# Chapter 8

# Outcome of Ventricular Tachycardia Ablation in Patients with Nonischemic Cardiomyopathy: The Impact of Noninducibility

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## ABSTRACT

### Background

Ablation failure and recurrence rates after ventricular tachycardia (VT) ablation in nonischemic cardiomyopathy (NICM) are high and the optimal procedural endpoint is not well defined. This study assessed the outcome after ablation, the impact of noninducibility and other potential predictors of VT recurrence.

### Methods and Results

Forty-five patients with NICM (60±16 years, LVEF 44±14%) accepted for VT ablation were included. Epicardial mapping was performed in 29 (64%). A median of 2 (first-to-third quartile, 2–4) VTs (cycle length [CL] 342±77ms) were induced per patient. After ablation, the complete programmed electrical stimulation protocol (3 drive CL, 3 extrastimuli ≥200ms, burst, ≥2 sites) was repeated. Complete success (non-inducibility of any monomorphic VT) was achieved in 17 patients (38%), partial success (elimination of clinical VT, persistent inducibility of non-clinical VT) in 17 patients (38%), and failure (persistent inducibility of clinical VT) in 11 patients (24%). During 25±15 months follow-up VT occurred in 24 patients (53%), but the 6-month VT burden was reduced by ≥75% in 79%. Recurrence rates were low after complete procedural success (18%), but high after both partial success (77%) and failure (73%). Non-complete procedural success was the strongest predictor of VT recurrence (hazard ratio 8.20, 95% confidence interval 2.37-28.43, p=0.001).

### Conclusions

Although 53% of patients had VT during follow-up, the 6-month VT burden was decreased by ≥75% in 79%. Recurrence rates are low after complete procedural success, but high after both partial success and failure. Non-complete procedural success was the strongest predictor of VT recurrence.

## INTRODUCTION

In patients with left ventricular (LV) non-ischemic cardiomyopathy (NICM) several aspects of ventricular tachycardia (VT) ablation require elucidation.

First, the procedural endpoint is not well defined. Although non-inducibility of VT by programmed electrical stimulation (PES) is frequently used as an endpoint, data supporting its predictive value for VT recurrence are mainly derived from patients after myocardial infarction (MI)[1,2] who are likely to have different substrates, higher procedural success and lower VT recurrence rates.[1,3] In addition, studies in post-MI patients are inconsistent, perhaps due to different induction protocols, incomplete application of protocols and differences between patient populations.[1,2,4-6] Data on the value of PES as a procedural endpoint in NICM are limited to two small series.[3,7] Recently, alternative endpoints have been proposed such as elimination of abnormal bipolar electrograms or late potentials consistent with slow conduction[4,8], late potentials are however less frequently found in patients with NICM than in post-MI patients.[3]

Second, risk factors for VT recurrence in NICM are not established. Risk stratification may allow an individually tailored treatment strategy. A conservative approach may be appropriate in patients at low risk, whereas patients at high risk may require either more extensive ablation or concomitant drug therapy.

Third, the role of VT ablation early in the therapeutic course (e.g. for a first VT, symptomatic ATP or a single ICD shock) is unclear in NICM patients. The indication for VT ablation in patients with structural heart disease has changed over time.[9] Recent recommendations apply to all patients with structural heart disease, although evidence is limited and based on trials conducted in post-MI patients.[10,11] The risk-benefit ratio of VT ablation early in the therapeutic course may be different in patients with NICM, in whom VT ablation is reported to be less effective[1,3] and may more often requires epicardial ablation, which is associated with a higher procedural risks.[12,13]

The aims of the current study are fourfold: 1) to determine the outcomes of VT ablation in NICM, 2) to assess the value of PES as a procedural endpoint, 3) to identify predictors of acute and long-term outcome, 4) to evaluate the role of VT ablation early in the therapeutic course in NICM.

## METHODS

### Patients

The study population consisted of 45 consecutive NICM patients who underwent VT ablation at the Leiden University Medical Centre between 1/2007 and 6/2011, including patients in whom no radiofrequency (RF) energy was delivered. All patients had systolic

impairment and evidence of scar in the LV based on contrast-enhanced MRI and/or electroanatomical mapping. Patients with significant coronary artery disease (>50% stenosis, assessed by coronary angiography in all patients), congenital heart disease, hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, left ventricular noncompaction, restrictive cardiomyopathy, (sub)acute myocarditis, cardiac sarcoidosis, toxic cardiomyopathy, tachycardia-induced cardiomyopathy or primary valvular abnormalities were excluded. All patients were treated according to the routine clinical protocol and provided informed consent.

### Clinical presentation and procedural strategy

In patients presenting with incessant VT, ≥2 implantable cardioverter defibrillator (ICD) shocks or multiple VT recurrences after prior endocardial ablation, VT ablation was classified as 'late in the therapeutic course'. In these patients, epicardial mapping was always attempted if endocardial ablation did not result in complete success. In patients presenting with a first VT, symptomatic ATP or a single ICD shock, VT ablation was classified as 'early in the therapeutic course'. In these patients, epicardial mapping was not attempted in case of 1) prior surgery, 2) a septal or basal anterior substrate likely not reachable from the epicardium due to coronary arteries and/or a basal fat layer, 3) only remaining non-clinical very fast VT (cycle length [CL] ≤250ms), 4) patient preference.

### Ventricular tachycardia induction

The procedure was performed under conscious sedation (n=43) or general anesthesia (n=2); anti-arrhythmic drugs (AADs) were discontinued for ≥5 half-lives with the exception of amiodarone (n=19; 42%). In patients who were not under general anesthesia, PES was performed before sedation and opioid administration. PES consisted of three drive CLs (600, 500 and 400ms) with 3 ventricular extrastimuli (≥200ms) from ≥2 right ventricular sites and burst pacing. Positive endpoint was induction of sustained monomorphic VT lasting >30s or requiring termination because of hemodynamic compromise. Isoprenaline was used if the (presumptive) clinical VT could not be induced. Induced VTs were regarded clinical if the 12-lead ECG matched that of a spontaneous VT, or presumptive clinical when the CL matched that of an ICD-recorded VT (difference <30ms).

### Electroanatomical mapping and ablation

Electroanatomical LV endocardial mapping was performed retrogradely during pacing or sinus rhythm using a 3.5mm, irrigated-tip catheter and an electroanatomical mapping system (NaviStar ThermoCool and CARTO XP™, Biosense Webster Inc, Diamond Bar, CA, USA). Epicardial mapping was performed through a subxyphoid puncture. Electrograms were filtered at 30-400Hz (bipolar) and 1-240Hz (unipolar). Endocardial areas with low bipolar voltage (≤1.50mV) or low unipolar voltage (≤8.27mV[14]), and epicardial areas

with low bipolar voltage (≤1.81mV[15]) and low unipolar voltage areas (≤7.95mV[15]) were considered abnormal and consistent with scar if ≥1cm$^2$ in size and accompanied by double potentials, fragmented electrograms, late potentials or other prolonged electrograms ≥50ms.[15] Substrates were classified as septal if they were predominantly located in one of the anteroseptal or inferoseptal segments. Endocardial and epicardial ablation target sites were identified based on the combination of substrate, pace, activation and entrainment mapping for stable VT, and based on substrate and pace mapping for unstable VT (defined as VTs requiring prompt termination[9]). At the epicardium, ablation was usually withheld when the estimated distance to a coronary artery was <5mm, as assessed by integrated CT-derived coronary anatomy and coronary angiography.[16] High output pacing (10mA, 2ms) was performed to determine the location of the phrenic nerve. RF energy was applied at 30-45W (maximum temperature 45ºC, flow 20-30mL/min, 60s) for endocardial sites and ≤50W (flow 20mL/min) for epicardial sites.

### Acute procedural outcome and reasons for non-complete procedural success

After the last RF application, the entire PES protocol was repeated in each patient. Isoprenaline was administered if required to induce VT before ablation. Complete procedural success was defined as non-inducibility of any sustained monomorphic VT regardless of VT CL; partial success as elimination of the (presumptive) clinical VT but persistent inducibility of ≥1 nonclinical VT; failure as persistent inducibility of the (presumptive) clinical VT.

Reasons for non-complete procedural success (partial success and failure) were categorized as 1) vicinity of coronary arteries and/or epicardial fat, 2) proximity of the His bundle, 3) pericardial adhesions, 4) prolonged low cardiac output after electrical cardioversion, 5) no identifiable target site for fast clinical VT, 6) multiple cardioversions for non-clinical fast VT with hemodynamic collapse, 7) patient preference for medical therapy.

### Follow-up

ICDs were offered to all patients regardless of acute procedural outcome. ICDs were typically programmed to include 3 zones: monitor zone (150-188bpm, ATP if indicated), fast VT zone (188-210bpm, ATP and shock), VF zone (>210bpm, if available ATP during charging, and shock). Patients were followed at 3, 6 and 12 months after ablation and at 6- to 12-monthly intervals thereafter. Recordings were analyzed by two experienced observers. Recurrence was defined as any VT treated with ATP or shock and any sustained VT occurring in the monitor zone, including VTs that occurred before discharge from the hospital. In patients without an ICD, VT recurrence was defined as sustained VT documented on a 24h Holter ECG or any complaints suggestive for VT. The reduction of

VT burden was calculated as follows: 1 – (# of VT episodes in period post-ablation / # of VT episodes in same period pre-ablation).

### Disease progression

To analyze the effect of disease progression on VT recurrence, the LV end-diastolic volume (LVEDV) and LV ejection fraction (LVEF) were assessed by transthoracic echocardiography before the procedure and during follow-up. The annual changes in LVEDV and LVEF were calculated as follows: (value last echocardiogram – value baseline echocardiogram)/time interval in years.

### Statistical analysis

Categorical variables are displayed as number (percentage) and continuous variables are expressed as mean±SD when normally distributed or median (first-to-third quartile [Q1-to-Q3]) when non-normally distributed. Categorical variables were compared using the $\chi^2$ test or the Fisher's exact test when the expected value in any cell was below 5. Continuous variables were compared using the Student's *t* test when normally distributed or the Mann-Whitney *U* test when non-normally distributed. The VT burden before and after ablation was compared using the Wilcoxon signed-rank test. Survival curves were estimated by the Kaplan-Meier method and compared by the log-rank test. Univariable logistic regression and Cox regression analysis were performed to identify predictors of acute procedural success and predictors of VT recurrence, respectively. Start of cardiac resynchronization therapy (CRT) during follow-up was included as a time-dependent covariate. Multivariable analyses were not performed due to the limited number of patients and events. Probability values are all 2-sided and, if not otherwise specified, a probability value <0.05 was considered statistically significant. Analyses were performed using SPSS 20.0 software (SPSS Inc, Chicago, Ill).

## RESULTS

### Patients

Forty-five consecutive patients with NICM (76% male, age 60±16 years) were included after failure of 1.8±1.0 AADs. Twelve patients (27%) had previously undergone endocardial VT ablation, 2 of them at another center. Baseline characteristics are displayed in Table 1, the procedural strategy in Figure 1.

### Procedure

A median of 2 (Q1-to-Q3, 2–4) VTs with a mean CL of 342±77ms was induced per patient. Clinical VTs (mean CL 363±98ms) were induced in 43 patients (96%) and only non-clinical

VT in 2 patients (4%), which was based on the 12 lead ECG in 36 patients (80%) and on ICD recordings in 9 patients (20%). In only one patient isoprenaline administration was required to induce the clinical VT before ablation (2%). Bundle branch re-entry (BBR) VT was induced in 3 patients (7%).

**Table 1. Baseline characteristics.**

| | n=45 |
|---|---|
| Male | 34 (76%) |
| Age, years | 60±16 |
| NYHA classification | |
| I | 17 (38%) |
| II | 13 (29%) |
| III or IV | 15 (33%) |
| LV ejection fraction, % | 44±14 |
| LV end-diastolic volume, mL | 171±70 |
| History of atrial flutter/fibrillation | 14 (31%) |
| History of hypertension | 16 (36%) |
| Body mass index, kg/m$^2$ | 27±5 |
| Diabetes mellitus | 5 (11%) |
| Estimated GFR | |
| 30-60 mL/min | 6 (13%) |
| <30 mL/min | 4 (9%) |
| VT burden 6 months (episodes) | 7 (3 - 25) |
| VT burden 12 months (episodes) | 8 (3 - 31) |
| Incessant VT | 5 (11%) |
| VT storm[9] | 17 (38%) |
| ICD shocks in last 12 months | |
| 0 | 23 (51%) |
| 1 | 9 (20%) |
| ≥2 | 13 (29%) |
| Electrical storm in last 12 months | 8 (18%) |
| Clinical VTs >1 morphology | 13 (29%) |
| Cycle length of clinical VT(s) | 363±98 |
| Failed anti-arrhythmic drugs | |
| Class I | 9 (20%) |
| β-blocker | 33 (73%) |
| Sotalol | 15 (33%) |
| Amiodarone | 22 (49%) |
| Calcium-antagonist | 2 (4%) |
| ICD before ablation | 30 (67%) |
| Prior endocardial VT ablation | 12 (27%) |

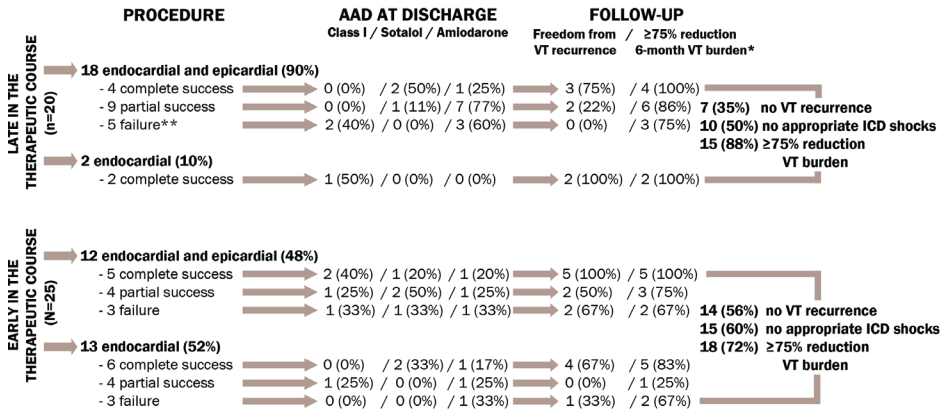


**Figure 1. Procedural strategy**

* In patients who have ≥6 months follow-up. ** Despite intraoperative cryoablation in 2 patients

Endocardial mapping was performed in all patients, percutaneous epicardial mapping in 29 patients (64%) and intraoperative epicardial mapping in 2 patients (4%, in one both percutaneous and intraoperative). Abnormal low bipolar or low unipolar voltage areas were present in all patients who underwent both endocardial and epicardial substrate mapping. Neither RF catheter ablation, nor intraoperative cryoablation was performed in 2 patients (4%) because no target site could be identified. Procedural data are summarized in Table 2.

## Acute procedural outcome and reasons for non-complete success

Complete success was achieved in 17 patients (38%), partial success in 17 (38%) and failure in 11 (24%, including the 2 patients in whom neither RF nor cryoablation was performed). In 2 patients the clinical VT was abolished but the final induction protocol could not be completed due to prolonged low cardiac output after non-clinical VT induction; partial success was achieved in both.

The reasons for non-complete procedural success were proximity of coronary arteries and/or epicardial fat in 5 (18%), the proximity of the His bundle in 2 (7%), adhesions due to prior surgery in 1 (4%), prolonged low cardiac output after cardioversion in 2 (7%), no identifiable target site for fast clinical VT in 5 (18%), multiple cardioversions due to non-clinical fast VT with hemodynamic collapse in 11 (39%) and patient preference for medical therapy in 2 patients (7%).

Seven patients did not undergo epicardial mapping despite non-complete procedural success, because of prior surgery in one, a basal septal substrate likely not reachable from the epicardium based on contrast-enhanced MRI in one, patient preference in one and only remaining very fast non-clinical VT in the setting of ablation early in the therapeutic course in 4 patients.

**Table 2. Procedural data.**

| | n=45 |
|---|---|
| Number of VTs induced | |
| 1 | 10 (22%) |
| 2 | 16 (36%) |
| ≥3 | 19 (42%) |
| Bundle branch re-entry VT | 3 (7%) |
| Hemodynamic stability of VTs | |
| Only stable VT | 14 (31%) |
| Only unstable VT | 11 (24%) |
| Stable and unstable VT | 20 (44%) |
| Cycle length of induced VTs (ms) | |
| Shortest | 294±69 |
| Mean | 342±77 |
| Longest | 395±116 |
| Pericardial puncture | 29 (64%) |
| Endocardial substrate mapping | 42 (93%) |
| Bipolar voltage area ≤1.50mV | 29/42 (69%) |
| Unipolar voltage area ≤8.27mV | 39/42 (93%) |
| Epicardial substrate mapping | 27 (60%) |
| Bipolar voltage area ≤1.81mV | 23/27 (85%) |
| Unipolar voltage area ≤7.95mV | 23/27 (85%) |
| Predominantly septal substrate | 19/42 (45%) |
| Substrate location/extent involves | |
| Any basal segment | 40/42 (95%) |
| Any mid segment | 25/42 (56%) |
| Any apical segment | 12/42 (27%) |
| Radiofrequency energy applications | |
| Only endocardial | 22 (49%) |
| Only epicardial | 2 (4%) |
| Endocardial and epicardial | 18 (40%) |
| None | 3 (7%) |
| Intra-operative cryoablation | 2 (4%) |
| Procedural duration (min) | 206±86 |
| Fluoroscopy time (min) | 45±21 |



## Predictors of acute procedural outcome

A higher age (odds ratio [OR] 1.78, p=0.01) and lower creatinine clearance (OR 1.28 per 10 mL/min decrease, p=0.03) were associated with non-complete procedural success (Figure 2). A trend was observed for lower LVEF (OR 1.52 per 10% decrease, p=0.09) and induction of unstable VT (OR 3.26, p=0.08).

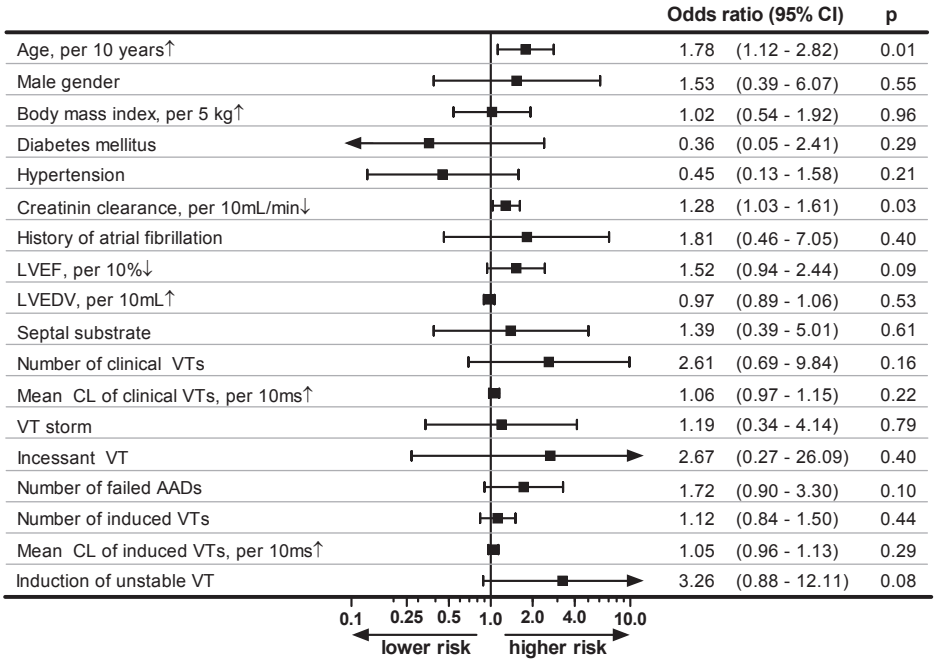


**Figure 2. Predictors of non-complete procedural success**
CI denotes confidence interval. CL, Cycle length

## Complications

One patient developed a pseudo-aneurysm of the femoral artery. Acute pericardial bleeding >80mL occurred in 2/29 patients (7%) who underwent pericardial puncture. One patient (3%) who accidentally received heparin developed tamponade after the procedure managed by drainage.

## VT recurrence during follow-up

All but 4 patients were discharged with an ICD; 8 patients (18%) were discharged on class I AADs, 29 (64%) on β-blocker, 10 (22%) on sotalol and 17 (38%) on amiodarone. During median 24 (Q1-to-Q3, 12–37) months follow-up (no patient lost to follow-up; at least 6 months follow-up in 42 patients, remaining 3 patients died within 6 months) 24 patients (53%) had VT recurrence, 20 (44%) received ≥1 ICD shock and 6 patients (13%) experienced an episode of electrical storm (defined as ≥3 appropriate ICD shocks within 24 hours). Only 1/8 patients with electrical storm before ablation had electrical storm recurrence.

The 6-month VT burden was reduced by ≥75% in 33/42 patients (79%) with at least 6 months follow-up (Figure 3). The 6-month VT burden was reduced equally in patients with and without an ICD before ablation (78% vs. 80% of patients ≥75% reduction,

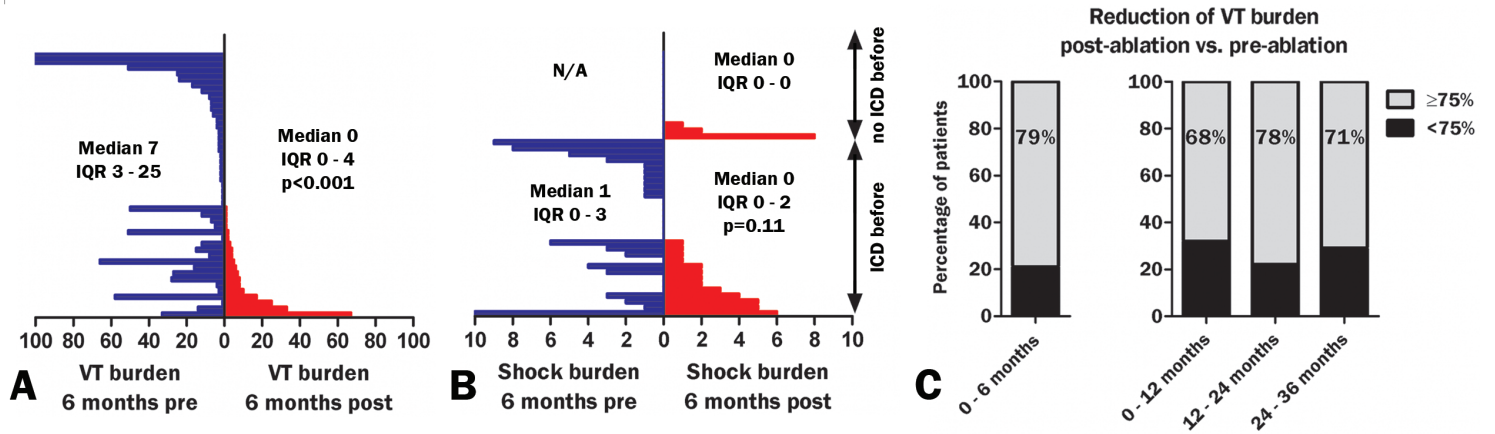


**Figure 3. Reduction of ventricular tachycardia and shock burden after ablation**

Panel A: All 45 patients are sorted according to 6-month ventricular tachycardia (VT) burden during follow-up on the right side of the y-axis (red bars), with the corresponding 6-month VT burden before ablation on the left side of the y-axis (blue bars). The VT burden is truncated at 100. Panel B: All 45 patients are sorted according to 6-month appropriate shock burden. Patients with (n=30) and without (n=15) an implantable cardioverter defibrillator (ICD) before ablation are displayed separately in the lower and upper parts of the graph, as indicated. The shock burden is truncated at 10. Panel C: Percentage of patients with ≥75% reduction of VT burden.

p>0.05). The 12-month VT burden was reduced by ≥75% in 68%, 78% and 71% of patients in the first, second and third year after ablation, respectively.

Eleven of 24 patients (46%) with VT recurrence had ≥1 fast VT (CL≤300ms) and 20/24 patients (83%) with VT recurrence received ≥1 appropriate ICD shock. A median of 23% (Q1-to-Q3, 5–64%) of all VTs per patient required a shock for termination.

### Impact of noninducibility

Only 3/17 patients (18%) with complete procedural success had VT recurrence, compared with 13/17 patients (77%) with partial procedural success and 8/11 patients (73%) with procedural failure (Figure 4). The 6-month VT burden was reduced by ≥75% in 94%, 67% and 70%, respectively. Importantly, 6/11 patients (55%) with induction of a very fast VT (CL≤250ms) at the end of the procedure had VT recurrence, including 2/3 patients (67%) with persistent inducibility of clinical very fast VT and 4/8 patients (50%) with inducibility of non-clinical very fast VT.

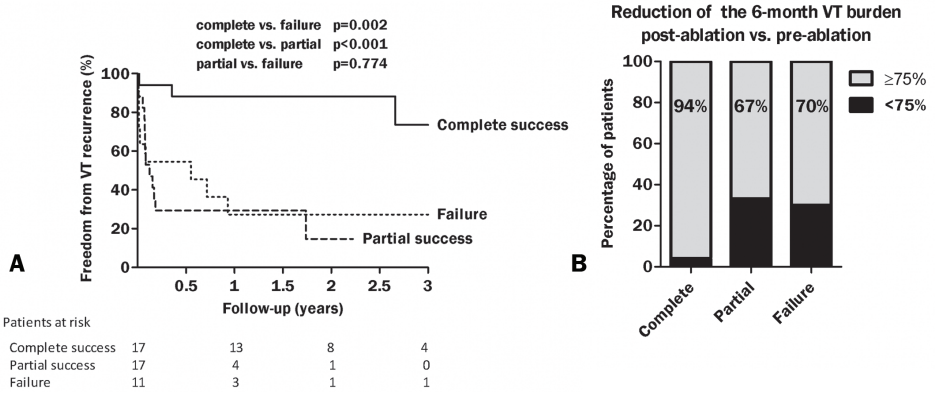


**Figure 4. Ventricular tachycardia recurrence and reduction of the 6-month VT burden according to acute procedural outcome**

### Predictors of VT recurrence

Non-complete procedural success (hazard ratio [HR] 8.20, p=0.001), lower LVEF (HR 1.61 per 10% decrease, p=0.004), VT storm (HR 2.50, p=0.03), a higher number of failed AADs (HR 1.62, p=0.01) and a longer mean CL of induced VTs (HR 1.08 per 10ms increase, p=0.02) were identified as predictors of VT recurrence (Figure 5). A trend was observed for the number of induced VTs (HR 1.08 per VT, p=0.09).

### Disease progression and VT recurrence

Disease progression was assessed by repeat echocardiography up to 19±9 months after baseline echocardiography in the 21/42 patients (50%) with at least 6 months follow-up.

The LVEF decreased by a median of 1.4% (Q1-to-Q3, -3.0–4.5%) and the LVEDV increased by a median of 10mL (Q1-to-Q3, -10–26mL) per year. In 5 patients (24%) the LVEF decreased by ≥5%/year, all had VT recurrence (100%). In 11 patients (31%) the LVEDV increased by ≥10mL/year, 7 had VT recurrence (64%).

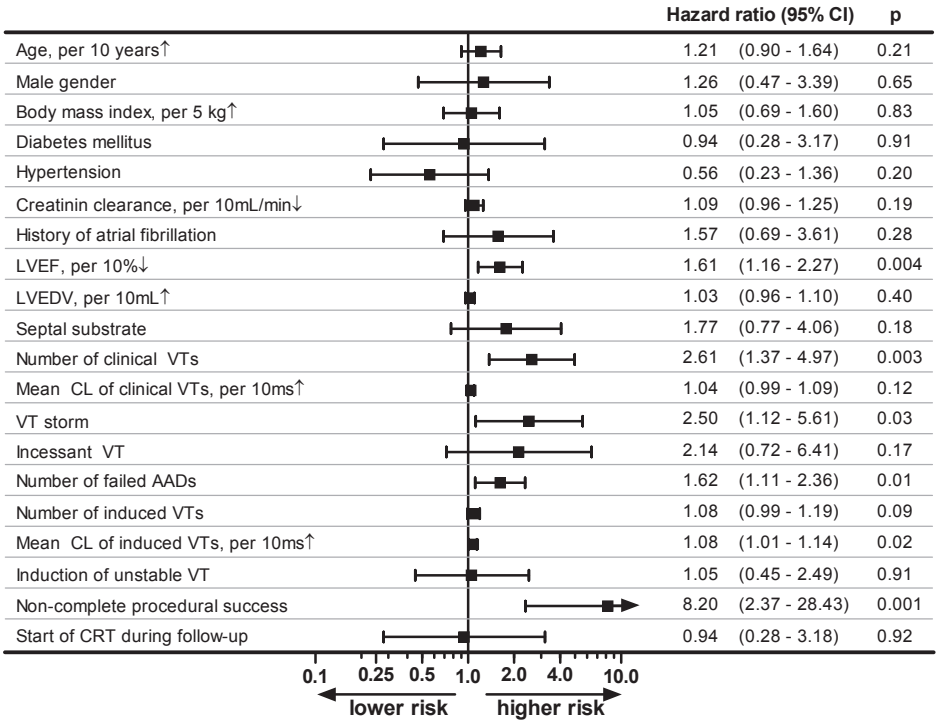


**Figure 5. Predictors of ventricular tachycardia recurrence**
CI denotes confidence interval; CRT, cardiac resynchronization therapy

## VT ablation early in the therapeutic course

Epicardial mapping was performed in 12/25 patients (48%, Figure 1) who underwent VT ablation early in the therapeutic course (i.e. for a first VT, symptomatic ATP or a single ICD shock). Complete success was achieved in 11 (44%), partial success in 8 (32%) and ablation failed in 6 (24%). The procedure was complicated by a pseudo-aneurysm of the femoral artery in 1 patient (4%) and tamponade after the procedure in another (4%). During a median follow-up of 24 months (Q1-to-Q3, 13–37 months), 14 patients (56%) were free from VT and 15 (60%) were free from appropriate ICD shocks. Twelve of 25 patients (48%) were both off amiodarone and without recurrent VT during follow-up.

The acute success rate and VT recurrence rate were not significantly different between patients undergoing ablation early in the therapeutic course and the other patients (p=0.58 and p=0.17, Figure 1).

### Repeat ablation

Repeat VT ablation was performed in 8/45 patients (18%) 11±11 months after the index procedure because of incessant VT and/or ≥1 appropriate ICD shock. Seven had prior partial success and one complete success. Pericardial puncture was performed in 4 (50%), but was unsuccessful due to adhesions in 2 patients who underwent epicardial mapping at baseline, despite intravenous steroids after the procedure. Complete procedural success was achieved in 3/8 patients (38%), partial success in 4 (50%) and failure in 1 (13%). During a mean follow-up of 17±13 months, 4 patients (50%) had VT recurrence and 2 (25%) received one appropriate ICD shock. Three of 6 patients (50%) with ≥6 months follow-up had ≥75% reduction of the 6-month VT burden.

### Mortality during follow-up

Six patients (13%) died during follow-up. The cause of death was terminal heart failure (n=2), incessant VT in the setting of progressive heart failure (n=2), respiratory insufficiency after cardiac surgery (n=1) and cancer (n=1). Two patients (4%) underwent cardiac transplantation.

## DISCUSSION

The main findings of this study can be summarized as follows: 1) although VT occurs in 53% of NICM patients after ablation, the 6-month VT burden was substantially reduced in 79%, 2) complete procedural success, defined as non-inducibility of any VT after the last RF application, was associated with low VT recurrence rates, whereas partial success and procedural failure were both associated with high recurrence rates, 3) non-complete procedural success, a lower LVEF, a higher number of clinical VTs, VT storm, a higher number of failed AADs and a higher mean CL of induced VTs are predictors of VT recurrence and 4) after VT ablation early in the therapeutic course, 56% of NICM patients remain free from VT recurrence.

### Prior reports

To our knowledge, this series of NICM patients undergoing VT ablation and complete PES after the last RF delivery is the largest reported to date. Patients had a higher LVEF than patients in prior studies (44% vs. 27-34%[3,7,13,17-20]), had less frequently an ICD before ablation (67% vs. 71-100%[3,7,13,17-20]) and were less often on amiodarone (42% vs. 43-88%[3,13,17-20]), suggesting that VT ablation was employed at an earlier stage, which is in line with recently extended indications for VT ablation.[9]

Complete procedural success was achieved in 38% of patients, which is lower than some prior studies[7,17,18] but similar to others.[3,13,21] However, the currently reported recur-

rence rate of 53% during median 24 (Q1-to-Q3, 12–37) months follow-up is, considering differences in follow-up duration, favorable when compared to two studies employing epicardial mapping in the majority of patients[3,13] and similar to one study with epicardial mapping in all patients.[17] An overview of studies analyzing outcome of VT ablation in NICM is provided in a supplemental Table.

### Noninducibility as a procedural endpoint

The majority of available data on the predictive value of non-inducibility is derived from post-MI patients.[1,2,4-6] NICM patients may however have a different arrhythmogenic substrate.[3,22] Of interest, 96% of our patients were inducible for the clinical VT, suggesting the presence of a fixed substrate. The small number of patients under general anesthesia and the fact that initial PES was performed before sedative and opioid administration may also have contributed to this finding.

Only 2 small prior studies (including 13 and 16 patients) have analyzed the value of PES at the end of VT ablation procedures in patients with NICM.[3,7] In the present study PES was performed after the last RF application in all 45 patients. Perhaps due to the consistent application of the induction protocol, patients remained more often inducible for non-clinical and in particular fast VTs, and therefore partial success may have been achieved more frequently compared to prior studies (supplemental Table). Prolonged depression of cardiac output prevented completion of the induction protocol in only 2 patients, which may be partly due to the higher LVEF and our strategy to perform substrate mapping and only limited mapping during VT in all patients independent of VT CL.

Both partial procedural success and failure were associated with high VT recurrence rates, indicating that partial success may not be superior to ablation failure. Importantly, 55% of patients with induction of a very fast VT (CL≤250ms) after ablation had VT recurrence, suggesting that induction of these VTs after ablation is not a non-specific finding. However, the latter does not necessarily imply that very fast, nonclinical VTs should always be targeted. Persistent inducibility of very fast VTs may be a marker for a more complex or functional arrhythmogenic substrate less amenable to VT ablation. This is in line with the observation that 83% of patients required one or more ICD shocks to terminate ≥1 VT which may be due to ATP failure or short VT CL. Further studies are needed to assess whether additional ablation can abolish these nonclinical, usually rapid VTs and improve long-term outcomes after ablation.

### Predictors of acute procedural success and VT recurrence

Higher age was strongly associated with non-complete procedural success, also after adjustment for epicardial access, LVEF and AADs (data not shown), perhaps due to a

different substrate in older patients. Interestingly, although age was associated with non-complete procedural success, it seemed not to predict VT recurrence.

All patients with a significantly decreasing LVEF and 64% of patients with a significantly increasing LVEDV had VT recurrence during follow-up, perhaps indicating that patients with deteriorating LV function and dimensions may be at high risk for VT recurrence. Previous studies in post-MI patients demonstrated that a lower LVEF[6,23], a higher number of induced VTs[23,24], a higher number of clinical VTs[6] and acute procedural failure[6] are associated with VT recurrence. The current study suggests that most of these factors also apply to patients with NICM. Different substrates may however result in comparable clinical features, such as lower LVEF, and to date little is known about the VT substrates in NICM. Therefore, more studies are needed to identify potentially different substrates and their impact on VT occurrence. So far, PES after the last RF application is the strongest predictor of VT recurrence and may therefore be an important tool to identify patients who may need additional ablation, epicardial mapping and/or enhanced drug therapy.

### VT ablation early in the therapeutic course

This is the first study reporting on the results of VT ablation in NICM patients presenting with a first VT, symptomatic ATP or a single ICD shock. Importantly, no complication resulted in serious sequelae. Fifty-six percent had no VT recurrence and 60% were free from ICD shocks during follow up. Twelve of 25 patients (48%) were off amiodarone and without recurrent VT during follow-up. These findings suggest that VT ablation may be considered for indications such as a first VT, symptomatic ATP or a single ICD shock in NICM patients and perhaps even be considered as an alternative to life-long amiodarone therapy, particularly in young patients. The risks of VT ablation should be weighed carefully against the risks of medical therapy, which persist during follow-up and may include serious side effects. When considering epicardial ablation, the risk of pericardial adhesions preventing future pericardial access should also be taken into account, which may occur even after administration of intrapericardial steroids.

### Limitations

Non-complete procedural success may have been caused by lack of epicardial access in 7 patients (16%). One patient preferred not to undergo epicardial mapping and in the remaining 6 patients the potential benefits were considered not to outweigh the risks based on the clinical presentation. In a significant proportion of patients an ICD was implanted only after the procedure and therefore, ICD therapy for non-sustained VT after the procedure may have led to an underestimation of the reduction of VT burden. Echocardiography was performed in 50% of patients who survived ≥6 months after ablation and therefore, the relation between LVEF decrease and LVEDV increase and VT recurrence should be interpreted with caution.

## CONCLUSION

Although VT recurs in 53% of the patients during follow-up, the 6-month VT burden is reduced by ≥75% in 79% of patients. Noninducibility may be an appropriate endpoint in patients with NICM, as recurrence rates are low after complete procedural success, but high after both partial success and failure. Importantly, induction of very fast VT after ablation appears not to be a non-specific finding. Non-complete procedural success, a lower LVEF, VT storm, a higher number of clinical VTs, a higher number of failed AADs and a higher mean CL of induced VTs are predictors of VT recurrence. After ablation for a first VT, symptomatic ATP or a single ICD shock, 56% of NICM patients remain free from VT recurrence.

## CLINICAL PERSPECTIVE

There are limited data on ventricular tachycardia (VT) ablation in patients with nonischemic left ventricular cardiomyopathy, in particular, on the procedural end point. The present study comprised 45 patients with nonischemic cardiomyopathy who underwent VT ablation. The complete programmed electric stimulation protocol was consistently applied after the last radiofrequency energy application in each patient, resulting in noninducibility of any VT in 38%, induction of nonclinical VT in another 38%, and inducibility of the clinical VT in 24%. Although VT recurred in approximately half of the patients during follow-up, the VT burden was substantially reduced in the majority. In 25 patients VT ablation was performed because of a first VT, symptomatic ATP, or a single implantable cardioverter defibrillator shock; 56% of these patients remained free from VT during follow-up, suggesting that catheter ablation may also be considered early in the therapeutic course. Programmed electric stimulation after ablation seemed to provide important prognostic information. Noninducibility of any VT was associated with a very low recurrence rate during long-term follow-up, whereas persistent inducibility of clinical or nonclinical VT was associated with a poor prognosis. Induction of very fast VT, which has previously been considered a nonspecific finding, also seemed to be associated with a high recurrence rate. Inducibility of VT after ablation was the strongest predictor of VT recurrence. These data support the role of programmed electric stimulation to assess the procedural end point in patients with nonischemic cardiomyopathy and may, therefore, significantly aid clinicians who perform VT ablation in this population.

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**Supplemental Table 1. Studies analyzing outcome of VT ablation in nonischemic cardiomyopathy**

| First author and year of publication | Hsia[19] 2003 | Soejima[20] 2004 | Cano[17] 2009 | Nakahara[3] 2010 | Schmidt[13] 2010 | Arya[7] 2010 | Haqqani[18] 2011 | Current study |
|---|---|---|---|---|---|---|---|---|
| **Population** | Only endocardial | Only LVEF≤50% | All endo-epicardial | - | All endo-epicardial | Electrical storm | Isolated septal substrate | - |
| **Number of patients** | 19 | 28 | 22 | 16 | 16 | 13 | 31 | 45 |
| **Age** | 61±16 | 54±14 | 56±13 | 59±11 | 57±11 | 57±18% | 59±12 | 60±16 |
| **LV ejection fraction (%)** | 34±11 | 30±11 | 30±13 | 27±12 | 32±8 | 33±9 | 30±14 | 44±14 |
| **Failed antiarrhythmic drugs** | - | - | All ≥1 | All ≥1 | 2±2 | All ≥2 | All ≥1 | 1.8±1.0 |
| **ICD before** | 84% | 71% | 95% | 94% | 81% | 100% | 84% | 67% |
| **Prior ablations** | - | 7% | mean 1.8 | 38% | 100% | - | 32% | 27% |
| **Pericardial access** | 0% | 29% | 100% | 75% | 94% | 24% | 45% | 64% |
| **Anesthesia during epicardial mapping** | NA | - | General | General | - | - | CS or general | 96% CS, 4% General |
| **VTs induced per patient** | 3±1 | 2.9±1.7 | mean 3.3 | 2.6±1.6 | 1.9±1.7 | range 1 – 4 | mean 4.9 | 2 (2 - 4) |
| **Mean cycle length (ms)** | 373±91 | - | 392±109 | 421±88 | 409±94 | 384±75 | 396±90 | 342±77 |
| **Amiodarone at time of procedure** | 63% | 43% | 59% | 88% | 69% | - | 74% | 42% |
| **Complete success** | 74% | 61% | 67% | 44% | 38% | 62% | 66% | 38% |
| **Partial success** | 26% | 14% | 33% | 44% | 38% | 38% | 20% | 38% |
| **Failure** | | 25% | | 13% | 24% | 0% | 14% | 24% |
| **Follow-up duration in months** | 22±12 | 9±9 | 18±7 | 15±13 | median 12 | median 23 | 20±28 | median 24 |
| **VT recurrence rate** | 58% | 36% | 29% | 50% | 47% | 38% | 32% | 53% |
| **VT recurrence rate per year** | 32% | 48% | 19% | 40% | 47% | 20% | 19% | 27% |

The table includes all studies including ≥10 patients with nonischemic cardiomyopathy who underwent VT ablation.
CS denotes conscious sedation; LV, left ventricle; ICD, implantable cardioverter defibrillator; VT, ventricular tachycardia