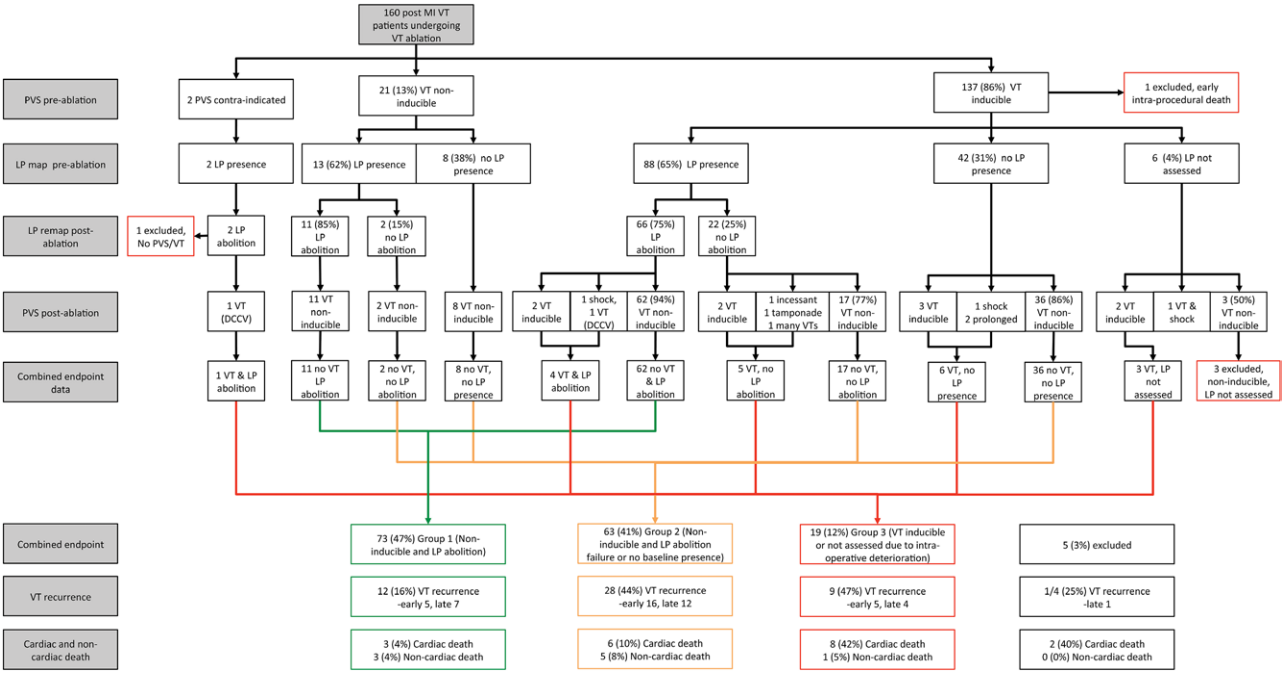

Figure 4. Procedural flowchart of 160 post–myocardial infarction (MI) patients undergoing ventricular tachycardia (VT) ablation. Results of pre- and postablation VT inducibility and late potential (LP) status are presented. Patients were classified using the combined end point into 3 groups, where possible (155/160 patients), and respective VT recurrence and mortality rates are presented. PVS indicates programmed ventricular stimulation.

Discussion

We have previously shown that successful catheter ablation for VT, as judged by postprocedural inducibility, can favorably affect VT recurrence and cardiac mortality in the setting of a dedicated VTU.[8] In this report, we have focused on our current procedural strategy that is based on both VT and SR mapping, targeting VT and LPs when present, in post-MI patients with a high prevalence (94%) of previously implanted ICDs. The main study findings are as follows:

1. Two thirds of post-MI patients presenting for VT ablation have mappable LPs, and in 80% these can be eliminated with current techniques. Considering that 13% were noninducible at baseline, a combined end point approach allowed 97% of patients to be treated systematically.
2. Achieving the combined procedural end point of VT noninducibility and LP abolition, in patients needing single or multiple interventions, reduces VT recurrence to exceptionally low levels (16%), now comparable with other complex arrhythmias, such as paroxysmal atrial fibrillation ablation.
3. VT inducibility using the narrow (excluding VF), as opposed to the broad, definition is a superior predictor of VT recurrence.
4. Early VT recurrence is highly predictive of cardiac death.
5. In the setting of a dedicated VTU, VT ablation can be safely undertaken with an acceptably low periprocedural death and complication rates, including the use of an epicardial approach, when LPs were found to be remarkably prevalent (≈60%).

End Points: VT Noninducibility

Important acute diagnostic issues with PVS include daily baseline variability, effects of changing antiarrhythmic/sedation/general anesthetic therapy, drive cycle, extrastimuli protocol and pacing site dependence, inconsistent clinical/nonclinical VT induction, and induction of VF in healthy individuals using aggressive protocols, the so-called nonspecific response.[9,13] We have presented our data using narrow and broad definitions of VT inducibility.[11] In accordance with the Multicenter Automatic Defibrillator Implantation Trial (MADIT) II, the narrow definition of noninducibility was more predictive of VT recurrence.[11] Taking into consideration the above limitations, we consider any inducible sustained monomorphic VT as a marker for arrhythmogenic substrate and possible VT recurrence and therefore use this as an indispensable procedural end point. Furthermore, in one third of patients we did not identify LPs necessitating an approach based mostly on VT mapping and ablation. We observed that a large proportion of noninducible patients recur; however, with the additional proof of substrate modification, such as with LP abolition and other techniques under investigation, the prognostic value of noninducibility as an end point can be enhanced.

End Points: LP Abolition

Because VT inducibility testing is hampered by unsatisfactory reproducibility and in 13% of our cases baseline noninducibility, a strategy aiming to abolish all potential circuits is additive. Additionally, mapping and ablating during SR improve hemodynamic stability, especially when faced with patients who have poorly tolerated VT, several VTs, VTs with rapidly changing morphologies, polymorphic VT/VF, or VTs

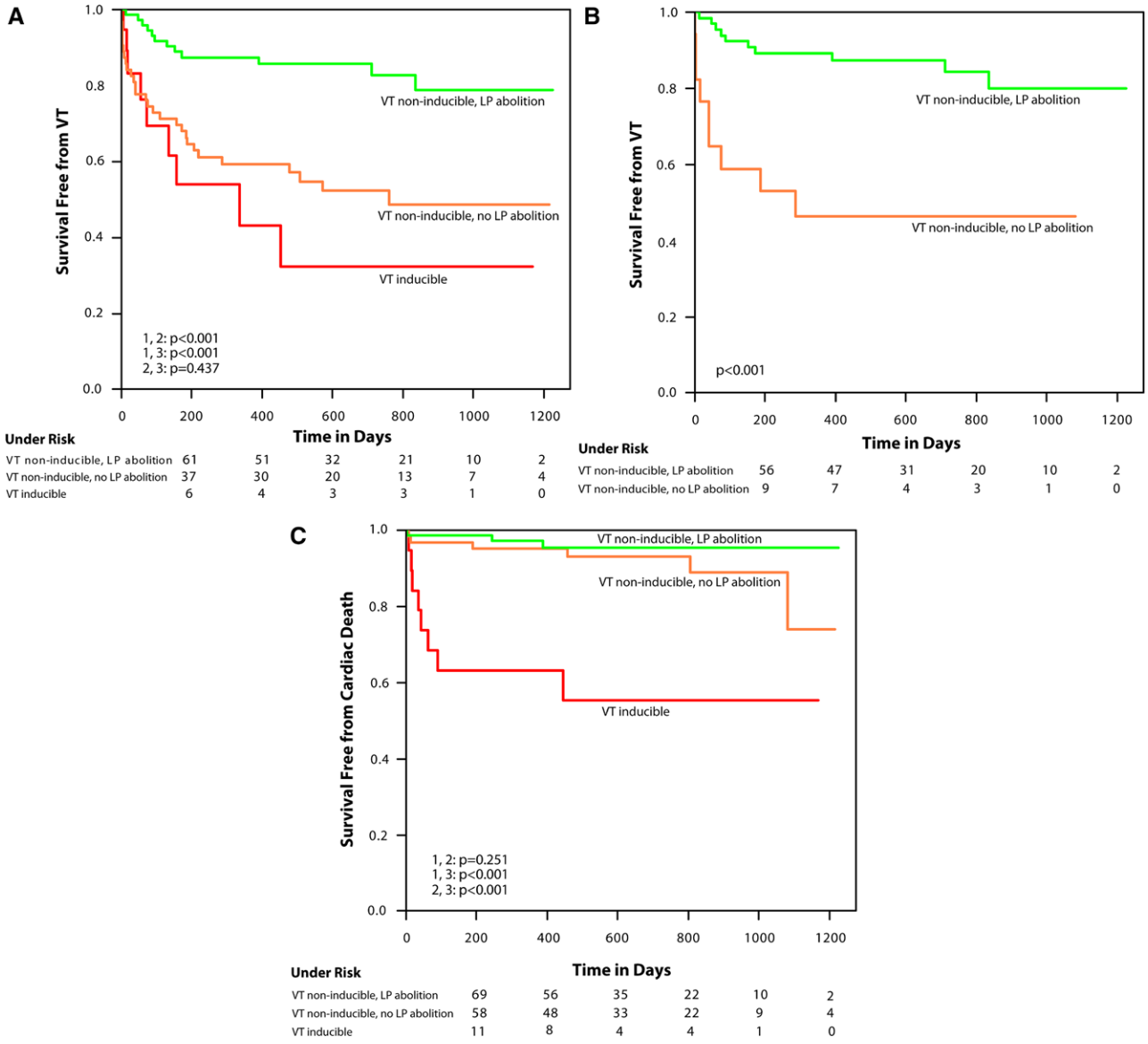

Figure 5. Kaplan–Meier curves comparing freedom from ventricular tachycardia (VT) recurrence according to group (**A**), and in only those with baseline late potential (LP) presence (**B**). **C**, Kaplan–Meier curve comparing freedom from cardiac death according to group.

that are difficult to terminate within a reasonable time frame. One may consider invasive hemodynamic support, but this is an escalation of care, necessitating postoperative intensive care unit, thus increasing postoperative risk. Thus, we reserved this for the minority of cases (8%) who developed severe hypotension and low cardiac output state despite high-dose inotropic support.

Other strategies for VT ablation in SR include scar-based ablation using linear or encircling lesions to divide the VT re-entry isthmus.[14–17] Isolated LPs and conducting channels in SR have been shown to correlate with VT circuit isthmuses and can be used as a target for substrate ablation in SR.[18,19] We have previously demonstrated that successful LP abolition reduces VT recurrence, and we have systematically instituted this as a second procedural end point in patients with structural heart disease.[7] This end point can be clearly defined by systematically remapping and documenting the presence or the absence of LPs after ablation, with further ablation if necessary and feasible. We consider high-density mapping using 3-dimensional EAM systems mandatory for this approach.

Prior VT Ablation Studies

In the randomized Substrate Mapping and Ablation in Sinus Rhythm to Halt Ventricular Tachycardia (SMASH-VT) trial (128 patients), catheter ablation reduced ICD therapies by 65% during a 2-year follow-up in post-MI patients receiving ICDs for secondary prevention.[5] The main ablation strategy used pace mapping and subsequent scar-based ablation in SR, although VTs and LPs were targeted in some cases. The Ventricular Tachycardia Ablation in Coronary Heart Disease (VTACH) study randomized 107 post-MI patients

Table 3. Univariate Cox Regression Analysis of VT Recurrence and Cardiac Mortality

	VT Recurrence		Cardiac Mortality	
	HR (95% CIs)	*P* Value	HR (95% CIs)	*P* Value
Age, y	0.99 (0.96–1.03)	0.70	1.02 (0.96–1.08)	0.59
Female sex	1.27 (0.31–5.23)	0.74	4.80 (1.08–21.32)	0.04
Ejection fraction, %	0.97 (0.94–1.00)	0.03	0.97 (0.92–1.03)	0.32
NYHA class	1.26 (0.88–1.79)	0.20	2.69 (1.47–4.95)	0.01
ES/incessant VT (yes/no)	1.11 (0.63–1.96)	0.77	0.84 (0.34–2.41)	0.90
Endocardial LP presence	0.53 (0.32–0.87)	0.01	0.35 (0.16–0.78)	0.01
LP presence	0.55 (0.31–0.97)	0.04	0.45 (0.16–1.23)	0.12
LP abolition*	0.24 (0.11–0.50)	<0.01	0.39 (0.09–1.75)	0.22
LP abolition	0.30 (0.16–0.56)	<0.01	0.32 (0.10–1.00)	0.05
EP ablation	1.06 (0.53–2.12)	0.87	2.19 (0.81–5.95)	0.12
Nontolerated VT	1.59 (0.90–2.79)	0.11	1.14 (0.42–3.06)	0.80
Baseline VT inducibility (narrow)	1.94 (0.70–5.38)	0.21	2.82 (0.37–21.33)	0.32
VTs in procedure (≠)	1.29 (1.00–1.66)	0.05	1.38 (0.91–2.10)	0.13
VTs terminated (≠)	1.05 (0.75–1.48)	0.79	1.36 (0.86–2.45)	0.27
Final VT inducibility (broad)	1.66 (0.89–3.08)	0.11	3.70 (1.43–9.62)	0.01
Final VT inducibility (narrow)	2.35 (1.13–4.86)	0.02	8.71 (3.23–21.9)	<0.01
Combined end point vs VT inducibility		<0.01		<0.01
VT noninducible and LP abolition	0.21 (0.09–0.50)	<0.01	0.08 (0.02–0.28)	<0.01
VT noninducible without LP abolition	0.76 (0.35–1.56)	0.42	0.17 (0.06–0.49)	<0.01
Discharge amiodarone	1.76 (0.97–3.20)	0.06	1.92 (0.63–5.87)	0.26

CI indicates confidence interval; EP, early potential; ES, electrical storm; HR, hazard ratio; LP, late potential; NYHA, New York Heart Association; and VT, ventricular tachycardia.

*Only patients with baseline LP presence (n=102).

with stable VT to ICD implantation and VT ablation (VT mapping and scar-based linear lesions without targeting LPs) or ICD implantation alone.[6] At 2 years, VT-free survival was 47% in the ablation group and 29% in the control group. In the Cooled RF trial (146 patients), 46% of patients developed a VT recurrence with a mean follow-up of 243 days, and this was unrelated to VT inducibility at the end of the procedure.[10] In the multicenter Thermocool Ventricular Tachycardia Ablation Trial (231 post-MI patients) catheter ablation focused on VT noninducibility was highly effective in reducing VT recurrence, yet the 1-year cardiac mortality rate remained high at 13%. In our study, with a median follow-up time of 1.5 years, the redo rate was low at 16%, with a VT recurrence rate of 32% after 1 procedure and 21% after redo procedures, comparing favorably with prior studies. The yearly cardiac mortality rate was 7% including an in-hospital death rate of 2.5%, which is relatively low in a population characterized by heart failure and multiple comorbidities. In 70 patients with ischemic and idiopathic dilated cardiomyopathy, Jaïs et al[20] assessed the impact of successful ablation of local abnormal ventricular activity as a single procedural end point on the combined outcome of VT recurrence and all-cause mortality. The observed benefit was primarily driven by LP abolition on VT recurrence, consistent with our findings.[20]

Table 4. Multivariate Cox Regression Analysis of VT Recurrence and Cardiac Mortality

	HR (95% CIs)	*P* Value
VT recurrence		
Combined end point vs VT inducibility		<0.01
VT noninducible and LP abolition	0.21 (0.09–0.49)	<0.01
VT noninducible without LP abolition	0.70 (0.33–1.49)	0.35
Cardiac death		
Combined end point vs VT inducibility		<0.01
VT noninducible and LP abolition	0.11 (0.03–0.42)	<0.01
VT noninducible without LP abolition	0.21 (0.07–0.62)	<0.01
NYHA class	2.03 (1.11–3.70)	0.02

CI indicates confidence interval; HR, hazard ratio; LP, late potential; NYHA, New York Heart Association; and VT, ventricular tachycardia.

Study Findings

The combined end point of VT noninducibility and LP abolition was associated with a 5-fold reduction in VT recurrence and a 10-fold reduction in cardiac mortality as compared with inducible patients and was achievable in 47% of cases. In a further 41%, only noninducibility was achieved, and this was associated with a similar mortality but markedly higher VT recurrence. In this group, only 30% had mappable LPs suggestive of a different substrate that is less amenable to ablation that is associated with a higher VT recurrence rate. Early VT recurrence was closely linked to cardiac death, suggesting that the lack of an observed mortality difference

between groups A and B may have been because of an insufficient study population size or follow-up duration as the annual cardiac mortality rate was low among noninducible patients (≈4%). A striking observation from this study relates to sex differences, with a high prevalence of men undergoing VT ablation yet a higher mortality in women. This is partly explained by the lower prevalence of women with ICDs (≈20% of the overall ICD population), but it is also concerning to note that women may receive less mortality benefit from ICDs and, possibly, VT ablation as well.[21] Remarkably, electrical storm and incessant VT presentations did not predict VT recurrence or death suggesting that our management of these patients in particular has improved in recent years.

Post-MI patients present the prototype substrate for SR-based mapping and ablation, yet we only achieved a combined end point in half of these patients. Reasons for this are several fold. First, current LP abolition rates only reach 80%, mainly because of limitations of radiofrequency as an energy source. Second, LPs may be intramural or epicardial and thus unmapped. Additionally, LPs may recover postablation, and ablation itself may introduce LPs. LPs present a clear end point for substrate ablation; however, the same is not true for EPs, as at present, there is no SR mapping technique for rapidly discerning those that relate to VT isthmuses. Pacing maneuvers can help but are time consuming to undertake in a systematic fashion when using high-density mapping. New contact multipolar mapping catheter technologies, allowing greater point density and definition and faster mapping, may allow us to overcome these issues with EP characterization and subsequent documentation of their disappearance postablation.

Limitations

This is a single-center prospective analysis of our current ablation strategy, not a randomized controlled trial assessing catheter ablation against medical therapy or one strategy versus another.

Conclusions

Achieving a combined catheter ablation procedural end point of VT noninducibility and LP abolition reduces VT recurrence and cardiac mortality in post-MI patients who already have implanted ICDs. In the setting of a specialized VTU, using modern mapping and ablation techniques, this allows overall VT recurrence and mortality rates to be significantly reduced as compared with prior reports.

Acknowledgments

We thank all the staffs at the San Raffaele VTU and intensive care unit for their tireless work and professionalism.

Disclosures

Dr Della Bella is a consultant for St. Jude Medical and has received honoraria for lectures from Biosense Webster, St Jude Medical, and Biotronik. Drs Silberbauer and Oloriz are Advanced European Heart Rhythm Association Fellows with grants funded by Biosense Webster. The other authors report no conflicts.

References

1. Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, Levine JH, Saksena S, Waldo AL, Wilber D, Brown MW, Heo M. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med*. 1996;335:1933–1940.
2. Goldenberg I, Gillespie J, Moss AJ, Hall WJ, Klein H, McNitt S, Brown MW, Cygankiewicz I, Zareba W; Executive Committee of the Multicenter Automatic Defibrillator Implantation Trial II. Long-term benefit of primary prevention with an implantable cardioverter-defibrillator: an extended 8-year follow-up study of the Multicenter Automatic Defibrillator Implantation Trial II. *Circulation*. 2010;122:1265–1271.
3. Poole JE, Johnson GW, Hellkamp AS, Anderson J, Callans DJ, Raitt MH, Reddy RK, Marchlinski FE, Yee R, Guarnieri T, Talajic M, Wilber DJ, Fishbein DP, Packer DL, Mark DB, Lee KL, Bardy GH. Prognostic importance of defibrillator shocks in patients with heart failure. *N Engl J Med*. 2008;359:1009–1017.
4. Anderson KP. Sudden cardiac death unresponsive to implantable defibrillator therapy: an urgent target for clinicians, industry and government. *J Interv Card Electrophysiol*. 2005;14:71–78.
5. Reddy VY, Reynolds MR, Neuzil P, Richardson AW, Taborsky M, Jongnarangsin K, Kralovec S, Sediva L, Ruskin JN, Josephson ME. Prophylactic catheter ablation for the prevention of defibrillator therapy. *N Engl J Med*. 2007;357:2657–2665.
6. Kuck KH, Schaumann A, Eckardt L, Willems S, Ventura R, Delacrétaz E, Pitschner HF, Kautzner J, Schumacher B, Hansen PS; VTACH study group. Catheter ablation of stable ventricular tachycardia before defibrillator implantation in patients with coronary heart disease (VTACH): a multicentre randomised controlled trial. *Lancet*. 2010;375:31–40.
7. Vergara P, Trevisi N, Ricco A, Petracca F, Baratto F, Cireddu M, Bisceglia C, Maccabelli G, Della Bella P. Late potentials abolition as an additional technique for reduction of arrhythmia recurrence in scar related ventricular tachycardia ablation. *J Cardiovasc Electrophysiol*. 2012;23:621–627.
8. Della Bella P, Baratto F, Tsiachris D, Trevisi N, Vergara P, Bisceglia C, Petracca F, Carbucicchio C, Benussi S, Maisano F, Alfieri O, Pappalardo F, Zangrillo A, Maccabelli G. Management of ventricular tachycardia in the setting of a dedicated unit for the treatment of complex ventricular arrhythmias: long-term outcome after ablation. *Circulation*. 2013;127:1359–1368.
9. Cooper MJ, Hunt LJ, Richards DA, Denniss AR, Uther JB, Ross DL. Effect of repetition of extrastimuli on sensitivity and reproducibility of mode of induction of ventricular tachycardia by programmed stimulation. *J Am Coll Cardiol*. 1988;11:1260–1267.
10. Calkins H, Epstein A, Packer D, Arria AM, Hummel J, Gilligan DM, Trusso J, Carlson M, Luceri R, Kopelman H, Wilber D, Wharton JM, Stevenson W. Catheter ablation of ventricular tachycardia in patients with structural heart disease using cooled radiofrequency energy: results of a prospective multicenter study. Cooled RF Multi Center Investigators Group. *J Am Coll Cardiol*. 2000;35:1905–1914.
11. Daubert JP, Zareba W, Hall WJ, Schuger C, Corsello A, Leon AR, Andrews ML, McNitt S, Huang DT, Moss AJ; MADIT II Study Investigators. Predictive value of ventricular arrhythmia inducibility for subsequent ventricular tachycardia or ventricular fibrillation in Multicenter Automatic Defibrillator Implantation Trial (MADIT) II patients. *J Am Coll Cardiol*. 2006;47:98–107.
12. Mizuno H, Vergara P, Maccabelli G, Trevisi N, Eng SC, Brombin C, Mazzone P, Della Bella P. Contact force monitoring for cardiac mapping in patients with ventricular tachycardia. *J Cardiovasc Electrophysiol*. 2013;24:519–524.
13. Brugada P, Green M, Abdollah H, Wellens HJ. Significance of ventricular arrhythmias initiated by programmed ventricular stimulation: the importance of the type of ventricular arrhythmia induced and the number of premature stimuli required. *Circulation*. 1984;69:87–92.
14. Soejima K, Suzuki M, Maisel WH, Brunckhorst CB, Delacretaz E, Blier L, Tung S, Khan H, Stevenson WG. Catheter ablation in patients with multiple and unstable ventricular tachycardias after myocardial infarction: short ablation lines guided by reentry circuit isthmuses and sinus rhythm mapping. *Circulation*. 2001;104:664–669.
15. Stevenson WG, Wilber DJ, Natale A, Jackman WM, Marchlinski FE, Talbert T, Gonzalez MD, Worley SJ, Daoud EG, Hwang C, Schuger C, Bump TE, Jazayeri M, Tomassoni GF, Kopelman HA, Soejima K, Nakagawa H; Multicenter Thermocool VT Ablation Trial Investigators. Irrigated radiofrequency catheter ablation guided by electroanatomic mapping for recurrent ventricular tachycardia after myocardial infarction: the

multicenter thermocool ventricular tachycardia ablation trial. *Circulation*. 2008;118:2773–2782.
16. Marchlinski FE, Callans DJ, Gottlieb CD, Zado E. Linear ablation lesions for control of unmappable ventricular tachycardia in patients with ischemic and nonischemic cardiomyopathy. *Circulation*. 2000;101:1288–1296.
17. Tanner H, Hindricks G, Volkmer M, Furniss S, Kühlkamp V, Lacroix D, DE Chillou C, Almendral J, Caponi D, Kuck KH, Kottkamp H. Catheter ablation of recurrent scar-related ventricular tachycardia using electroanatomical mapping and irrigated ablation technology: results of the prospective multicenter Euro-VT-study. *J Cardiovasc Electrophysiol*. 2010;21:47–53.
18. Bogun F, Good E, Reich S, Elmouchi D, Igic P, Lemola K, Tschopp D, Jongnarangsin K, Oral H, Chugh A, Pelosi F, Morady F. Isolated potentials during sinus rhythm and pace-mapping within scars as guides for ablation of post-infarction ventricular tachycardia. *J Am Coll Cardiol*. 2006;47:2013–2019.
19. Arenal A, Glez-Torrecilla E, Ortiz M, Villacastín J, Fdez-Portales J, Sousa E, del Castillo S, Perez de Isla L, Jimenez J, Almendral J. Ablation of electrograms with an isolated, delayed component as treatment of unmappable monomorphic ventricular tachycardias in patients with structural heart disease. *J Am Coll Cardiol*. 2003;41:81–92.
20. Jaïs P, Maury P, Khairy P, Sacher F, Nault I, Komatsu Y, Hocini M, Forclaz A, Jadidi AS, Weerasooryia R, Shah A, Derval N, Cochet H, Knecht S, Miyazaki S, Linton N, Rivard L, Wright M, Wilton SB, Scherr D, Pascale P, Roten L, Pederson M, Bordachar P, Laurent F, Kim SJ, Ritter P, Clementy J, Haïssaguerre M. Elimination of local abnormal ventricular activities: a new end point for substrate modification in patients with scar-related ventricular tachycardia. *Circulation*. 2012;125:2184–2196.
21. Santangeli P, Pelargonio G, Dello Russo A, Casella M, Bisceglia C, Bartoletti S, Santarelli P, Di Biase L, Natale A. Gender differences in clinical outcome and primary prevention defibrillator benefit in patients with severe left ventricular dysfunction: a systematic review and meta-analysis. *Heart Rhythm*. 2010;7:876–882.

CLINICAL PERSPECTIVE

Catheter ablation is an effective treatment option in post–myocardial infarction patients with ventricular tachycardia (VT) refractory to medical therapy. The classical procedural end point is abolition of inducible VTs, targeting either the clinical VTs or all inducible VTs. We recently found that abolition of all inducible VTs is associated with better outcomes, and in this article we demonstrate that the addition of late potential abolition is associated with further benefit. Two thirds of post–myocardial infarction patients had late potentials, and in 80%, these were eliminated. The combined end point of VT noninducibility and late potential abolition was achieved in half of the patients and was associated with a VT recurrence rate of 16% that was significantly better than when noninducibility without late potential abolition was achieved. Considering that 13% of patients were noninducible at baseline, late potential abolition allows all patients to be treated systematically. In patients without late potentials or inducible VT at baseline, a strategy targeting abnormal early potentials that are inscribed within the QRS, but exposed by pacing maneuvers, was used. Further work is needed to understand how best to assess early potentials and clarify the additive value of late and early potential ablation on patient outcomes.