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New insights on post-myocardial infarction ventricular tachycardia ablation: defining patient-tailored endpoints to improve outcome

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Part II

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Re-assessing non-inducibility as ablation endpoint of post-infarction ventricular tachycardia: The impact of left ventricular function

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ABSTRACT

Background

Noninducibility is frequently used as procedural end point of ventricular tachycardia (VT) ablation after myocardial infarction. We investigated the influence of left ventricular (LV) function on the predictive value of noninducibility for VT recurrence and cardiac mortality.

Methods and Results

Ninety-one patients (82 men, 67 ± 10 years) with post-myocardial infarction VT underwent ablation between 2009 and 2012. Fifty-nine (65%) had an LV ejection fraction (EF) $>30\%$ (mean 41 ± 7) and 32 (35%) an $LVEF \leq 30\%$ (mean 20 ± 5). Thirty patients (51%) with $EF > 30\%$ and 13 (41%) with $EF \leq 30\%$ were noninducible after ablation ($P=0.386$). During a median follow-up of 23 (Q1–Q3 16–36) months, 35 patients (38%) experienced VT recurrences and 17 (18%) cardiac death. At 1 year follow-up, survival free from VT recurrence and cardiac death for patients with $LVEF > 30\%$ was 80% (95% confidence interval [CI], 70–90) compared with 42% (95% CI, 33–51) for those with $LVEF \leq 30\%$ ($P=0.001$). Noninducible patients with $LVEF > 30\%$ had a recurrence-free survival from cardiac death of 90% (95% CI, 71–100) compared with 65% (95% CI, 47–83) for inducible patients ($P=0.015$). In the subgroup of patients with $LVEF \leq 30\%$, the survival free from VT recurrence and cardiac death was 31% (95% CI, 0%–60%) for noninducible compared with 39% (95% CI, 27–52) for those who remained inducible ($P=0.842$).

Conclusions

Noninducible patients with moderately depressed LV function have a favorable outcome compared with patients who remained inducible after ablation. On the contrary, patients with severely depressed LV function have a poor prognosis independent of the acute procedural outcome.

INTRODUCTION

In patients late after myocardial infarction (MI), noninducibility of any sustained monomorphic ventricular tachycardia (VT) with programmed electric stimulation (PES) after ablation has been associated with favorable long-term outcome (lower VT recurrence rate and mortality).¹⁻⁵

Noninducibility is therefore currently used as procedural end point in many electrophysiology laboratories and the only endorsed by the current expert consensus.⁶ However, the predictive value of noninducibility for VT recurrence is limited because $\leq 30\%$ of patients who are rendered noninducible experience VT recurrences and more than half of the patients who remain inducible for nonclinical VTs do not present recurrence on short-term follow-up.⁵

In line with prior recommendations, the majority of patients included in former studies of post-MI VT ablation had an advanced disease with poor left ventricular function, presenting with multiple VT episodes refractory to antiarrhythmic drugs (AAD), including amiodarone.^{1-5,7} More recently, ablation early in the course of the arrhythmic disease has been recommended based on 2 randomized trials.^{8,9}

Because of the reported high recurrence rates, despite noninducibility, new ablation end points like elimination of late or abnormal potentials have been suggested for all patients with scar-related VT, irrespective of baseline patient characteristics and clinical presentation. Achieving these end points may require more invasive and extensive procedures likely to be associated with patient discomfort and procedure-related complications.¹⁰⁻¹²

We hypothesize that differences between patients, in particular in left ventricular (LV) function, may not only affect procedural and long-term outcome but also the optimal procedural end point for an individual patient.

The main objective of this study was to analyze the influence of individual patient characteristics on the predictive value of noninducibility for VT recurrence and cardiac mortality in the population currently referred for VT ablation after MI.

METHODS

Patient Population

The study population consisted of consecutive patients with prior MI and spontaneous symptomatic sustained monomorphic VT who underwent a first catheter ablation procedure at the Leiden University Medical Center between January 2009 and December 2012. Diagnosis of MI was based on the presence of wall motion abnormalities, nonreversible perfusion defects, and subendocardial or transmural late gadolinium enhancement areas in the perfusion territory of a significant stenotic coronary artery (>75%). Patients who underwent surgical ablation or presented with frequent premature ventricular contractions or nonsustained VT without documented spontaneous sustained VT were excluded. All patients provided informed consent and were treated according to the institutional clinical protocol.

Preprocedural Evaluation

Before the procedure, patients underwent a comprehensive clinical evaluation. VT clinical presentation was classified as electrical storm (≥ 3 implantable cardioverter defibrillator [ICD] shocks/24 h), incessant VT (recurrent sustained VT despite repeated intervention for termination), recurrent ICD therapies, VT below detection of ICD, and first episode of VT. A special effort was taken to obtain 12-lead documentation of the spontaneous VTs.

All patients underwent 2-dimensional and color Doppler echocardiography to assess LV ejection fraction (LVEF). LV end-diastolic and end-systolic volumes were obtained from the apical 2- and 4-chamber views and LVEF was calculated according to the biplane Simpson's method. Echocardiographic analyses were performed by an experienced observer blinded to all clinical and procedural data.

In 25 patients without ICD, contrast-enhanced MRI was performed. Seventy-nine patients (87%) underwent coronary angiography, and in 23 patients (25%), percutaneous coronary intervention was performed before catheter ablation.

Electrophysiological Study

Studies were performed in the fasting state under conscious sedation. In stable patients, all AAD with the exception of amiodarone (n=39, 43%) were discontinued for 5 half-lives before the study.

The PES protocol consisted of burst pacing and extrastimulation with 3 drive cycle lengths (CL; 600, 500, and 400ms) from at least 2 sites (right ventricular apex and right

ventricular outflow tract) with 1, 2, and 3 extrastimuli until 200 ms or refractoriness. Positive end point for stimulation was considered the induction of a sustained monomorphic VT lasting for >30 s or requiring termination because of hemodynamic instability. Induced VTs were classified as (1) clinical when there was a 12/12 electrocardiographic morphology match with a previously documented VT, (2) presumptive clinical when the CL was ± 30 ms of an ICD recorded VT, or (3) nonclinical VT when the previous criteria were not fulfilled.

Electroanatomical Mapping and Catheter Ablation

The initial approach was endocardial in all but one patient (after 2 failed attempts of endocardial ablation in another center). If noninducibility could not be achieved from the endocardium and an epicardial site of origin was assumed based on endocardial activation and substrate mapping, epicardial mapping as secondary approach was considered depending on VT clinical presentation and patient preference. Electroanatomical LV mapping was performed through a retrograde aortic approach (n=88) or a combination of retrograde and transeptal approach (n=3) during sinus or paced rhythm (n=9). Bipolar voltage maps were created with a 3.5 mm irrigated-tip catheter with a 2-5-2 mm interelectrode spacing (NaviStar ThermoCool; Biosense Webster, Inc, Diamond Bar, CA) and the CARTO system. Electrograms were filtered at 30 to 400 Hz (bipolar) and 1 to 240 Hz (unipolar). The area with bipolar voltages under 0.5 mV was defined as dense scar. The area with bipolar voltages between 0.5 to 1.5mV was defined as scar border zone. Re-entry isthmus sites were identified with entrainment and activation mapping for stable VTs and with substrate mapping for unstable VTs. Potential ablation targets based on electrogram characteristics and pace mapping ($\geq 10/12$ morphology match with induced VT and stimulus-to-QRS delay > 40 ms) were tagged on the map. Once the area of interest was localized, VT was reinduced. Whenever possible, poorly tolerated VTs were at least briefly mapped during VT to either perform entrainment mapping or slow and terminate VT during radiofrequency application. Only areas specifically related to induced VTs based on entrainment and pace-mapping were targeted. Radiofrequency energy was delivered between 35 and 50 W with a temperature limit of 43°C and a flow rate of 20 to 30 mL/min until the capture threshold postablation was >10 mA/2 ms.

Procedural End Point

All clinical and nonclinical sustained monomorphic VTs were targeted for ablation. Only nonclinical fast VTs, defined as VTs with a VTCL close to ventricular refractory period, that were not reproducible inducible were considered to be of unknown clinical relevance and were not targeted. Safety was taken into major consideration; therefore, the procedure was stopped if multiple electric cardioversions were required or the patient had prolonged hemodynamic instability.

Acute Procedural Outcome

After the last radiofrequency application, the entire PES protocol was repeated. Complete acute success was defined as noninducibility of any sustained monomorphic VT; partial success as elimination of all clinically documented VTs but inducibility of any nonclinical VT independent from VTCL and morphology also including nontargeted fast VTs and failure as persistent inducibility of any clinical VT.

Postprocedural Management

An ICD was offered to all patients regardless of acute procedural outcome. Preablation AAD were maintained until the first follow-up visit. Thereafter, the AAD regimen was left at the discretion of the referring cardiologist

Follow-Up

Patients were followed at the outpatient clinic 3 and 6 months after the procedure and every 6 months afterward, including a careful history regarding symptoms for VT and ICD interrogation. For patients followed at other institutions and in case of death, the referring cardiologist or general physician was contacted for VT recurrence and cause of death. VT recurrence was defined as occurrence of any documented VT after ablation, independently of CL or clinical presentation. In-hospital recurrences were also included in the analysis. During follow-up, VT recurrence was classified as electrical storm (≥ 3 ICD shocks/24 h), incessant VT (recurrent sustained VT despite repeated intervention for termination), VT terminated by ICD shock, VT terminated by ATP, VT in monitor zone, or ECG-documented VT. A clinically relevant VT recurrence was defined as any VT that was treated with ICD shock or led to hospitalization, reablation, or modification of the antiarrhythmic therapy.

Statistical Analysis

Continuous variables are reported as mean \pm SD or medians with upper and lower quartiles (Q1–Q3). Categorical variables are presented as numbers and frequencies (%). Categorical variables were compared using the Chi-squared test or the Fisher exact test and continuous variables with the Student's t test or the Mann–Whitney U test when appropriate. The VT and ICD shock frequency before and after ablation and the CL of the spontaneous, remaining, and recurrent VTs were compared with the Wilcoxon signed-rank test. Freedom from VT recurrence and cardiac death was estimated by Kaplan–Meier method and compared by log-rank test between groups. Predictors of acute procedural outcome, VT recurrence, and mortality were assessed with univariate logistic regression and Cox regression analysis, respectively. For the regression analysis of predictors of mortality on follow-up, VT recurrence was treated as time-dependent variable. Independent predictors of acute procedural outcome and VT recurrence were

analyzed with multivariable models using a backward stepwise selection. Variables with a P value <0.10 were initially included. At each step, the least significant variable was removed from the model, until all variables reached a P value <0.20 . All tests were 2-sided and a P value <0.05 was considered statistically significant. All statistical analyses were performed with SPSS version 20.0 (SPSS Inc, Chicago, IL).

RESULTS

During the study period, 116 patients with prior MI and symptomatic ventricular arrhythmias were referred for ablation. Twenty patients (17%) with nonsustained VT and premature ventricular contractions, 4 (3%) who underwent surgical ablation, and 1 (1%) with pleomorphic VT at presentation were excluded. Finally, 91 patients (82 men, 67 ± 10 years) with remote MI and history of spontaneous sustained monomorphic VT comprised the study population. Ten (11%) patients had previously undergone ≥ 1 failed endocardial VT ablation in another center. Fifty-seven patients (63%) had an ICD implanted before the procedure. Fifteen patients (17%) presented with electrical storm and 14 (15%) with incessant VT. Twenty-eight patients (31%) were referred for ablation after the first documented VT episode.

Fifty-nine patients (65%) had a moderately depressed LVEF (defined as $LVEF > 30\%$, mean 41 ± 7) and 32 (35%) a severely depressed LVEF (defined as $LVEF \leq 30\%$, mean 20 ± 5). Patients with severely depressed LVEF were younger (64 ± 13 versus 69 ± 8 years-old, $P=0.048$) and had more frequently a history of an anterior MI (53% versus 29%, $P=0.026$), atrial fibrillation (47% versus 22%, $P=0.018$), heart failure hospitalizations (72% versus 29%, $P<0.0001$), ICD implantation before the procedure (84% versus 51%, $P=0.002$), a previous VT ablation in another center (22% versus 5%, $P=0.030$), and slower VTs at presentation (438 ± 69 versus 353 ± 77 ms, $P<0.0001$). Patients with $LVEF > 30\%$ were more often referred for ablation after the first episode of a symptomatic VT (42% versus 9%, $P=0.001$). In most of these patients, the procedure was performed clinically, before ICD implantation. Baseline characteristics of the patients according to LVEF are displayed in **Table 1**.

Ablation Procedure

Eighty-five patients (93%) were either inducible (median 3 VTs per patient, Q1–Q3 2–5; mean CL 355 ± 87 ms) or in VT at the beginning of the procedure. Clinical VTs were present or induced in 75 patients (82%). VT was classified as clinical based on the 12 lead-ECG in 60 patients (66%) and on ICD recordings in 15 (16%). Ten patients (11%) were only inducible for nonclinical VTs. Sixty-four (70%) had at least one hemodynamically unstable VT inducible.

Table 1. Baseline characteristics of the patients according to left ventricular ejection fraction

	All (n=91)	EF > 30% (n=59)	EF ≤ 30% (n=32)	P
Age, y	67 ± 10	69 ± 8	64 ± 13	P=0.048
Male sex	82 (90%)	53 (90%)	29 (91%)	P=1.000
Hypertension	41 (45%)	30 (51%)	11 (34%)	P=0.186
Diabetes mellitus	13 (14%)	8 (14%)	5 (16%)	P=0.764
Hypercholesterolemia	32 (35%)	23 (39%)	9 (28%)	P=0.362
History of Stroke/TIA	8 (9%)	6 (10%)	2 (6%)	P=0.708
History of atrial fibrillation	28 (31%)	13 (22%)	15 (47%)	P=0.018
History of renal failure	29 (32%)	15 (25%)	14 (45%)	P=0.063
Prior admissions for heart failure	40 (44%)	17 (29%)	23 (72%)	P<0.0001
Anterior MI	34 (37%)	17 (29%)	17 (53%)	P=0.026
MI acute reperfusion	15 (16%)	10 (17%)	5 (16%)	p=1.000
Time since MI, y	19 ± 9	20 ± 9	18 ± 7	P=0.441
Prior CABG	37 (41%)	25 (42%)	12 (38%)	P=0.823
Prior PCI	36 (39%)	23 (39%)	13 (41%)	P=1.000
LV ejection fraction, %	34±12	41 ± 7	20 ± 5	P<0.0001
ICD before ablation	57 (63%)	30 (51%)	27 (84%)	P=0.002
Prior VT ablation	10 (11%)	3 (5%)	7 (22%)	P=0.030
Clinical VT mean CL, ms	382±84	353 ± 77	438 ± 69	P<0.0001
Medication at admission				
Statins	81 (89%)	53 (90%)	28 (88%)	P=0.737
Antialdosteronic	31 (34%)	20 (34%)	11 (34%)	P=1.000
ACE inhibitor/ARB	76 (84%)	51 (86%)	25 (78%)	P=0.378
Betablockers	69 (76%)	43 (73%)	26 (81%)	P=0.448
Amiodarone	39 (43%)	21 (36%)	18 (56%)	P=0.076
VT clinical presentation				
Electrical storm	15 (17%)	8 (14%)	7 (22%)	P=0.378
Incessant VT	14 (15%)	7 (12%)	7 (22%)	P=0.234
ICD therapies	24 (26%)	13 (22%)	11 (34%)	P=0.221
Below ICD detection	10 (11%)	6 (10%)	4 (13%)	P=0.737
First episode	28 (31%)	25 (42%)	3 (9%)	P=0.001

TIA indicates transitory ischemic attack; MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; LV, left ventricular; ICD, implantable cardioverter defibrillator; VT, ventricular tachycardia; CL, cycle length; ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers.

Compared with patients with LVEF>30%, patients with LVEF≤30% were inducible for a higher number of VTs (2.8±2.0 versus 5.0±2.9, P<0.0001), which were slower (mean CL 323±63 versus 409±97 ms, P<0.0001) and had more often left bundle branch block morphology (51% versus 78%, P=0.033). Procedural data according to LVEF are summarized in **Table 2**.

Table 2. Electrophysiological and procedural characteristics according to left ventricular ejection fraction

	All (n=91)	EF > 30% (n=59)	EF ≤ 30% (n=32)	P
Inducible before ablation	85 (93%)	54 (92%)	31 (97%)	P=0.419
Number of Induced VTs	3.6 ± 2.5	2.8 ± 2.0	5.0 ± 2.9	P<0.0001
Induced VT max CL, ms	418 ± 116	367 ± 86	507 ± 108	P<0.0001
Induced VT mean CL, ms	355 ± 87	323 ± 63	409 ± 97	P<0.0001
Induced VT min CL, ms	295 ± 79	282 ± 61	319 ± 101	P=0.036
HD unstable VT inducible	64 (70%)	39 (72%)	25 (81%)	P=0.443
LBBB VT inducible	55 (60%)	30 (51%)	25 (78%)	P=0.033
Epicardial mapping	7 (8%)	4 (7%)	3 (9%)	P=0.236
Complete success	43 (47%)	30 (51%)	13 (41%)	P=0.386
Partial success	44 (49%)	25 (42%)	19 (59%)	P=0.132
Remaining VT mean CL, ms	279 ± 59	275 ± 59	286 ± 59	P=0.531
Procedural duration, min	207 ± 92	202 ± 80	216 ± 113	P=0.516
Fluoroscopic time, min	38 ± 23	36 ± 21	41 ± 25	P=0.434
ICD after ablation	77 (85%)	47 (80%)	30 (94%)	P=0.126
Amiodarone post-ablation	44 (48%)	22 (37%)	22 (54%)	P=0.005

VT indicates ventricular tachycardia; CL, cycle length; LBBB, left bundle branch block; ICD, implantable cardioverter defibrillator.

All patients underwent endocardial mapping and ablation. In 8 of 52 patients (15%) who remained inducible after endocardial ablation, an epicardial approach was attempted. Of the 7 patients who finally underwent epicardial mapping (one was not successful because pericardial adhesions) only in 4 epicardial radiofrequency was applied. Three patients were rendered noninducible and one remained inducible for nonclinical VTs only after combined endo-epicardial approach.

At the end of the procedure, all patients underwent PES. Complete acute success was achieved in 43 patients (47%) and partial in 44 (49%). Procedural failure occurred in 4 patients (4%). Of note, there was no difference between patients with severely and moderately depressed LV function regarding the acute procedural success rate (non-inducibility was achieved in 30 patients [51%] with EF>30% versus 13 [41%] with EF≤30%; P=0.386).

The majority of inducible patients after ablation (41/48, 85%) had remaining VTs, which were faster than all spontaneous VTs (mean CL 280±59 versus 389±89 ms, P<0.0001), 35/48 patients (73%) had only VTs with a CL≤300 ms. Importantly, in 38 of 48 patients (79%), remaining fast VTs were not targeted because they were considered to be of unknown clinical relevance (mean CL 263±42 ms).

Complications

There was no procedure-related mortality. One patient with multiple ICD shocks and a basoseptal central isthmus site developed anticipated complete AV block after ablation. Ten patients had vascular access-related complications. None of them needed surgical intervention. Cardiac tamponade requiring percutaneous drainage after endocardial ablation occurred in one patient and late tamponade after an epicardial approach in one other patient. There was no difference in the occurrence of procedural-related complications according to baseline LVEF (EF>30%; 18% versus EF≤30%; 6%, P=0.129).

Predictors of Acute Outcome

Noncomplete acute success was associated with a higher number of induced VTs (odds ratio 1.42 per additional VT induced; 95% confidence interval [CI] 1.15–1.76; P=0.001) and the induction of faster (odds ratio 2.79 per 50 ms decrease in minimum VT CL; 95% CI 1.66–4.72; P<0.0001) and hemodynamically unstable VTs (odds ratio 6.55; 95% CI 2.11–20.32; P=0.001; **Figure 1**). On multivariate analysis, the number of induced VTs (odds ratio 1.23 per additional VT induced; 95% CI 1.00–1.57; P=0.047) and the CL of the fastest induced VT (odds ratio 2.78 per 50 ms decrease in minimum VT CL; 95% CI 1.60–4.76; P<0.0001) remained independently associated with the acute procedural outcome.

This was observed for both patient groups, those with LVEF>30% and LVEF≤30% with the exception of the number of induced VTs that was not associated with worse acute outcome for patients with LVEF≤30% (odds ratio 1.30 per additional VT induced; 95% CI 0.97–1.77; P=0.080).

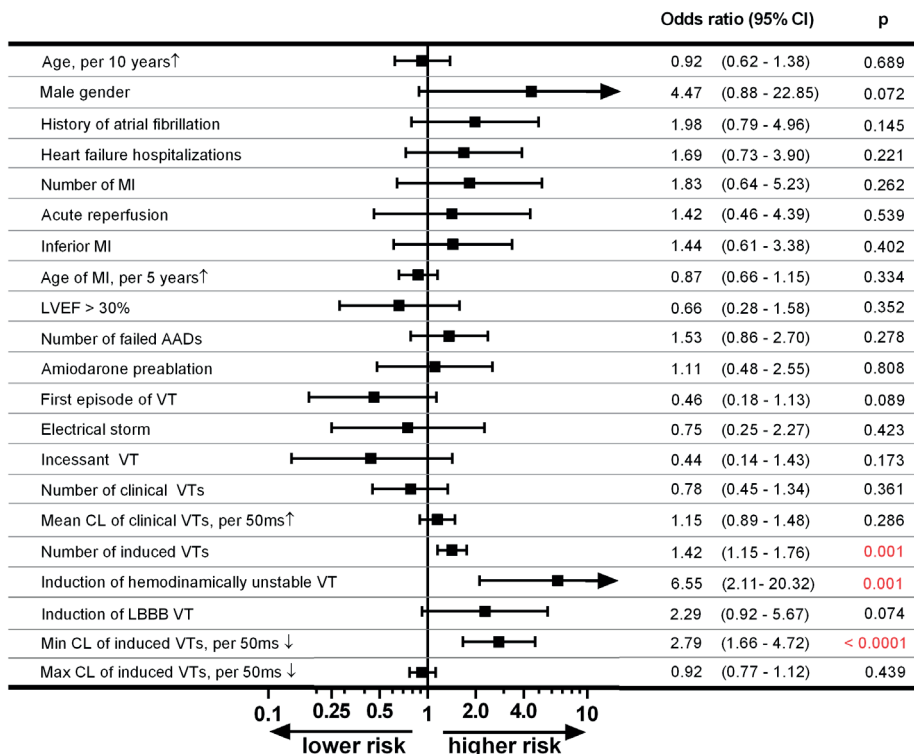
Postprocedural Management

Seventy-seven (85%) patients were discharged with an ICD. Fourteen (15%) patients refused ICD implantation. These patients were older (odds ratio 0.35 per 10 years increase; 95% CI 0.16–0.75; P=0.007), had better LVEF (odds ratio 0.69 per 5% increase EF; 95% CI 0.51–0.92; P=0.011, all but 2 EF>30%), and were more often noninducible after ablation (odds ratio 20.37; 95% CI 2.53–163.82; P=0.005). Seventy-two (79%) patients were discharged on AAD other than conventional β -blockers (44 [48%] on amiodarone and 28 [31%] on sotalol).

VT Recurrence

During a median follow-up of 23 (Q1–Q3 16–36) months, 35 patients (38%) experienced any VT recurrence with a median time to recurrence of 133 (Q1–Q3 36–608) days (only one patient was lost for follow-up, all but 2 had a follow-up longer than 1 year, 9 patients died during the first year).

Figure 1.
Predictors of inducibility after ablation



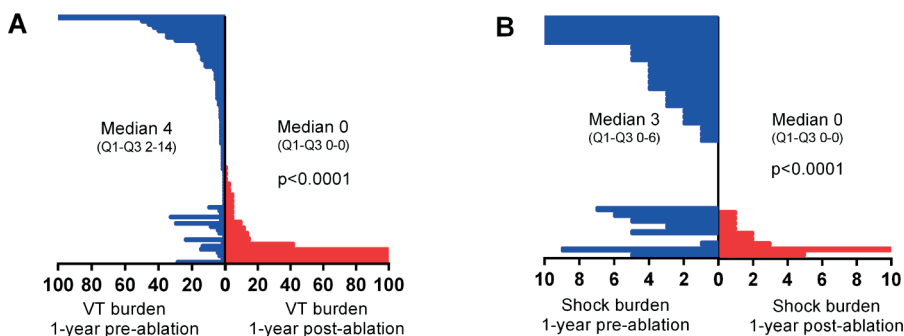
AAD indicates antiarrhythmic drugs; CL, cycle length; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; Max, maximum; MI, myocardial infarction; Min, minimum; and VT, ventricular tachycardia.

Patients with a LVEF>30% had a lower incidence of VT recurrence than patients with LVEF≤30% (34% versus 48%, hazard ratio [HR] 0.43; 95% CI 0.21–0.87; P=0.02).

The 1-year VT burden was reduced in the entire group from a median of 4 (Q1–Q3 2–14) episodes before ablation to a median of 0 (Q1–Q3 0–0) episodes after ablation (P<0.0001). Sixty-five of 79 (82%) patients with a follow-up longer than 1 year had a ≥75% reduction of the VT burden (**Figure 2A**). In patients with ICD before ablation, the frequency of shocks per year was reduced from a median of 3 (Q1–Q3 0–6) to a median of 0 (Q1–Q3 0–0) after ablation (P<0.0001; **Figure 2B**).

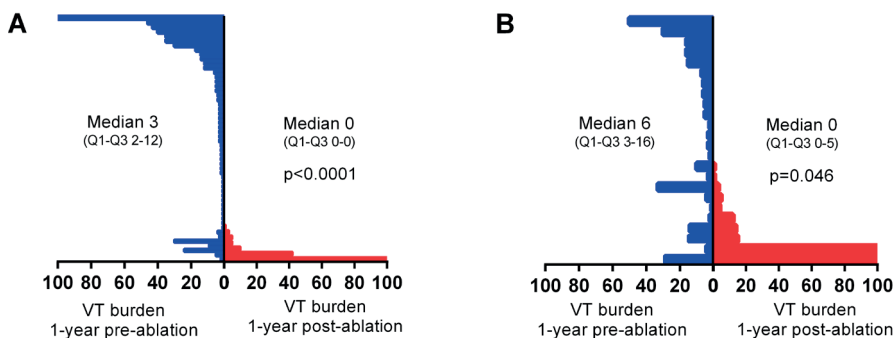
A significant reduction of the 1-year VT burden was observed in patients with both severely and moderately depressed LV function (**Figure 3**).

Figure 2.



A: One-year ventricular tachycardia (VT) burden before (blue lines) and after ablation (red lines) of 77 patients with follow-up longer than 1 year. The number of VT episodes is truncated at 100. **B:** One-year shock burden before (blue lines) and after ablation (red lines) in patients with prior ICD and follow-up longer than 1 year. The number of shocks is truncated at 10. IQR indicates interquartile range.

Figure 3.



One-year ventricular tachycardia (VT) burden before (blue lines) and after ablation (red lines) in patients with LVEF>30% (Panel A) and LVEF≤30% (Panel B). The number of VT episodes is truncated at 100.

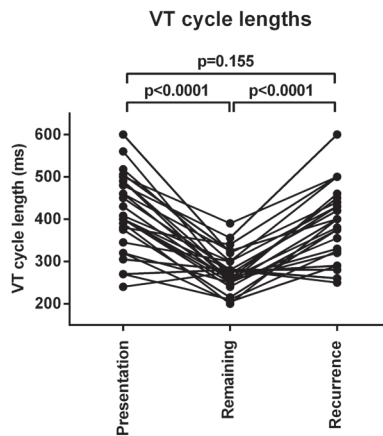
Mode and Predictors of VT Recurrence

Based on the provided definition, only 27 patients (29%) presented with clinically relevant VT recurrences (3 (3%) electrical storm, 5 (5%) incessant VT, 12 (13%) ≥ 1 ICD shock, 4 (4%) VT below detection of ICD, 3 (3%) frequent symptomatic ATP). Eight patients (9%) presented with sporadic ATP or asymptomatic self-terminating VTs in the monitor zone that did not require any intervention. Thirteen patients (42%) with LVEF≤30% presented with relevant VT recurrences compared with 14 (24%) with LVEF>30% (P=0.150). In 21 of 27 patients (81%) with relevant VT recurrences, these occurred during the first year of follow-up (18 (67%) in the first 6 months). No VT recurrence was documented in patients discharged without ICD.

Recurrent VTs were significantly slower than the remaining VTs in patients with non-complete acute procedural success (378 ± 74 versus 285 ± 63 ms; $P < 0.0001$). In fact, in 23 of 28 patients (82%) with noncomplete acute success and recurrences on follow-up, the CL of the recurrent VT was at least 30 ms longer than the CL of the slowest remaining VT after ablation, suggesting that remaining fast VTs were not the cause of recurrence in these patients. **Figure 4** shows the CL of spontaneous, remaining, and recurrent VTs in individual patients with partial acute success and VT recurrence during follow-up.

On multivariate analysis, after adjusting for age, sex, hypertension, ejection fraction, history of atrial fibrillation, renal failure, history of heart failure hospitalizations, electrical storm, incessant VT at presentation, and amiodarone use after ablation, a higher number of induced VTs (HR 1.22 per additional VT induced; 95% CI 1.08–1.40; $P = 0.002$) and inducibility after ablation (HR 2.49; 95% CI 2.49–5.61; $P = 0.028$) were independently associated with VT recurrence for the entire population. Ablation after the first documented VT episode was independently associated with lower VT recurrence (HR 0.30; 95% CI 0.10–0.89; $P = 0.029$).

Figure 4.



The cycle length of the spontaneous ventricular tachycardia (VT), slowest remaining VT after ablation, and recurrent VT from 28 patients with partial success and VT recurrence on follow-up are plotted.

Mortality on Follow-Up

Twenty-five patients (27%) died during follow-up with a median time to death of 442 days (IQR 245–655), and 17 (19%) died of cardiac causes. Patients with LVEF > 30% had better prognosis with cardiac mortality of 10% compared with 35% for patients with LVEF ≤ 30% over the follow-up period (HR 0.21; 95% CI 0.08–0.58; $P = 0.003$). VT recurrence (HR 2.46; 95% CI 0.93–6.51; $P = 0.070$) and inducibility after ablation (HR 0.8; 95% CI

0.31–2.10; $P=0.647$) were not associated with cardiac mortality for the entire population. The most frequent cause of death was terminal heart failure ($n=15$, 60%), in particular for patients with severely depressed LV function ($n=9$, 75%). In 3 patients, death was of arrhythmic/presumed arrhythmic origin (one 80-year-old patient with 45% LVEF and complete acute success without ICD died unwitnessed while sleeping, 2 patients with severely depressed LVEF (26 and 19%) died because of an electrical storm that was not targeted by ablation). Seven of 13 patients (54%) with $EF>30\%$ died from noncardiac causes compared with 1 of 12 with $LVEF\leq 30\%$ ($P=0.073$).

VT Recurrence and Cardiac Mortality According to LV Function, VT Inducibility, and Clinical Presentation

During follow-up, the combined end point of VT recurrence or cardiac death occurred in 24 of 59 patients with $LVEF>30\%$ (41%; 34% had VT recurrence, and 10% cardiac death) had VT recurrence and 38% cardiac death).

Patients with an $LVEF>30\%$ had a higher probability of survival free from VT recurrence and cardiac death compared with those with $LVEF\leq 30\%$ (81% [95% CI 71–91] versus 61% [95% CI 43–79] at 6 months and 80% [95% CI 70–90] versus 42% [95% CI 33–51] at 1 year follow-up, $P=0.001$; **Figure 5A**).

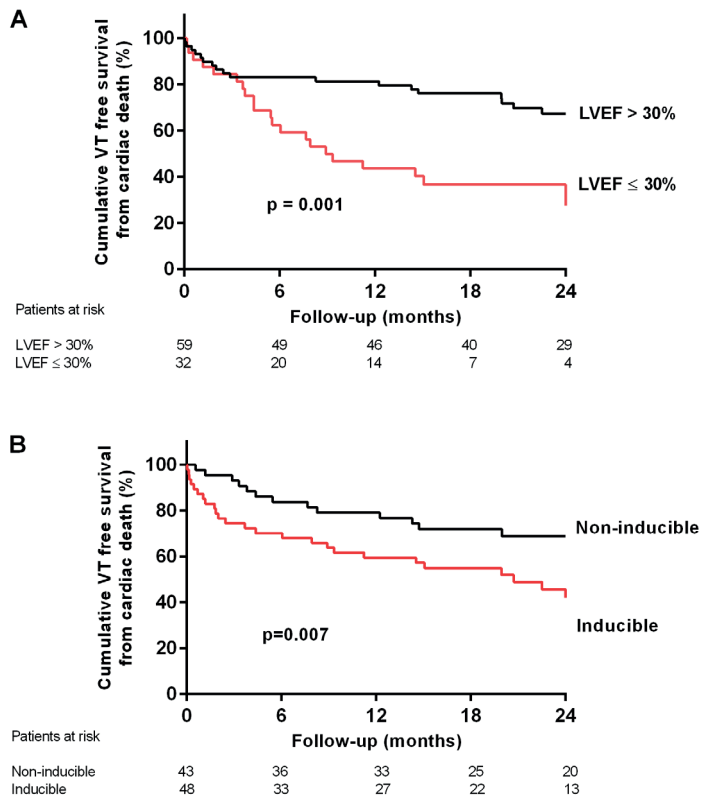
Survival free from VT recurrence and cardiac death was also higher for patients who were rendered noninducible compared with patients who remained inducible after ablation (81% [95% CI 69–93] versus 77% [95% CI 65–89] at 6 months and 68% [95% CI 54–82] versus 57% [95% CI 43–71] at 1 year follow-up: $P=0.007$; **Figure 5B**).

In the subgroup of patients with $LVEF>30\%$, survival free from VT recurrence and cardiac death at 1 year follow-up was 90% (95% CI 71–100) for noninducible patients compared with 65% (95% CI 47–83) for those who remained inducible for any VT after ablation ($P=0.015$; **Figure 6**). This was mainly because of a higher incidence of VT recurrence in inducible patients. In fact, the probability of VT recurrence was higher in those who remained inducible after ablation (HR 4.26; 95% CI 1.54–11.78; $P=0.005$), whereas no significant difference was found in the incidence of cardiac death (HR 1.23; 95% CI 0.26–6.28; $P=0.774$). A higher number of induced VTs (HR 1.55 per additional VT induced; 95% CI 1.23–1.88; $P<0.0001$) was associated with VT recurrence in these patients with $LVEF>30\%$, whereas ablation after the first documented VT episode was associated with lower VT recurrence (HR 0.25; 95% CI 0.08–0.74; $P=0.012$). No patient with $LVEF>30\%$ and who was rendered noninducible by ablation after the first symptomatic VT episode had VT recurrence or died of a cardiac cause during the first year of follow-up.

On the contrary, patients with LVEF \leq 30% had a poor prognosis that was independent from the acute outcome of the procedure. At 1 year follow-up, the cumulative incidence of VT free survival from cardiac death was 31% (95% CI 0–60) for noninducible patients compared with 39% (95% CI 27–52) for those who remained inducible after ablation (P=0.842).

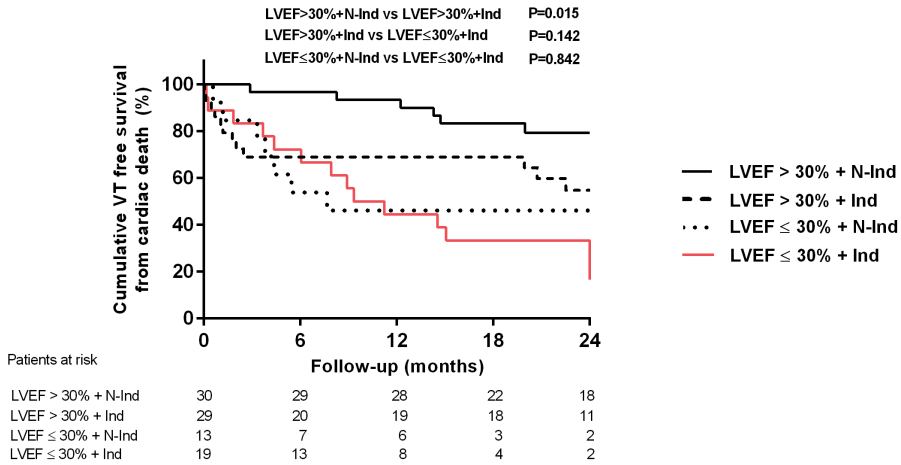
Noninducibility was neither associated with VT recurrence (HR 2.7; 95% CI 0.78–9.69; P=0.121) nor with cardiac mortality (HR 0.31; 95% CI 0.09–1.11; P=0.073) in this subgroup of patients. There was a nonsignificant trend to a higher number of inducible VTs in patients who experienced VT recurrence (HR 1.19 per additional VT induced; 95% CI 0.99–1.42; P=0.054). Ablation after the first VT episode was not associated with lower VT recurrence in these patients (HR 0.39; 95% CI 0.00–35.63; P=0.352).

Figure 5.



Ventricular tachycardia-free survival from cardiac death according to left ventricular ejection fraction (LVEF; A) and inducibility after ablation (B).

Figure 6.



Ventricular tachycardia (VT)–free survival from cardiac death according to left ventricular ejection fraction (LVEF) and inducibility after ablation.

DISCUSSION

The present study is the first to evaluate the influence of individual patient characteristics—in particular LV function—on the predictive value of noninducibility for VT recurrence and cardiac mortality in the population currently referred for VT ablation after MI.

The predictive value of noninducibility for VT recurrence and cardiac mortality was influenced by the baseline LVEF. At 1 year follow-up, only 10% of the patients with moderately depressed LV function that were rendered noninducible by ablation experienced VT recurrence or died from a cardiac cause compared with 35% of patients in whom noninducibility was not achieved. Furthermore, patients with LVEF>30% that were referred after the first documented episode of symptomatic VT and became noninducible by ablation had an excellent prognosis. No patient with these characteristics had VT recurrence or died from a cardiac cause during the first year of follow-up. On the contrary, patients with severely depressed LV function had a poor prognosis that was independent from the acute result of the procedure or the VT clinical presentation, mainly driven by heart failure–related death. In fact, >50% of the patients with LVEF<30% experienced VT recurrence or cardiac death or both during the first year of follow-up.

Prior Reports

A recent meta-analysis including 928 post-MI patients from 8 observational studies showed that lack of inducibility of any VT after ablation was associated with lower

VT/ventricular fibrillation recurrence and all-cause mortality during follow up and, therefore, proposes noninducibility as a reasonable end point for the procedure.⁵ This meta-analysis included, however, an unselected pool of patients that were referred for ablation over >20 years (1991–2011) and did not correct for individual patient characteristics that may per se influence outcome.

The recommendations and strategies of post-MI VT ablation have changed over time. In line with clinical guidelines, the majority of patients initially included in studies had an advanced disease, with poor LV function, symptomatic heart failure, and multiple VT episodes despite amiodarone.^{1–5,7,13} Since the publication of the last expert consensus, more patients with moderately depressed LV function after the first documented VT episode are referred for ablation.⁶ In this regard, our study is more representative of the current practice because it includes only patients treated after 2008, frequently referred after the first documented VT episode (31%) with a high prevalence of moderately depressed LV function (65%). The basal cardiac function and the stage of the arrhythmic disease may impact both the outcome and the appropriate end point of the ablation procedure for an individual patient.

Ablation Late in the Therapeutic Course of Disease

It has been shown that, in post-MI patients, the predictive value of PES to predict ventricular arrhythmic events depends on the basal cardiac function. In the MUST trial, the cause of death of inducible patients with LVEF>30% was arrhythmic in 61% of the cases. On the contrary, no difference in the incidence of arrhythmic death was observed between inducible and noninducible patients with LVEF<30%.¹⁴ In line with these results, in our study, noninducibility was not associated with lower VT recurrence and cardiac mortality in patients with severely depressed LV function. This finding might be explained by 2 factors. First, not all VTs have a fixed reentrant mechanism and, in particular, in patients with advanced cardiac remodeling and heart failure, other focal arrhythmic mechanisms not so accurate reproducible by PES and not so easily approachable by our current ablation techniques may play an important role.¹⁴ Secondary, in patients with poor LV function and end-stage heart failure, a high competing risk of nonarrhythmic cardiac death is present.¹⁵ In fact, the most prevalent cause of death in this population was terminal heart failure (75% of the cases).

Ablation Early in the Therapeutic Course of Disease

The evidence that supports the benefit of an early intervention in patients with post-MI VT is based on 2 recent randomized trials.^{8,9} However, in the VTACH trial, only patients with LVEF>30% had a significant higher survival free from VT/ventricular fibrillation after ablation.⁹ According to these results, in our study, 20% of the patients with moderately

depressed LV function had VT recurrence or died from a cardiac cause during the first year of follow-up compared with 58% of patients with severely depressed LV function in spite of a similar rate of acute procedural success.

Patients with LVEF>30% that were rendered noninducible by ablation had a good prognosis because only 10% experienced VT recurrence or cardiac death 1 year after ablation. In line with a recent publication, if these patients were referred for ablation after the first documented VT episode, the outcome was excellent.¹⁶ No patient fulfilling these criteria had events during the first year of follow-up, further supporting an early ablation in this patient population. Inducibility of any VT after ablation seems to be therefore a good predictor of VT recurrence in patients with moderately depressed LV function, and noninducibility might be a sufficient end point for the ablation procedure in these patients.

Patients with LVEF>30% in whom noninducibility was not achieved had a worse prognosis mainly related to a higher VT recurrence rate. If noninducibility is not achieved, analyzing and understanding the reasons for ablation failure is mandatory to select the appropriate next step for each individual patient (eventually epicardial).¹⁷ The clinical significance of nonclinical VTs, in particular fast and nonreproducible inducible VTs, remains still unclear. Prior studies, based on the analysis of ICD recordings, suggested that the cause of recurrence in patients with noncomplete acute success were nonclinical VTs that were either not targeted or not successfully abolished during ablation.^{1,2} In the present study, in 82% of patients with partial success and VT recurrence on follow-up, VTCL was at least 30 ms longer than remaining VTs, suggesting that these VTs were not the cause of recurrence. VT recurrence might be related to lesion healing but may also be caused by new reentry circuits, and inducibility of nonclinical fast VTs might just indicate a more complex arrhythmic substrate. These findings support the need for additional ablation end points based on substrate mapping and the development of new ablation tools able to perform deeper and long-lasting lesions for patients with moderately depressed LV function in whom noninducibility is not achieved.

Limitations

This study is limited by its observational nature. The reported acute and long-term outcomes after ablation come from a high-volume referral center and may therefore not apply for smaller less experienced centers. The antiarrhythmic regimen after ablation was left at the discretion of the referral physician, and this might have influenced the outcome of some patients. The number of patients with severely depressed LV function that were referred for ablation after the first episode of symptomatic VT was small, limiting its power to determine whether this factor was associated with better outcome.

To discern between remaining VTs after ablation and recurrent VTs on follow-up, only the CL of the VTs was taken into account. Routine analysis of ICD-stored VT electrogram morphology was not performed.

CONCLUSION

Patients with prior MI and moderately depressed LV function that are rendered noninducible by ablation, in particular if they are referred after the first episode of symptomatic VT, have an excellent prognosis. Therefore, in this population, an early intervention aiming noninducibility seems to be appropriate. On the contrary, patients with severely depressed LV function have a poor prognosis that is independent of the acute outcome of the procedure and is mainly driven by heart failure–related death. In this subgroup of patients, a more conservative approach, prioritizing symptoms relief, patient comfort, and safety might be preferable.

CLINICAL PERSPECTIVE

What is known

- In patients with prior MI, non-inducibility is frequently used as VT ablation endpoint.
- Non-inducibility has been associated with improved outcomes.

What the study adds

- The LV function has an important impact on the predictive value of non-inducibility for VT recurrence and cardiac mortality.
- Patients with moderately depressed LV function who are rendered uninducible by ablation have an excellent prognosis. Non-inducibility seems to be an appropriate ablation endpoint in this population.
- Patients with severely depressed LV function have a poor prognosis, independent of the acute result of the procedure, mainly due to heart failure related death. In these patients, a more conservative approach might be preferable.

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