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Clinical Outcomes in Patients With Dilated Cardiomyopathy and Ventricular Tachycardia

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ABSTRACT

BACKGROUND Recurrent ventricular tachycardia (VT) due to dilated cardiomyopathy (DCM) is difficult to treat, and long-term outcome data are limited.

OBJECTIVES The aim of this study was to identify predictors of mortality or heart transplantation (HTx) and VT recurrence.

METHODS Consecutive patients with DCM accepted for radiofrequency catheter ablation (RFCA) of VT at 9 centers were prospectively enrolled and followed.

RESULTS Of 281 consecutive patients (mean age 60 ± 13 years, 85% men, mean left ventricular ejection fraction [LVEF] 36% ± 12%), 35% had VT storm, 20% had incessant VT, and amiodarone was unsuccessful in 68%. During follow-up of 21 months (IQR: 6-30 months), 67 patients (24%) died or underwent HTx, and 138 (49%) had VT recurrence (45 within 30 days, defined as early); the 4-year rate of VT recurrence or mortality or HTx was 70%. Independent predictors of mortality or HTx were early VT recurrence (HR: 2.92; 95% CI: 1.37-6.21; $P < 0.01$), amiodarone at discharge (HR: 3.23; 95% CI: 1.43-7.33; $P < 0.01$), renal dysfunction (HR: 1.92; 95% CI: 1.01-3.64; $P = 0.046$), and LVEF (HR: 1.36; 95% CI: 1.0-1.84; $P = 0.052$). LVEF ≤32% identified patients at risk for mortality or HTx (area under the curve: 0.75). Mortality or HTx per 100 person-years was 40.4 events after early, compared with 14.2 events after later VT recurrence and 8.5 events with no VT recurrence after RFCA ($P < 0.01$ for both). Patients with early recurrence and LVEFs ≤32% had a 1-year rate of mortality or HTx of 55%. VT recurrence was predicted by prior implantable cardioverter-defibrillator shocks, basal anteroseptal VT origin, and procedural failure but not LVEF.

CONCLUSIONS Patients with DCM needing RFCA for VT are a high-risk group. Following RFCA, approximately one-half remain free of VT recurrence. Early VT recurrence with LVEF ≤32% identifies those at very high risk for mortality or HTx, and screening for mechanical support or HTx should be considered. Late VT recurrence after RFCA does not predict worse outcome. (J Am Coll Cardiol 2022;80:1045-1056) © 2022 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

AAD = antiarrhythmic drug

DCM = dilated cardiomyopathy

HTx = heart transplantation

ICD = implantable cardioverter-defibrillator

IHD = ischemic heart disease

LBBB = left bundle branch block

LV = left ventricular

LVEF = left ventricular ejection fraction

NYHA = New York Heart Association

PES = programmed electric stimulation

RFCA = radiofrequency catheter ablation

VT = ventricular tachycardia

Radiofrequency catheter ablation (RFCA) is being increasingly performed to reduce symptomatic recurrent ventricular tachycardia (VT) and implantable cardioverter-defibrillator (ICD) therapy in patients with ischemic heart disease (IHD) and nonischemic dilated cardiomyopathy (DCM). Persistent inducibility after catheter ablation and VT recurrence during follow-up have been associated with higher mortality in retrospective cohorts.[1-5] Accordingly, it has been suggested that aggressive initial and repeated ablation after VT recurrence may positively affect survival by reducing VT episodes and ICD shocks.[1] Procedural failure and VT recurrence may, however, be surrogate markers for both disease severity and the complexity of the underlying VT substrate.

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VT recurrence has been reported to be significantly higher in patients with DCM compared with those with IHD, although mortality after ablation did not differ.[6] In IHD, a lower left ventricular ejection fraction (LVEF) and a higher New York Heart Association (NYHA) functional class have been consistently associated with VT recurrence after ablation.[5,7] In DCM, there are conflicting data concerning the association between cardiac function and VT recurrence.[2,8] In contrast, in both patients with IHD and those with DCM, a low LVEF is a strong and consistent predictor of (cardiac) mortality.[9,10] These data suggest that in DCM, substrate-specific parameters that are not necessarily related to cardiac function and mortality may determine freedom from VT. Most of the available data on ablation outcome, VT recurrence, and prognosis are derived from patient cohorts with IHD, which cannot be extrapolated to patients with DCM. Large, prospective, multicenter data on VT recurrence and mortality after RFCA in contemporary patients with DCM receiving optimal heart failure management are lacking.

The aims of this international multicenter DCM VT study are to: 1) evaluate acute and long-term outcomes after RFCA; 2) identify predictors of VT recurrence and mortality; and 3) evaluate the prognostic impact of VT recurrence and the timing of recurrence on mortality in a contemporary cohort of patients with DCM enrolled according to an intention-to-treat principle.

METHODS

STUDY DESIGN. The DCM VT study is a prospective, international, multicenter cohort study to evaluate acute and long-term outcomes after VT ablation in consecutive patients with DCM enrolled according to an intention-to-treat principle.

PATIENT POPULATION. Consecutive patients with nonischemic DCM who were accepted for ablation of recurrent sustained VT occurring within the 6 months before treatment were enrolled at 9 participating centers. Patients were also included if they had entered the electrophysiology laboratory for potential ablation but ablation was not performed. The start and duration of the enrollment period varied across institutions, but all procedures were performed between September 2013 and January 2017. Patients with prior myocardial infarctions, significant coronary artery disease (>75% stenosis in any major coronary artery), right-dominant cardiomyopathy, hypertrophic cardiomyopathy, left ventricular (LV) noncompaction cardiomyopathy, restrictive cardiomyopathy, prior acute or subacute myocarditis, cardiac sarcoidosis, Chagas disease, tachycardia-induced cardiomyopathy, primary significant valvular heart disease, prior valve replacement, or congenital heart disease were excluded.

All patients provided informed consent for treatment according to local institutional requirements. Data regarding baseline characteristics, heart failure management, arrhythmic presentation and prior treatment, details of mapping and ablation, acute procedural success, procedure-related complications, VT recurrence, mortality, and cause of death during follow-up were anonymized and gathered online in a secured central database. Genetic testing and cardiac magnetic resonance imaging were encouraged but not required for inclusion. The study was approved by the Leiden, den Haag ethics committee.

ELECTROPHYSIOLOGICAL STUDY AND CATHETER ABLATION. Initial programmed electric stimulation (PES) was performed, and the number, cycle length, and configurations of all induced VTs were collected.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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TABLE 1 Baseline Characteristics (N = 281)

Age, y	60 ± 13
Male	238 (85)
Hypertension	127 (45)
Diabetes mellitus	54 (19)
COPD	21 (8)
Renal dysfunction (eGFR <50 mL/min)	90 (32)
History of atrial fibrillation	105 (37)
Family history of DCM	39 (14)
Time since diagnosis DCM, y	5 (2-9)
(Likely) pathogenic mutation/number tested	28/101 (28)
LVEF, %	36 ± 12 35 (27-42)
LVEF >35%	123 (43)
NYHA functional class	
I	111 (40)
II	91 (32)
III/IV	67 (24)
Prior treatment	
ICD	250 (89)
CRT-D	80 (28)
Failed AADs	
Sotalol	74 (26)
Amiodarone	192 (68)
Amiodarone plus class I AAD	51 (18)
Prior VT ablation	126 (44)
Arrhythmic presentation	
Electrical storm	100 (35)
Incessant VT	55 (20)
ICD shocks	191 (68)
Hemodynamically tolerated VT	143 (51)
Rhythm at admission	
Sinus rhythm	182 (65)
Atrial fibrillation	37 (13)
Atrial pacing	61 (22)
Ventricular pacing	81 (29)
Median QRS duration, ms	133 (102-170)
Nonpaced QRS, ms	114 (100-145)
Medication at admission	
Beta-blocker	237 (84)
ACE inhibitor or ARB	219 (80)
Mineralocorticoid receptor antagonist	113 (40)
Diuretic agent	155 (55)
Amiodarone	152 (54)
Sotalol	42 (15)
Class I AAD	80 (28)
Combination class I and III	49 (19)

Values are mean ± SD, n (%), or median (IQR).

AAD = antiarrhythmic drug; ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; COPD = chronic obstructive long disease; CRT-D = cardiac resynchronization therapy-defibrillator; DCM = dilated cardiomyopathy; eGFR = estimated glomerular filtration rate; ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; VT = ventricular tachycardia.

The use of state-of-the-art mapping and ablation techniques was encouraged, including a combined endo- and epicardial approach for intramural or subepicardial substrates, high-density electroanatomical substrate mapping and activation mapping for tolerated VTs, followed by irrigated-tip catheter ablation targeting all induced VTs and the VT substrate. After ablation, PES was repeated from at least 2 right ventricular sites and ≥1 LV site. A protocol including a baseline train of 350 ms and up to 4 extrastimuli and the use of isoproterenol was encouraged to determine acute procedural outcome at the end of RFCA procedure whenever considered safe. Procedural success was defined as noninducibility of any monomorphic sustained VT. The procedure was considered unsuccessful if any sustained monomorphic VT remained inducible irrespective of VT cycle length or if PES was not performed at the end of the procedure. VTs with an inferior axis and left bundle branch block (LBBB)-like configuration were considered to originate from an anteroseptal substrate, and, among these, those with an early transition (dominant R in leads V_2 and V_3) to originate from a basal anteroseptal substrate. Pleomorphic VTs, VTs that caused hemodynamic compromise, and VTs that degenerated to ventricular fibrillation were considered unmappable.

FOLLOW-UP. Patients were followed up at 6-month intervals. VT recurrence was defined as the occurrence of any sustained VT requiring ICD therapy or recorded within the ICD monitor zone lasting >30 seconds or documented on 12-lead electrocardiography, including VTs that occurred before discharge from the hospital. Mortality and its cause were recorded as reported by the investigators. The national social security death index database was queried for vital status if appropriate.

STUDY ENDPOINTS. The primary endpoint was a composite endpoint of all-cause mortality or heart transplantation (HTx) and VT recurrence.

Secondary endpoints were: 1) acute procedural success; 2) any VT recurrence; 3) early VT recurrence, defined as VT recurrence within 30 days from the ablation procedure; and 4) all-cause mortality or HTx.

STATISTICAL ANALYSIS. Continuous variables are reported as mean ± SD or median (IQR) and were compared using Student's *t*-test or the Mann-Whitney *U* test, as appropriate. Categorical variables are expressed as number (%) and were compared using the chi-square or Fisher exact test. The survival curves were estimated using the Kaplan-Meier method. A Cox proportional hazards model was created to detect significant predictors of mortality or HTx, VT recurrence, and a combined endpoint of mortality or HTx and VT recurrence (reported as the HR with its 95% CI). Independent predictors of these endpoints were analyzed with multivariable models using backward stepwise selection. Variables for the

TABLE 2 Procedural Data (N = 281)

Procedure	
General anesthesia	176 (63)
Number of induced VTs	2 (1-4)
Minimal VT CL, ms	310 (270-360)
Maximal VT CL, ms	380 (334-460)
Noninducible at baseline	33 (12)
Any unmappable VT inducible	163 (58)
Mapping	
LV endocardium	255 (91)
RV endocardium	111 (40)
Epicardium	162 (58)
Target site definition	
Activation/entrainment mapping	130 (46)
Substrate mapping	253 (90)
Abnormal EGM/LP	
LV endocardium (n mapped = 255)	190 (75)/111 (44)
RV endocardium (n mapped = 111)	45 (41)/27 (24)
Epicardium (n mapped = 162)	123 (76)/71 (44)
Ablation sites	
LV endocardium	207 (73)
RV endocardium	67 (24)
Epicardium	125 (44)
Aortic root	16 (6)
Procedural time, min	220 (170-275)
Fluoroscopy time, min	31 (22-49)
Acute outcome	
Complications	32 (11)
Procedure-related death	2 (1)
Pericardial bleeding/tamponade	5/2 (2)
AV block	7 (2)
Vascular complications	10 (3)
Bail-out ablation procedures	
Bipolar ablation	8 (3)
Transcoronary alcohol ablation	2 (<1)
Surgical ablation	5 (2)
PES performed after ablation	220 (78)
Any VT inducible	89 (32)
Clinical VT inducible	33 (12)
PES not performed (reasons)	61 (22)
Noninducible baseline	11
Patient condition/complications	19
No ablation performed	8
Discharge treatment	
ICD at discharge	267 (95)
CRT-D	95 (34)
AAD at discharge	
Amiodarone	132 (47)
Sotalol	46 (16)
Class I	43 (15)
Combination class I and class III	14 (5)

Values are n (%), median (IQR), or n.

AV = atrioventricular; CL = cycle length; EGM = electrogram; LP = late potential; LV = left ventricular; PES = programmed electric stimulation; RV = right ventricular; other abbreviations as in Table 1.

multivariable model were selected on the basis of the result of univariable evaluation ($P < 0.10$) and known predictive value for the endpoint on the basis of previous studies. At each step, the least significant variable was removed from the model, until all variables reached P values <0.20.

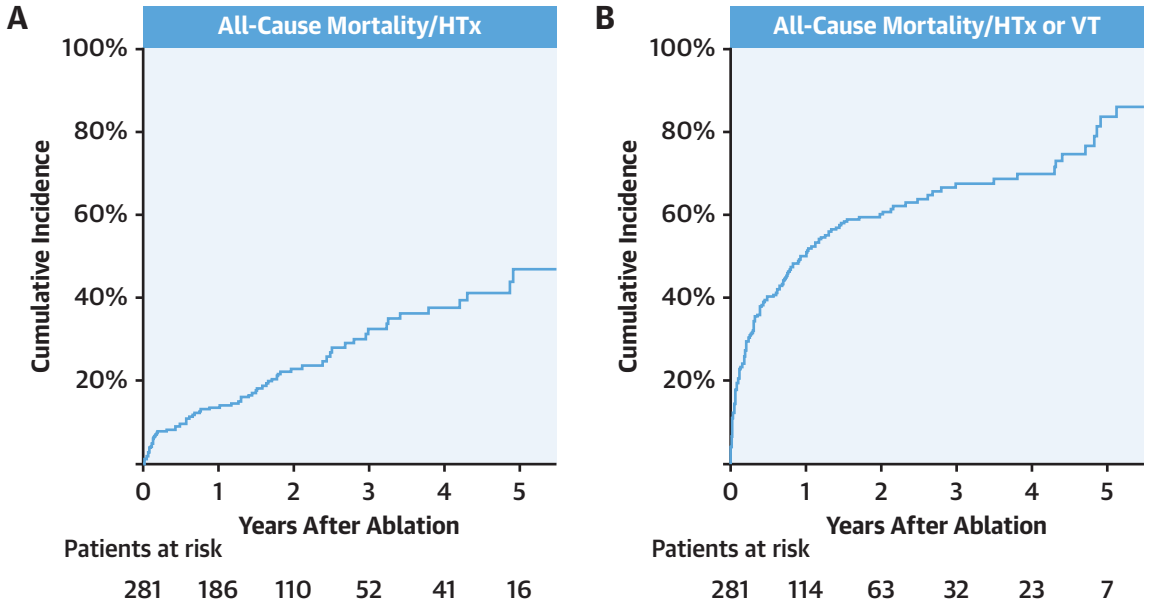
To account for the competing risk for mortality and VT recurrence during follow-up, the cumulative incidence of each individual event was estimated using the competing-risk method, in which death of any cause was considered a competing risk. For comparisons between exposure groups, the Gray test was used. Receiver-operating characteristic curve analysis was performed to determine the optimal cutoff value of LVEF for all-cause mortality or HTx, defined as the values maximizing the sum of sensitivity and specificity.

The time to event from the date of the procedure to the date of the event of interest was used to estimate the incidence rates of all-cause mortality that occurred between the catheter ablation procedure and the first recurrence of VT or the end of follow-up (whichever occurred first) and between the first recurrence of VT and the end of follow-up. Incidence rates are expressed as events per 100 person-years with 95% CI. All tests were 2-sided, and a P value <0.05 was considered to indicate statistical significance. Cumulative incidence function analyses and incidence rates with 95% CIs were determined using R version 4.0.3 (R Foundation for Statistical Computing). Other analyses were performed using SPSS version 27.0 (IBM).

RESULTS

PATIENT CHARACTERISTICS. Baseline characteristics are presented in Table 1. A total of 281 consecutive patients (mean age 60 ± 13 years, 85% men) with DCM were enrolled at 9 centers (median 26 patients per center [IQR: 14-56 patients per center] during a median inclusion period of 20 months [IQR: 13-26 months]). Patients presented after a median of 5 years (IQR: 2-9 years) since the first diagnosis of DCM. The mean LVEF at admission was 36% ± 12%, and 71% of patients were in NYHA functional class I or II. Genetic testing was performed in 101 patients and revealed pathogenic or likely pathogenic (class IV or V) mutations in 28% of those tested. A total of 100 patients (35%) presented with VT storm and 55 (20%) with incessant VT. In 191 patients (68%), ICD shocks were required to terminate VT. Amiodarone in 192

FIGURE 1 **Cumulative Incidence of All-Cause Mortality and the Composite Endpoint**



Survival curves were estimated using the Kaplan-Meier method. Death or heart transplantation (HTx) rates were substantial. The cumulative incidence of all-cause mortality or HTx **(A)** was 38% at 4 years after the index ablation. The cumulative incidence of the combined endpoint **(B)** was 50%, 60%, and 70% **(B)**, respectively, at 1, 2, and 4 years after the index procedure. VT = ventricular tachycardia.

patients (68%) and a combination of amiodarone and class I antiarrhythmic drugs (AAD) in 51 patients (18%) failed to control VT. A median of 1 (IQR: 1-2) prior VT ablation procedure had been performed in 126 patients (44%). The baseline characteristics of patients, according to prior ablation procedure, are provided in Supplemental Table 1.

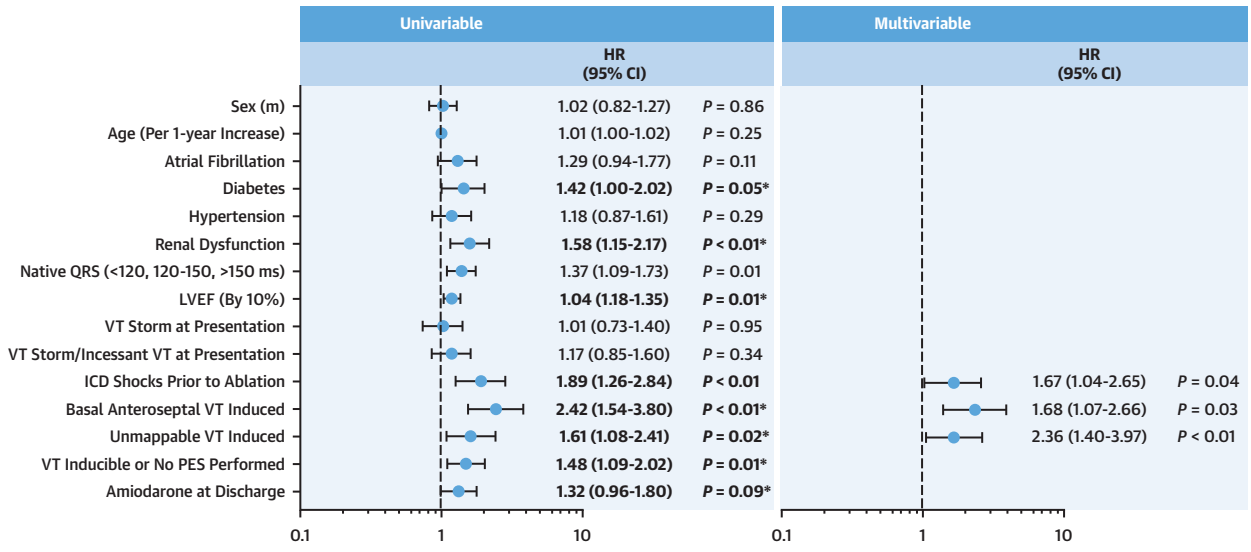
PROCEDURAL DATA. Table 2 summarizes the procedural data. A median of 2 (IQR: 1-4) VTs per patient could be induced, and 163 patients (58%) had at least 1 unmappable VT. Thirty-three patients (12%) had no inducible VT at baseline. An inferior-axis, LBBB-like VT and an inferior-axis, LBBB-like VT with transition from lead V_2 to V_3 consistent with an anteroseptal (basal) substrate could be induced in 82 (29%) and 30 (12%) patients, respectively. Epicardial access was attempted in 172 patients (61%) and successfully achieved in 162 (58%). Ablation target site identification was on the basis of substrate mapping in 90% of patients and additional activation and entrainment mapping in 46%. In 18 patients, no ablation was performed because of the absence of an accessible VT target site.

Any abnormal electrogram at the LV endocardium was identified in 75% of the patients, including 44% who had LV endocardial late potentials. Of the 162 patients with epicardial mapping, abnormal epicardial electrograms were identified in 123 of 162 (76%), with late potentials present in 44% of patients.

After the last radiofrequency application, 131 of 220 patients (60%) in whom PES was performed had no sustained VT inducible, while in 38 (11%), the clinical documented VT remained inducible. In 61 (22%), PES was not performed at the end of the procedure, mainly because of the desire to avoid hemodynamic effects on the patient or procedural complications (n = 19), noninducibility at baseline (n = 11), or if no effective ablation could be performed (n = 8) (such as because of inaccessibility of an ablation site with close proximity to coronary arteries or overlying epicardial fat). Half-normal saline or needle ablation was not performed. Procedure-related complications occurred in 32 patients (11%), the majority due to vascular access (n = 10 [31%]), pericardial bleeding (n = 7 [22%]), and (anticipated) atrioventricular block (n = 7 [22%]). There were 2 procedure-related deaths (refractory cardiogenic shock and sepsis). Worsening of heart failure after ablation in additional patients was not reported.

At discharge, 267 patients had ICDs, with cardiac resynchronization therapy in 95 patients (34%), and 221 were on AADs. Amiodarone was prescribed in 132

FIGURE 2 Prediction of All-Cause Mortality or Heart Transplantation and VT Recurrence



HRs were estimated using univariable and multivariable Cox regression analysis for the prediction of the composite endpoint of all-cause mortality or heart transplantation and ventricular tachycardia (VT) recurrence. In multivariable analysis, implantable cardioverter-defibrillator (ICD) shocks prior to ablation, induction of basal anteroseptal VTs, and induction of unmappable VTs remained independently associated with the composite endpoint. *Variables included in multivariable evaluation in **bold**. LVEF = left ventricular ejection fraction; PES = programmed electric stimulation.

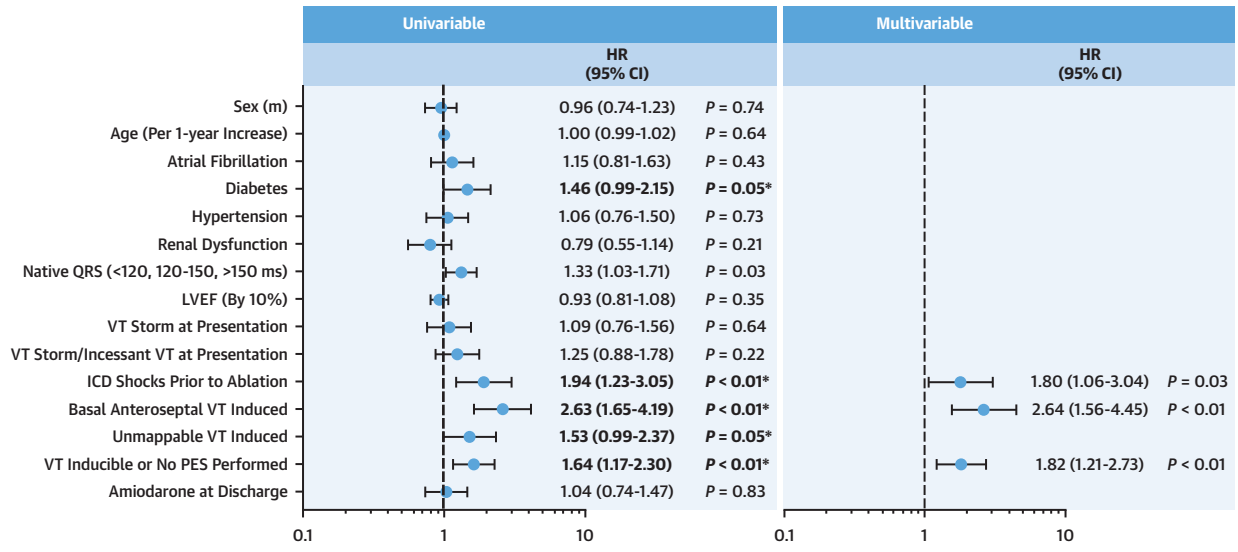
patients, 46 patients were on sotalol, 43 were on class I AADs, and 14 received combinations of class I and III AADs.

OUTCOMES AFTER ABLATION. During a median follow-up period of 21 months (IQR: 6-30 months), the composite endpoint of VT recurrence or all-cause mortality or HTx occurred in 167 patients (59%). The cumulative event rates of the combined endpoint were 50%, 60%, and 70%, respectively, at 1, 2, and 4 years after the index procedure (Figure 1). In univariable analysis, LVEF, QRS duration, renal dysfunction, and ICD shocks prior to ablation and the procedural parameters basal anteroseptal VT, induction of unmappable VT, and procedural failure were associated with the composite endpoint (Figure 2). Of note, the cumulative incidence of the composite endpoint did not differ between patients who remained inducible and those who were not tested at the end of the procedure (Supplemental Figure 1). A prior ablation procedure was not associated with outcomes (Supplemental Table 2). In multivariable analysis, ICD shocks prior to ablation (HR: 1.67; 95% CI: 1.04-2.65; $P = 0.04$), induction of basal anteroseptal VTs (HR: 1.68; 95% CI: 1.07-2.66; $P = 0.03$), and induction of unmappable VTs (HR: 2.36; 95% CI: 1.4-3.97; $P < 0.01$) remained independently associated with the composite endpoint.

VT RECURRENCE. VT recurred in 138 patients (49%) after a median of 82 days (IQR: 21-286 days), and 63% of patients received ICD shocks. The cumulative rates of VT recurrence were 46%, 54%, and 61% at 1-, 2-, and 4-year follow-up and were identical after adjustment for the competing risk for death. Among all patients with VT recurrences, VT recurred early within 30 days in 45 patients (33%), between 30 and 180 days in 49 patients (35%), and after 180 days in 44 patients (32%). Of note, among the 45 patients with early recurrence, 19 (42%) died (n = 14; cause of death uncontrollable VT in 3, heart failure in 8, and noncardiac in 3) or underwent transplantation for end-stage heart failure (n = 5) at a median of 69 days (IQR: 32-526 days) after the index ablation.

In univariable analysis, QRS duration, ICD shocks prior to ablation, induction of anteroseptal VTs, and persistent inducibility or refrainment from PES after ablation were associated with VT recurrence. Of note, LVEF was not associated with VT recurrence on univariable analysis. ICD shocks prior to ablation (HR: 1.8; 95% CI: 1.06-3.04; $P = 0.03$), induction of basal anteroseptal VTs (HR: 2.64; 95% CI: 1.56-4.45; $P < 0.01$), and persistent inducibility or no PES testing (HR: 1.82; 95% CI: 1.21-2.73; $P < 0.01$) remained independent predictors of VT recurrence (Figure 3).

FIGURE 3 **Prediction of VT Recurrence After Ablation**



HRs were estimated using univariable and multivariable Cox regression analysis for the prediction of VT recurrence after ablation. LVEF was not associated with VT recurrence. VT recurrence was associated with factors that likely reflect specific nonischemic substrates. *Variables included in multivariable evaluation in **bold**. Abbreviations as in Figure 2.

MORTALITY OR HTx. A total of 67 patients (24%) either died (n = 59) or underwent HTx (n = 8) for end-stage heart failure. The mode of death was heart failure in 24 patients (41%), uncontrollable VT or arrhythmic death in 14 patients (24%), noncardiac causes in 9 patients (15%), and not specified in 12 patients (20%). The cumulative event rates of all-cause mortality or HTx were 13%, 23%, and 38% at 1-, 2-, and 4-year follow-up (Figure 1). Of the 67 deaths or HTx procedures, 9 (13%) occurred within 30 days after ablation. An additional 14 patients (21%) died or underwent transplantation between 30 and 180 days.

A lower LVEF, prior atrial fibrillation, renal dysfunction, induction of unmappable VT, procedural failure, amiodarone at discharge, and early VT recurrence were all associated with all-cause mortality or HTx on univariable analysis (Figure 4). According to receiver-operating characteristic analysis, LVEF ≤32% was the optimal threshold to identify patients at risk for mortality or HTx (area under the curve: 0.75) (Supplemental Figure 2).

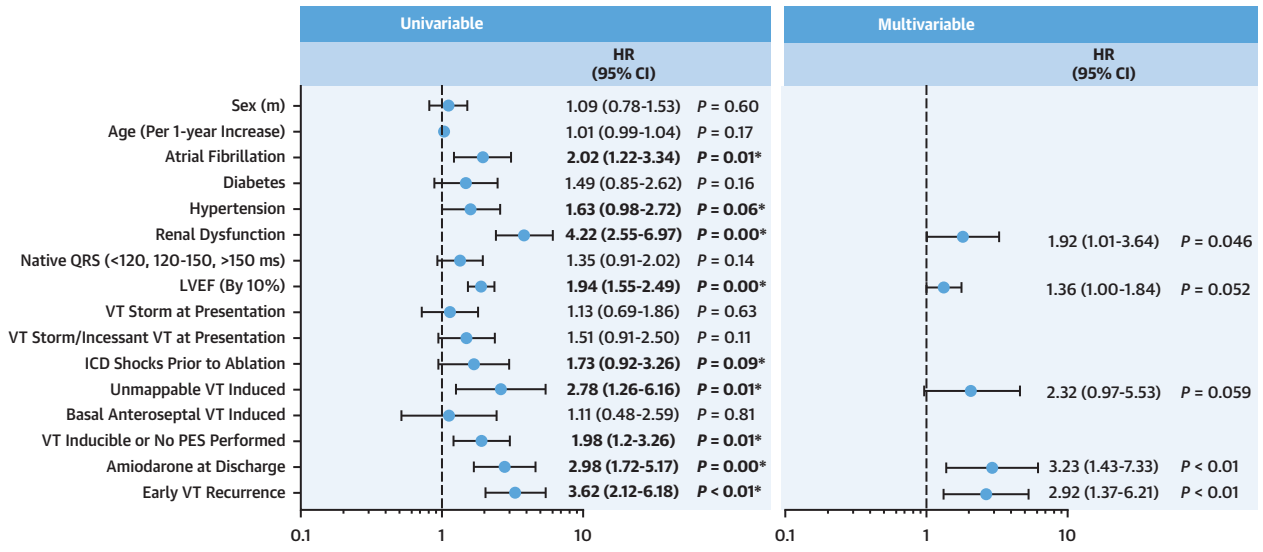
In multivariable analysis, early VT recurrence (HR: 2.92; 95% CI: 1.37-6.21; $P < 0.01$), amiodarone at discharge (HR: 3.23; 95% CI: 1.43-7.33; $P < 0.01$), renal dysfunction (HR: 1.92; 95% CI: 1.01-3.64; $P = 0.046$), and, with borderline significance, LVEF (HR: 1.36; 95% CI: 1.0-1.84; $P = 0.052$) and induction of unmappable VTs (HR: 2.32; 95% CI: 0.97-5.53; $P = 0.059$) remained independent predictors of all-cause mortality or HTx (Figure 4). If early VT recurrence was excluded from the model, procedural failure was not independently associated with mortality or HTx. After excluding patients with early VT recurrence, patients with procedural failure had the same mortality as those with procedural success (Supplemental Figure 3).

IMPACT OF THE TIMING OF VT RECURRENCE AND CARDIAC FUNCTION ON MORTALITY. All-cause mortality or HTx occurred in 39 patients after VT recurrence (20.1 events per 100 person-years after first VT recurrence) and in 28 patients without VT recurrence (8.5 events per 100 person-years) ($P < 0.001$). Death or HTx events per 100 person-years were significantly higher after early VT recurrence (40.4 events per 100 person-years) compared with VT recurrence from 30 to 180 days and >180 days (14.2 and 13.1 events per 100-person years [$P = 0.006$ and $P = 0.008$], respectively). Mortality/HTx rates for patients with VT recurrence after 30 days were not significantly higher than for patients with no VT recurrences (Central Illustration).

A comparison of baseline and procedural data between patients with early (within 30 days of the procedure) vs late vs no VT recurrence is presented in Table 3.

More patients with recurrences had pathogenic mutations identified, but the number of patients tested was small. Patients with early VT recurrence

FIGURE 4 Prediction of All-Cause Mortality or Heart Transplantation



HRs were estimated using univariable and multivariable Cox regression analysis for the prediction of all-cause mortality or heart transplantation. Amiodarone at discharge and early VT recurrence remained the strongest independent predictor of mortality. *Variables included in multivariable evaluation in **bold**. Abbreviations as in Figure 2.

had significantly lower LVEFs and higher NYHA functional class and were more likely to be inducible for VT or were not tested after RFCA compared with patients with late recurrence or no VT recurrence.

Of note, patients with LVEFs ≤32% and early VT recurrence had a cumulative 1-year mortality/HTx rate of 55%, compared with 19% in patients with LVEF ≤32% and no early VT recurrence and 6% in patients with LVEFs >32% and early VT recurrence ($P < 0.01$) (Central Illustration).

DISCUSSION

Recurrent monomorphic VT in patients with DCM is difficult to manage, and RFCA is increasingly performed to reduce symptomatic VT and ICD shocks.[5] To the best of our knowledge, this is the first prospective, international, multicenter cohort study to evaluate acute procedural outcome, VT recurrence, mortality, and the impact of timing of VT recurrence on mortality following RFCA for monomorphic sustained VT in consecutive and contemporary patients with DCM. A high proportion of our patients were receiving beta-blockers (84%), angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (80%), and mineralocorticoid receptor antagonists (40%), and 34% were receiving cardiac resynchronization therapy. The striking 71% rate of death, HTx, or recurrent VT at 4 years is indicative of the underlying disease severity.

CATHETER ABLATION FOR RECURRENT VT IN DCM. Although only 51% of patients remained free of VT after ablation, clinically, this represents a very meaningful result, given the severity and frequency of the arrhythmias in this cohort. It should also be recognized that in contrast to many reports, this outcome is after a single ablation procedure according to an "intention-to-treat" principle, as we included patients in whom ablation was intended but then not performed because of inability to identify or reach the arrhythmia substrate. Despite the severity of the underlying illness, procedure-related mortality was <1%.

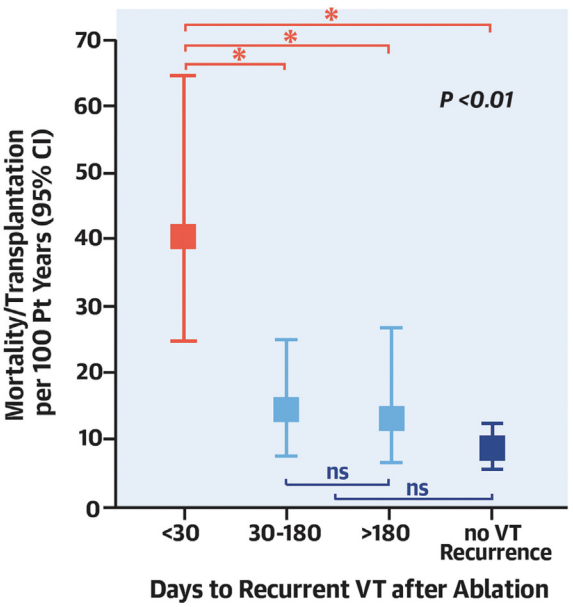
Complete noninducibility at the end of the ablation procedure or at noninvasive PES performed before discharge has been consistently associated with lower VT recurrence rates[2,5,8,11] and was also observed in our study. Applying a uniform and extensive PES protocol, noninducibility of any VT was achieved in 60% of those tested in our cohort. Prior studies have reported a wide range (38%-74%)[2,8,11-13] of noninducibility after RFCA. In these studies, LV stimulation was not consistently performed, and induction protocols and definitions of "noninducibility" varied. Of note, in our cohort, no final PES was performed in an additional 22% of the patients, which is higher than in prior reports, ranging from 8.0% to 8.5%.[2,8] This may reflect a higher proportion of patients in unstable condition as well as the inclusion of patients in whom no ablation was performed. Of note,

CENTRAL ILLUSTRATION **Outcome After Ablation for Ventricular Tachycardia in Patients With Dilated Cardiomyopathy**

9 Centers, 281 DCM Patients Referred for VT Ablation
Outcome After a Median Follow-Up of 21 Months (IQR: 6-30 Months)

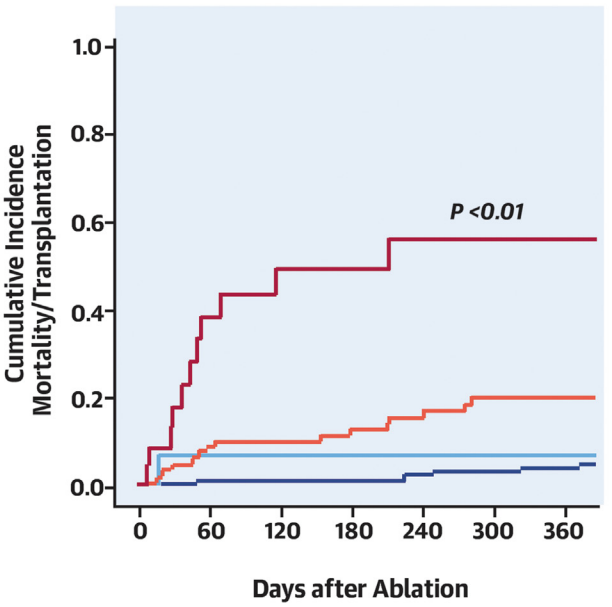
Mortality/Transplantation or VT	Mortality/Transplantation	VT
60% at 2 Years	23% at 2 Years	54% at 2 Years

Early VT Recurrence Predicts High Mortality



After early VT recurrence:
40.4 deaths/tranplants per 100 pt years

Survival <50% for Low LVEF + Early VT Recurrence



LVEF ≤32% + ER 55% at 1 year
LVEF ≤32% no ER 19% at 1 year
LVEF >32% + ER 6% at 1 year
LVEF >32% no ER 3% at 1 year

Low LVEF and Early VT Recurrence Warrants Early Consideration for Heart Transplantation or LVAD

Zeppenfeld K, et al. J Am Coll Cardiol. 2022;80(11):1045–1056.

Ventricular tachycardia (VT) recurrence and mortality or heart transplantation rates are high in patients with dilated cardiomyopathy (DCM) who need VT ablation **(top)**. All-cause mortality/heart transplantation per 100 person-years after ablation was determined **(bottom left)**. Event rates and 95% CIs are given for the time lived without VT recurrence, after a VT recurrence within 30 days after ablation and after a VT recurrence between 30 and 180 days or later than 180 days after ablation. After early VT recurrence, 40.4 events per 100 person-years occurred. The cumulative 1-year incidence of mortality or heart transplantation was significantly higher in patients with early VT recurrence and left ventricular ejection fraction (LVEF) ≤32% **(bottom right)**. ER = early recurrence; LVAD = left ventricular assist device.

TABLE 3 Baseline and Procedural Characteristics According to VT Recurrence

	Early Recurrence (n = 45)	Late Recurrence (n = 93)	No Recurrence (n = 143)	*P* Value: Early vs Late Recurrence	*P* Value: Early vs No Recurrence	*P* Value: Late vs No Recurrence
Baseline						
Age, y	59 ± 14	62 ± 12	60 ± 14	0.15	0.70	0.18
Time since diagnosis, y	6 (2-9)	5 (2-10)	5 (2-8)	0.47	0.36	0.80
Time since first VT, y	2 (2-5)	2 (1-7)	2 (2-5)	0.28	0.99	0.12
Male	36 (80)	85 (91)	117 (82)	0.09	0.83	0.06
Hypertension	48 (107)	43 (46)	64 (45)	1.00	1.00	1.00
Atrial fibrillation	18 (40)	34 (37)	53 (37)	0.71	0.72	1.00
Diabetes	11 (24)	24 (26)	19 (13)	1.00	0.10	0.03
Genetic testing done	13 (29)	41 (44)	47 (30)	0.09	0.6	0.08
Pathogenic mutation	6 (13)	15 (16)	7 (5)	0.75	0.04	0.02
eGFR normal	23 (51)	66 (71)	95 (66)	0.05	0.10	0.66
LVEF >35%	13 (29)	50 (54)	60 (42)	0.01	0.11	0.14
LVEF, %	31 ± 10	38 ± 12	35 (12)	<0.01	0.02	0.16
NYHA functional class III/IV	17 (38)	18 (19)	31 (22)	<0.01	0.01	0.74
VT storm at presentation	19 (42)	33 (35)	48 (34)	0.23	0.13	0.89
VT storm/incessant VT at presentation	24 (53)	43 (46)	59 (41)	0.24	0.04	0.41
Prior ICD shocks	35 (78)	64 (69)	92 (64)	0.046	<0.01	0.28
Failed sotalol	11 (24)	21 (23)	42 (29)	0.83	0.57	0.23
Failed amiodarone	35 (78)	67 (72)	90 (63)	0.53	0.07	0.20
Failed class I	24 (53)	18 (19)	37 (26)	<0.01	<0.01	0.27
Failed combination I/III	15 (33)	10 (11)	26 (18)	<0.01	0.04	0.14
Prior ablation	24 (53)	42 (45)	60 (42)	0.47	0.23	0.69
Procedure						
Epicardial access	25 (56)	57 (61)	80 (56)	0.58	0.63	0.50
Noninducibility baseline	5 (11)	7 (8)	22 (15)	0.53	1.00	0.10
Acute outcome						
Noninducible	14 (31)	46 (49)	82 (57)	0.046	<0.01	0.28
VT inducible or no PES performed	31 (69)	47 (51)	61 (43)			
Any unmappable VT induced	29 (64)	57 (61)	77 (54)	0.16	0.05	0.53
Basal anteroseptal VT induced	10 (22)	12 (13)	8 (6)	0.13	<0.01	0.10

Values are mean ± SD, median (IQR), or n (%).
Abbreviations as in Tables 1 and 2.

nontested patients had the same outcome as those who had persistently inducible VT. Adding these 2 groups resulted in a high "procedural nonsuccess" rate of 53%, which is in contrast to 31% in a prior study, evaluating the effect of noninducibility on outcome.[8]

Apart from procedural failure, overall VT recurrence was associated with factors that likely reflect specific nonischemic substrates. An anteroseptal VT substrate location has been consistently associated with higher VT recurrence rates.[11,14] In line with these reports, a VT configuration consistent with a (basal) anteroseptal LV substrate was the strongest independent predictor of VT recurrence. VT not responsive to antitachycardia pacing and requiring ICD shocks for termination was also independently associated with VT recurrence, suggesting that these VTs indicate the presence of a VT substrate that is more difficult to control by ablation. Of note, VT recurrence was not associated with a poor NYHA functional class, a low LVEF, or a severe arrhythmic presentation, which is consistent with the HELP-VT (Heart Centre of Leipzig VT) study[5] but differs from a study by Muser et al[2] in which outcomes reported were after the last of multiple ablation procedures in a large proportion of patients.

MORTALITY. Death or HTx rates were substantial, with a cumulative rate of 38% at 4 years. As expected, this outcome was associated with factors that indicate a poorer clinical status, including lower LVEF and renal dysfunction. Of note, the continuous use of amiodarone and early VT recurrence were stronger predictors. Continuation of amiodarone was left to the discretion of the operator and was likely influenced by the severity of the arrhythmic presentation, cardiac function, and procedural outcome. However,

the >3-fold higher risk for death after adjustment is in line with concerns for adverse effects of amiodarone during long-term follow-up.[14,15]

Procedural failure has been associated with poor survival in IHD and DCM cohorts[2,4,8] but was not an independent predictor of mortality or HTx in our cohort.

Previous studies have shown that VT recurrence was associated with increased mortality in patients with structural heart disease, but conflicting results have been reported in DCM cohorts.[2,3,8,16] In our cohort, only early VT recurrence was associated with mortality, while later recurrences did not affect mortality. Most of these deaths were attributable to heart failure, rather than arrhythmia, and indeed, a lower LVEF was the most important distinguishing feature between patients with early and late recurrence.

Of importance, patients with LVEFs ≤32% and early recurrence had a very high 1-year mortality or HTx rate of 55%, related mainly to heart failure, compared with the 18% mortality rate of patients with similar cardiac function but no early VT recurrence. These observations support an interdisciplinary approach of early screening for advanced heart failure management such as LV mechanical support and HTx for this group. Of note, patients with LVEFs >32% and early recurrence had a 1-year mortality rate of 6%, only slightly higher than patients with LVEFs >32% and no early recurrence. In these patients, repeat ablation may be beneficial to control VT but is unlikely to significantly affect mortality. Interestingly, late recurrence was also not related to an increased risk for mortality. Assessment of cardiac function immediately before "late" VT recurrence was not available, but the observations suggest that late arrhythmia outcome is dissociated from the severity of cardiac dysfunction and nonarrhythmic mortality.

STUDY LIMITATIONS. Although our data collection was prospective, treatment decisions were left to the treating physicians, including specific ablation techniques, decision to use epicardial mapping, continuation of antiarrhythmic medications, and ICD programming. Cause of death was assigned by the investigator. Genetic testing was not systematically performed, and hence the relation of genotype to outcome after ablation was not assessed.

CONCLUSIONS

Patients with DCM with recurrent VT despite AAD therapy who are referred for ablation have a high 4-year rate of mortality or need for transplantation of approximately 38%. Catheter ablation controls VT in approximately one-half of these patients. VT recurrence is predicted by markers of a specific VT substrate and persistent inducibility but not by LVEF. Early recurrent VT within 30 days is a marker of early heart failure-related mortality in patients with LVEFs ≤32%, such that early screening for mechanical support and HTx should be considered. In contrast, in patients with LVEFs >32% and early VT recurrence, 1-year mortality is relatively low. Late recurrence of VT occurs in 33% of patients and does not predict a worse outcome. Prospective studies are needed to determine whether attempts to achieve arrhythmia control earlier in the course of the disease will improve outcomes.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Patients with DCM who undergo RFCA for VT face a 70% incidence of recurrent VT, HTx, or mortality over 4 years.

TRANSLATIONAL OUTLOOK: Additional prospective studies are needed to determine whether earlier or more complete control of ventricular arrhythmias improves clinical outcomes for patients with DCM.

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KEY WORDS mortality, nonischemic cardiomyopathy, radiofrequency catheter ablation, VT recurrence

APPENDIX For supplemental figures and tables, please see the online version of this paper.