ORIGINAL RESEARCH

Ablation Outcomes and Predictors of Mortality Following Catheter Ablation for Ventricular Tachycardia: Data From the German Multicenter Ablation Registry

Roland Richard Tilz, MD; Tina Lin, MD; Lars Eckardt, MD; Thomas Deneke, MD; Dietrich Andresen, MD; Heinrich Wieneke, MD; Johannes Brachmann, MD; Stefan Kääb, MD; K. R. Julian Chun, MD; Paula Münkler, MD; Thorsten Lewalter, MD; Matthias Hochadel, MD; Jochen Senges, MD; Karl-Heinz Kuck, MD

***Background*—**Ventricular tachycardia (VT) causes significant morbidity and mortality. Implantable cardioverter-defibrillator shocks terminate VT but confer a significant morbidity and mortality risk. Therefore, VT ablation is increasingly common. Patients with structural heart disease (SHD) and patients with structurally normal hearts as well as the subgroup with and without ischemic heart disease were assessed for predictors of mortality and nonfatal VT recurrence. We present the first multicenter, prospective German VT registry.

***Methods and Results*—**In 334 patients, 118 structurally normal hearts and 216 SHD (74.5% ischemic heart disease), referred for VT ablation in 38 centers, long-term follow-up was assessed for a minimum of 12 months and analyzed for factors predicting VT recurrence rates and mortality. The VTs in SHD patients were more frequently hemodynamically unstable (34.7% versus 12.7%, $P<0.0001$) or incessant (9.7% versus 2.7%, $P<0.05$). More SHD patients underwent substrate modification than patients with structurally normal hearts who had more focal ablations. Ablation failure was 9% in both groups. Two-year mortality was higher in patients with SHD (18.7% versus 3.5%, $P<0.001$). Predictors of mortality include age >60 years, incessant VT, left ventricular ejection fraction ≤30%, procedural failure, and Class I and III anti-arrhythmic drug use at discharge. Only procedural failure is a predictor of nonfatal VT recurrence.

***Conclusions*—**Procedural failure was the sole independent predictor for nonfatal VT recurrence for our study cohort. This emphasizes the importance of a successful ablation procedure in experienced hands to reduce long-term mortality and nonfatal VT recurrence. **(*J Am Heart Assoc*. 2018;7:e007045. DOI: 10.1161/JAHA.117.007045.)**

Key Words: catheter ablation • multicenter registry • predictors of mortality • predictors of recurrence • ventricular tachycardia

It is well known that sustained ventricular tachycardia (VT) is an important cause of morbidity and mortality in patients with structural heart disease (SHD), particularly ischemic heart disease (IHD). Previous studies have demonstrated that in these patients, implantable cardioverter defibrillators (ICDs) can terminate sustained VT episodes with antitachycardia pacing and shocks[1]; however, shocks themselves, whether appropriate or inappropriate, also confer a significant increase in morbidity and mortality.[2–4] The use of ICDs in combination with oral anti-arrhythmic drug (AAD) therapy reduces a proportion of VT episodes; however, it does so with variable success and often with significant side effects.[5–7]

Catheter ablation for the management of VT is becoming increasingly common, and in patients with life-threatening, incessant sustained VT, it can play a critical role. Since the introduction of catheter ablation of VT, many studies assessing its efficacy in patients with and without SHD have been conducted.[8–12] However, several factors in this high-risk

From the Department of Cardiology, Asklepios Hospital St. Georg, Hamburg, Germany (R.R.T., T. Lin, K.-H.K.); Medical Clinic II, University Schleswig Holstein, University Heart Center Lübeck, Lübeck, Germany (R.R.T.); Rhythmologie Universitätsklinikum Muenster, Muenster, Germany (L.E.); Heart Center Bad Neustadt an der Saale, Bad Neustadt a.d. Saale, Germany (T.D.); Vivantes Klinikum Am Urban, Berlin, Germany (D.A.); Elisabeth-Krankenhaus Essen, Essen, Germany (H.W.); Klinikum Coburg, Coburg, Germany (J.B.); LMU, Campus Innenstadt, Munich, Germany (S.K.); Cardioangiologisches Centrum Bethanien, Frankfurt, Germany (K.R.J.C.); University Heart Center Hamburg, Hamburg, Germany (P.M.); University of Bonn, Germany (T. Lewalter); Stiftung Institut für Herzinfarktforschung, Ludwigshafen, Germany (M.H., J.S.).

Correspondence to: Roland Richard Tilz, MD, Medical Clinic II, University Schleswig Holstein, University Heart Center Lübeck, Ratzeburger Allee 160, 23538 Lübeck, Germany. E-mail: tilz6@hotmail.com

Received October 18, 2017; accepted January 9, 2018.

Clinical Perspective

What Is New?

- This study characterizes the patient population undergoing ventricular tachycardia (VT) ablation in Germany in a real-world cohort and reveals substantial variability with respect to age, comorbidities, and VT mechanism.
- Predictors of mortality after VT ablation included older age, worse left ventricular function, incessant VT, antiarrhythmic drug use, and procedure failure.
- Procedural failure defined as inducibility of the clinical VT at the end of the procedure was identified as predictor of both mortality and nonfatal VT recurrence.

What Are the Clinical Implications?

- Predictors of outcome after VT ablation are highly relevant for physicians' and patients' decision regarding the best therapeutic options.
- The identification of procedural failure as the sole independent predictor of nonfatal VT recurrence highlights the importance of noninducibility of the clinical VT as a procedural end point.

patient cohort continue to make this a complex procedure, such as hemodynamic instability, complex arrhythmia substrate, multiple VTs, noninducibility, and uncertainty over the best ablation method to undertake.[13–16] Radiofrequency ablation using an irrigated-tip ablation catheter in combination with a 3-dimensional (3D) electroanatomical mapping system is most commonly undertaken. However, the choice of activation-mapping, pace-mapping, or substrate-mapping, endocardial or epicardial or combined ablation, focal, linear, or substrate isolation ablation techniques are VT and operator dependent, and currently the best approach has yet to be defined.[17,18]

This is the first multicenter, prospective German registry of VT patients to date. This VT registry is the largest so far, and includes all patients who underwent catheter ablation for sustained VT, but without a primary electrical cause, at 38 centers in Germany. Patients with structurally normal hearts (SNH) and congenital or acquired SHD, including the specific subgroup of patients with IHD were included in this database and the procedural and 1-year clinical outcomes were assessed for predictors of mortality and recurrence.

Methods

The German Ablation Registry

The German ablation registry is a nationwide ablation registry. Participation in this registry was voluntary for both the patients and the operators. A total of 55 German electrophysiological centers agreed to participate in this prospective multicenter registry including 38 centers performing VT ablation. The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure. The study was driven by the scientific interest of the participating hospitals and supported by the Stiftung Institut fuer Herzinfarktforschung (IHF) Ludwigshafen, Germany. All enrolled patients gave informed consent for participation in the registry. Approval of the ethical review board of the Landesaerztekammer Rheinland-Pfalz was obtained.

Patient Selection

Between April 2007 and April 2011, 334 patients who underwent catheter ablation for sustained VT in 38 German centers were prospectively enrolled into the registry. Patients with SNH and SHD, including the specific subgroup of patients with IHD, were included. Exclusion criterion was primary electrical heart disease (eg, Brugada syndrome, long QT syndrome, and arrhythmogenic right ventricular cardiomyopathy). At the time of enrollment, demographic and baseline data were obtained. Baseline patient characteristics are shown in Table 1. Follow-up was scheduled to be performed with a telephonic interview with the patient 12 months after ablation.

Ablation Technique

All patients included in this study underwent a catheter ablation procedure to treat the clinical VT. No specific instructions were given for inclusion into the study. Ablation was performed according to the institutional standard of each participating center. Both conventional mapping using entrainment and pacemapping, as well as 3D electroanatomical mapping using various systems, were performed dependent on individual patient requirements. The type and techniques of ablation were also as per the procedural/institutional standards. Ablation failure was defined as inducibility of the clinical VT at the end of the procedure.

Complications

Major adverse cardiac events (MACE) were defined as death or myocardial infarction. Major adverse cardiac and cerebrovascular events (MACCE) were defined as death, myocardial infarction, or stroke. VT recurrence and adequate ICD therapy were not considered a MACE. In addition, major bleeding requiring intervention was considered a severe complication.

Clinical Data Collection and Monitoring

This registry was performed by the Stiftung IHF (Ludwigshafen, Germany) as previously described. It was

Table 1. Baseline Patient Characteristics (n=336)

Variable	Total (n=334)	SNH (n=118)	SHD (n=216)	No IHD (n=55)	IHD (n=161)
Age, mean (y)	59.3±14.6	50.4±14.8	64.2±12.0 *	55.1±16.0	67.3±8.3†
Male	72.2%	50.0%	84.3%*	78.2%	86.3%
LVEF ≤30%‡	27.6%	0%	42.0%*	29.6%	46.4%†
NYHA ≥ III	29.9%	NA	29.9%	18.0%	33.5%†
Hypertension§	53.1%	31.9%	63.5%*	37.9%	74.6%†
Diabetes mellitus	14.4%	5.9%	19.0%*	7.3%	23.0%†
Renal insufficiency§	13.9%	0.0%	20.6%*	10.3%	25.0%
Previous VT ablation	18.0%	16.9%	18.5%	30.9%	14.3%†
SHD	64.7%	0%	100%*	100%	100%
IHD	48.2%	0%	74.5%*	0%	100%
Valvular heart disease	9.6%	0%	14.8%*	36.4%	7.5%†
Cardiomyopathy (dilative+hypertrophic)	14.1%	0%	21.8%*	54.5%	10.6%†
Hypertensive cardiomyopathy	7.2%	0%	11.1%*	25.5%	6.2%†
Symptoms					
Palpitations	92.4%	94.9%	91.1%	90.4%	91.3%
Presyncope	13.0%	12.8%	13.1%	19.2%	11.2%
Syncope	10.3%	11.1%	9.9%	5.8%	11.2%
Previous resuscitation	3.6%	0.0%	5.6%*	3.8%	6.2%

Patients grouped into those without structurally normal hearts and with structural heart disease. In addition, a subgroup of patients from the structural heart disease group was analyzed. This subgroup included patients without and with ischemic heart disease. Percentages or means±SD are shown. IHD indicates ischemic heart disease; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SHD, structural heart disease; SNH, structurally normal heart; VT, ventricular tachycardia.

*Significant (P<0.05) compared with no SHD group.

†Significant (P<0.05) compared with no IHD group.

‡Data available in 94% of patients.

§Data available in 43% of patients because of later inclusion of the variable in the study.

responsible for project development, project management, data management, and clinical monitoring and was the central contract research organization for the study. Documentation and data management were paperless and were carried out as an Internet-based case report form system. The information was transmitted from the sites via a secure socket layer. The statistical analyses were done centrally at the biometrics departments of the IHF using anonymous patient data. Follow-up was performed by dedicated study personnel. The follow-up was scheduled at 12 months from the index ablation procedure. Contact was made via telephone interview with the patients themselves. In case of unapproachable patients, the registration offices were requested to ascertain the vital status.

Statistical Analysis

The patient population is described by absolute numbers and percentages with respect to categorical variables and medians with quartiles for continuous variables, and means with SD for age for better comparison with published literature. The distribution of binary or nominal categorical variables is compared between patient groups by Pearson χ^2 test or by Fisher exact test in case of infrequent events, and that of metrical and ordinal variables by Mann–Whitney test. Odds ratios with 95% confidence intervals were calculated for binary variables. These results were calculated from the available cases. The CHA_2DS_2-VASc risk score was calculated from the documented patients' characteristics according to the European Society of Cardiology guideline.[19]

Considering the actual follow-up, all-cause death up to 2 years after discharge from the index hospitalization was used for the survival analysis, censoring events that occurred later. The follow-up duration was defined as the time span from index discharge to the date of the follow-up contact (ie, when information on the patient's status was obtained). Estimates of survival probability were calculated with 95% confidence intervals by the Kaplan–Meier method, demonstrated in curves (Figure) and compared by log-rank test. Predictors of mortality after index discharge were analyzed using Cox regression, and predictors of recurrence of VT in survivors in proportional odds models using logistic

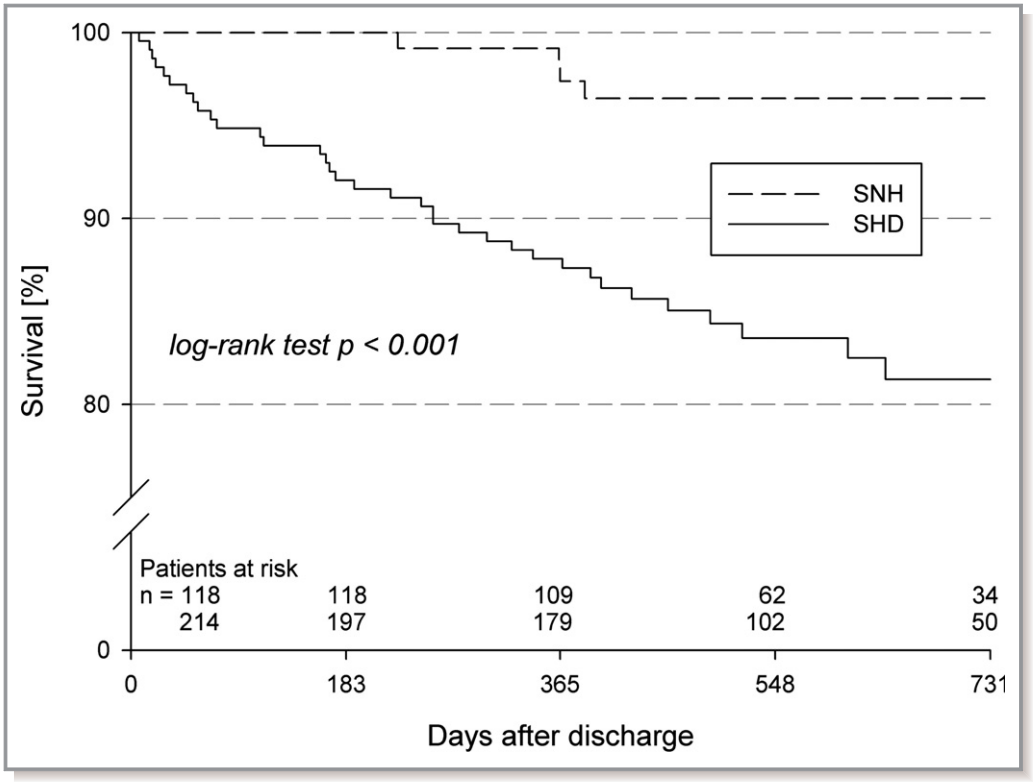

Figure. Kaplan–Meier analysis comparing patients with structural heart disease (SHD) and patients with structurally normal hearts (SNH). *x*-axis: Days after discharge; *y*-axis: proportion of patients surviving. n indicates number of patients included in the assessment of survival at the respective follow-up date.

regression including the logarithm of follow-up time as covariate.[20] Unadjusted hazard ratios or odds ratios with 95% confidence intervals were calculated in simple regression models as well as adjusted hazard ratios or odds ratios in multivariable regression models. Variables were selected regarding the results of forward and backward selection procedures applying $P<0.1$ as threshold for entry or stay, and statistically significant predictors were left in the final models. In addition to SHD and age ≥60 years, the following variables were considered clinically relevant and tested as potential predictors: sex, diabetes mellitus, implanted pacemaker or defibrillator, left ventricular ejection fraction (LVEF) known ≤30%, LVEF unknown, prior resuscitation, incessant VT (defined as continuous sustained VT lasting for several hours, which recurs promptly despite repeat intervention for termination), focal ablation, hemodynamic instability, procedural failure, length of stay, and antiarrhythmics class I, class II, and class III at index discharge. Variables selected for either event type are shown in Table 1. Missing values of the explanatory variables were imputed by means. $P\leq0.05$ were considered significant. All *P* values are results of 2-tailed tests. The statistical computations were performed using the SAS system release 9.3 (SAS Institute, Inc, Cary, NC) running on a personal computer.

Results

Baseline Characteristics

The study population consisted of 118 (35.3%) patients with SNH and 216 (64.7%) patients with SHD. Of the patients with SHD, 74.5% were secondary to IHD, 14.8% to valvular heart disease, 21.8% to dilative and hypertrophic cardiomyopathy, and 11.1% to hypertensive cardiomyopathy. No patients with primary electrical heart disease were included. Prior VT ablation had been performed in 18.0% of patients. Ablation was predominantly performed with patients in deep sedation (81.3%), and was rarely performed without sedation (17.8%) or in full anesthesia and intubation (0.8%).

Patients with SNH were significantly younger, with a higher proportion of females, and had lower CHA_2DS_2-VASc risk scores (1.1±0.8 versus 3.2±1.5, $P<0.0001$). Symptoms were not statistically different between the 2 groups, with most patients reporting symptoms of palpitations (SNH 91.1%, SHD 94.9%, $P=0.21$), which occurred at least once per month (SNH 85.2%, SHD 83.3%, $P=0.64$). Of note, no patients with SNH experienced previous resuscitation, whereas 5.6% of patients in the SHD group required resuscitation before enrollment. More patients had drug-resistant clinical arrhythmias in the SHD group (80.6% versus 61.9%, $P<0.001$).

In the SHD group, LVEFs were distributed as follows: 19.3% of patients had LVEF >50%, 38.7% LVEF 31% to 50%, and 42.0% LVEF ≤30%. New York Heart Association (NYHA) functional classes were as follows: 32.7% NYHA I, 37.4% NYHA II, 28.4% NYHA III, and 1.4% NYHA IV.

Of the patients with SHD, an analysis of patients with and without IHD (161 versus 55 patients) was performed. Patients without IHD were younger, with lower CHA_2DS_2-VASc risk scores (1.8±0.9 versus 3.8±1.2, $P<0.0001$), specifically with less diabetes mellitus and systemic hypertension. Clinical symptoms as well as their frequency of occurrence were similar between the 2 groups. Patients without IHD had generally better NYHA functional class classifications and LVEFs (Table 1).

Characteristics of the Clinical VT

The clinical VT was more frequently hemodynamically unstable in patients with SHD (34.7% versus 12.7%, $P<0.0001$), and was more frequently incessant (9.7% versus 2.7%, $P<0.05$). The VT origin was predominantly from the left ventricle (LV) in patients with SHD (84.4%), whereas in patients with SNH, the majority of the patients had VT originating from the right ventricle (78.5%). In the subgroup of IHD versus no IHD, there were no significant differences between the 2 groups for frequency of hemodynamic instability and incessant VT.

Procedural Techniques and Outcomes

Procedure techniques were as per the institutional standard of the individual centers. Access to the heart included retrograde aortic (56.4%) and antegrade transseptal (9.1%) access to the LV and epicardial access (5.8%) (Table 2). LV access was predominantly from a retrograde aortic approach compared with an antegrade transseptal approach (SNH 28.2% versus 3.4%; SHD 71.8% versus 12.2%, respectively). Epicardial access was required in 7.0% of the SHD group compared with 3.4% of the SNH group ($P=0.18$). Retrograde access to the LV was also more frequent compared with antegrade access in both the IHD and no IHD groups. Epicardial access was required more often in the no IHD group (14.8% versus 4.4%, $P<0.01$).

Electroanatomical mapping (3D) was performed in 67.9% of patients. Conventional mapping was performed significantly more frequently in patients with SNH (53.4% versus 19.2%, $P<0.0001$), whereas more complex mapping was performed with 3D-electroanatomical mapping in patients with SHD (79.9% versus 45.7%, $P<0.0001$). An average of 1.7 VTs were

Table 2. Clinical VT Characteristics and Ablation Technique Used

Variable	Total	SNH	SHD	*P* Value	Odds Ratio (95% CI)
Hemodynamically unstable VT	26.9% (90/334)	12.7% (15/118)	34.7% (75/216)	<0.0001	3.65 (1.98–6.72)
Incessant VT	7.2% (23/319)	2.7% (3/112)	9.7% (20/207)	0.021	3.89 (1.13–13.38)
Origin of VT					
RV	39.0% (124/318)	78.5% (84/107)	19.0% (40/211)	<0.0001	0.06 (0.04–0.11)
LV	64.2% (204/318)	24.3% (26/107)	84.4% (178/211)	<0.0001	16.80 (9.43–29.93)
Access					
Arterial access	56.4% (186/330)	28.2% (33/117)	71.8% (153/213)	<0.0001	6.49 (3.93–10.72)
Transseptal access	9.1% (30/330)	3.4% (4/117)	12.2% (26/213)	0.008	3.93 (1.34–11.55)
Epicardial access	5.8% (19/330)	3.4% (4/117)	7.0% (15/213)	0.18	2.14 (0.69–6.60)
3D mapping system	67.9% (224/330)	45.7% (53/116)	79.9% (171/214)	<0.0001	4.73 (2.88–7.76)
Number of VTs induced	1.8±1.4	1.7±1.5	1.8±1.4	0.29	
Length of procedure, min	160 (116;225)	134 (90;190)	180 (130;240)	<0.0001	
Length of RF application, s	574 (225;1359)	360 (180;876)	722 (298;1520)	0.001	
Length of fluoroscopy, min	21 (10;32)	12 (7;22)	24 (12;35)	<0.0001	
Fluoroscopy dose, cGy×cm^2	1977 (779;5500)	1055 (470;3708)	2770 (1116;6057)	<0.0001	
Acute ablation outcome					
Success	78.0% (259/332)	82.1% (96/117)	75.8% (163/215)	0.19	0.69 (0.39–1.21)
Partial success	12.7% (42/332)	8.5% (10/117)	14.9% (32/215)	0.10	1.87 (0.88–3.96)
No success	9.3% (31/332)	9.4% (11/117)	9.3% (20/215)	0.98	0.99 (0.46–2.14)

Percentages, medians with quartiles, or means±SD are shown. CI indicates confidence interval; 3D, 3 dimensional; LV, left ventricular; min, minutes; RF, radiofrequency; RV, right ventricular; s, seconds; SHD, structural heart disease; SNH, structurally normal heart; VT, ventricular tachycardia.

induced in the patients from the SNH group compared with 1.8 VTs in the SHD group (P=0.29), and there was no difference between the IHD and no IHD groups. In patients with SNH, more focal ablation was performed (96.3% versus 63.5%, P<0.0001), whereas more substrate modification/linear ablation was performed in patients with SHD (36.5% versus 3.7%, P<0.0001). For the IHD versus no IHD group, more patients received focal ablation in the no IHD group (73.1% versus 60.3%, P=0.10), whereas more substrate modification/linear ablations were performed in patients with IHD (39.7% versus 26.9%, P=0.10). Ablation success was achieved in a high number of patients in both groups (SNH 82.1% versus SHD 75.8%, P=0.19), with only partial success, defined as successful ablation of the clinical VT with persistence of a nonclinical VT, in more patients from the SHD group (14.9% versus 8.5%, P=0.10). Unsuccessful ablation was similar in both groups at 9.3%/9.4%. In the subgroup of IHD versus no IHD, ablation success was achieved more frequently in the IHD group (80.1% versus 63.0%, P<0.05).

Procedural data were as follows: The overall length of procedures was longer in the SHD group (median 180 versus 134 minutes, P<0.0001), as were overall radiofrequency application time (722 versus 360 s, P<0.01), overall fluoroscopy time (24 versus 12 minutes, P<0.0001), and overall fluoroscopy dose (2770 versus 1055 cGy×cm^2, P<0.0001). Overall, there were no significant differences in procedural data between the subgroups with IHD and without IHD (Table 2).

Anticoagulation was used during the procedure in the majority of patients with heparin (SNH 95.4% versus SHD 88.1%, P<0.05) (no IHD 92.7% versus IHD 96.3%, P=0.28) and levels were monitored using the activated clotting time.

Acute Complications and Outcomes

Periprocedural complications were low, with only 1 death reported in the SHD group (0.5% versus 0.0%, P=0.46), and this occurred in a patient with IHD. This was deemed to be from a cardiac cause. No patients developed any other MACE or MACCE end points periprocedurally. One patient from the SHD/no IHD group developed a major bleeding complication requiring intervention. Moderate complications included requirement for resuscitation, atrioventricular fistula formation, pericardial effusion, and third-degree atrioventricular block, the rates of which were not statistically different between the 2 groups. Nonfatal VT recurrence before discharge was 5.1% in the SNH group and 8.3% in the SHD group (P=0.27) (Table 3). Of the IHD subgroup, there was nonfatal VT recurrence in 8.1% with no IHD and 9.1% with IHD (P=0.81).

The median in-hospital stay was 3 days in the SNH group and 6 days in the SHD group (P<0.0001). There was no difference between the group of patients with IHD and without IHD.

Acute Complications and Outcomes in Re-do Procedure Versus First Ablation as the Index Procedure

The incidence of moderate nonfatal complications was higher in patients undergoing a re-do procedure as compared with

Table 3. Periprocedural Complications

Variable	Total	Structurally Normal Heart	Structural Heart Disease	*P* Value*	Odds Ratio (95% Confidence Interval)
Periprocedural death	1 (0.3%)	0 (0.0%)	1 (0.5%)	1.0	
MACE (death, MI)	1 (0.3%)	0 (0.0%)	1 (0.5%)	1.0	
MACCE (death, MI, stroke)	1 (0.3%)	0 (0.0%)	1 (0.5%)	1.0	
Major complications (death, MI, stroke, major bleeding)	2 (0.6%)	0 (0.0%)	2 (0.9%)	0.54	
Moderate complications	14/318 (4.4%)	5/114 (4.4%)	9/204 (4.4%)	1.0	1.01 (0.33–3.08)
Nonfatal resuscitation	2 (0.6%)	1 (0.9%)	1 (0.5%)	1.0	
AV fistula	7 (2.2%)	1 (0.9%)	6 (2.9%)	0.43	
Pericardial effusion	3 (0.9%)	2 (1.8%)	1 (0.5%)	0.29	
Third-degree atrioventricular block	2 (0.6%)	1 (0.9%)	1 (0.5%)	1.0	
Pulmonary embolism	1 (0.3%)	1 (0.9%)	0 (0.0%)	0.36	
Cardiac surgery (emergency)	1 (0.3%)	1 (0.9%)	0 (0.0%)	0.36	
VT recurrence before discharge	24 (7.2%)	6 (5.1%)	18 (8.3%)	0.38	1.70 (0.65–4.40)
Days in-hospital	5 (3; 10)	3 (2; 6)	6 (4; 11)	<0.0001	

Number (percentage) of patients, or median with quartiles are shown. MACE indicates major adverse cardiac events; MACCE, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; VT, ventricular tachycardia.

patients undergoing new-do procedures (10.5% versus 3.1%; *P*=0.024). This difference was because of a higher incidence of pericardial effusion, femoral atrioventricular fistula, and pseudoaneurysm and need for resuscitation. Re-do procedures were also associated with a higher recurrence rate before discharge (13.3% versus 5.5%; *P*=0.029) and higher rate of antiarrhythmic drug use (53.3% versus 39.1%; *P*=0.043).

During follow-up, recurrence rates and antiarrhythmic drug use did not differ between patients undergoing re-do and new-do procedures.

Acute Complications and Outcomes After Successful Versus Partially Successful Procedures

The procedure was classified as successful in 259 (86.0%) patients, and partially successful in 42 (14.0%) patients. Patients did not show any differences with respect to baseline characteristics and comorbidities. The complication rate, the use of antiarrhythmic drugs at discharge, the re-ablation rate, as well as the long-term success rate were similar between both groups. However, a successful procedure resulted in a lower in-house recurrence rate (4.6% versus 16.7%; *P*=0.003).

Discharge Management and Follow-Up

As expected, significantly more patients from the SNH group were discharged without medications (16.1% versus 1.4%, *P*<0.0001). A large number of patients from the SHD group were discharged with β-blockers (81.9%) and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (71.6%). Angiotensin-converting enzyme inhibitors/angiotensin receptor blockers were used more frequently in patients with IHD compared with those without IHD (76.3% versus 58.2%; *P*<0.05). With regard to AADs, more patients from the SNH received class I AADs (12.9% versus 7.9%, *P*=0.14), and more patients from the SHD received class III AADs (47.0% versus 13.8%, *P*<0.0001). There were no significant differences in AAD therapy between the IHD and no IHD groups. Anticoagulation with warfarin occurred more frequently in patients from the SHD group (31.6% versus 6.0%, *P*<0.0001). Aspirin, clopidogrel, and warfarin were used more frequently in patients with IHD versus no IHD (70.0% versus 49.1%; *P*<0.01; 19.4% versus 0.0%; *P*<0.001; 35.6% versus 20.0%; *P*<0.05, respectively) (Table 4).

Follow-up was successfully completed in 98.8% of patients discharged alive (SNH 100%, SHD 98.1%, *P*=0.14; no IHD 92.7%, IHD 100%, *P*<0.01). Median follow-up was 18.8 (quartiles 14.7–25.4) months after index discharge. At follow-up, a large number of patients with SNH ceased all medications (16.1%–33.0%), mainly in β-blocker and aspirin therapy. For the SHD group, medications were generally maintained, with the exception of Class I AADs (7.9%–4.4%). More patients in the IHD group maintained Class III AADs compared with the no IHD group (52.9% versus 32.5%; *P*<0.05).

In the SNH group, 6 patients (5.1%) were dead at the time of follow-up and 36 (17.1%) in the SHD group, with 5 deaths occurring in the no IHD and 31 in the IHD subgroup. Estimated 2-year mortality was significantly lower in the SNH group versus the SHD group (3.5% [95% confidence interval 1.3%–9.2%] versus 18.7% [13.5%–25.5%]; *P*<0.01) without significant difference between the no IHD and IHD subgroups (12.3% versus 20.5%; *P*=0.29). Similarly, MACE, MACCE, and major complications occurred at a significantly lower rate (MACE: 3.5% [1.3%–9.2%] versus 19.7% [14.3%–26.8%]; *P*<0.01. MACCE: 3.5% [1.3%–9.2%] versus 19.7% [14.4%–26.5%];

Table 4. Medications at Discharge

Variable	Total	SNH on Discharge	SHD on Discharge	*P* Value	Odds Ratio (95% Confidence Interval)
No medication	6.6% (22/331)	16.4% (19/116)	1.4% (3/215)	<0.0001	0.07 (0.02–0.26)
β-Blocker	71.0% (235/331)	50.9% (59/116)	81.9% (176/215)	<0.0001	4.36 (2.64–7.21)
Class I AAD	9.7% (32/331)	12.9% (15/116)	7.9% (17/215)	0.14	0.58 (0.28–1.21)
Class III AAD	35.3% (117/331)	13.8% (16/116)	47.0% (101/215)	<0.0001	5.54 (3.06–10.01)
Amiodarone	29.3% (97/331)	10.3% (12/116)	39.5% (85/215)	<0.0001	5.67 (2.94–10.93)
Digitalis	3.9% (13/331)	0.9% (1/116)	5.6% (12/215)	0.035	6.80 (0.87–52.95)
ACEi/ARB	52.0% (172/331)	15.5% (18/116)	71.6% (154/215)	<0.0001	13.74 (7.67–24.64)
Aspirin	59.8% (198/331)	50.9% (59/116)	64.7% (139/215)	0.015	1.77 (1.12–2.80)
Clopidogrel	9.7% (32/331)	0.9% (1/116)	14.4% (31/215)	<0.0001	19.38 (2.61–143.9)
Warfarin	22.7% (75/331)	6.0% (7/116)	31.6% (68/215)	<0.0001	7.20 (3.18–16.30)

AAD indicates anti-arrhythmic drugs; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; SHD, structural heart disease; SNH, structurally normal heart.

$P<0.01$) in the SNH group. Rehospitalization was more frequent for surviving patients with SHD (62.3% versus 46.5%; $P<0.05$) with no significant difference between the no IHD and IHD subgroups (52.4% versus 65.8%; $P=0.12$); however, both groups were predominantly re-admitted for cardiac causes (Table 5). There were no differences between the 2 groups for the number of days in-hospital after re-admission (SNH 11.8±13.6 versus SHD 19.3±27.5; $P=0.12$). Moderate complications include syncope, transient ischemic attack, pulmonary embolism, moderate bleeding, and revascularization and resuscitation, with only revascularization occurring significantly more frequently in the SHD group (5.5% versus 0%; $P<0.05$). However, within the SHD patients, MACE, MACCE, and major and moderate complication occurrences were similar between the no IHD versus IHD groups. Nonfatal VT recurrence was not different between the 2 groups (SNH 38.0% versus SHD 35.9%; $P=0.73$; no IHD 36.4% versus IHD 35.7%; $P=0.94$).

At discharge after the index procedure, 48.8% of the patients had an ICD implanted. The 2-year mortality rate in patients with an ICD was 21.4% as compared with 5.7% in patients without an ICD ($P<0.001$%). Following a successful procedure, 2.7% of the patients received an ICD versus 8.2% after a partially successful procedure or procedural failure ($P=0.032$).

Predictors of Nonfatal VT Recurrence and Mortality

During 21.0±8.0 months of follow-up, 42/329 (12.8%) patients died and 102/278 (36.7%) experienced nonfatal VT recurrence. Using proportional-hazards regression modeling, the unadjusted predictors of 2-year mortality included age >60 years old (hazard ratio [HR] 6.49 [2.54–16.60]), SHD (HR 5.21 [1.85–14.67]), prior resuscitation (HR 3.77 [1.34–10.63]), LVEF ≤30% (HR 4.37 [2.27–8.44]), incessant VT (HR 4.23 [1.85–9.67]), and the use of Class III AADs at discharge (HR 4.17 [2.14–8.12]). Procedural failure (HR 2.12 [0.89–5.07]) and the use of Class I AADs (HR 1.88 [0.79–4.49]) were not significant in unadjusted analysis. In a multivariable model, age >60 years old (adjusted HR 5.56 [2.08–14.86]), incessant VT (adjusted HR 2.99 [1.27–7.07]), LVEF ≤30% (adjusted HR 2.53 [1.21–5.31]), procedural failure (adjusted HR 2.99 [1.27–7.07]), the use of Class I AADs (adjusted HR 2.56 [1.05–6.26]) and of Class III AADs at discharge (adjusted HR 2.16 [1.12–4.57]) were predictive of mortality after ablation of VT.

In the proportional odds models, procedural failure was the only statistically significant predictor of nonfatal VT recurrence after catheter ablation in unadjusted (odds ratio [OR

Table 5. Follow-Up Outcomes

Variable	Total (Discharged Alive: n=333)	Structurally Normal Heart (n=118)	Structural Heart Disease (n=215)	*P* Value	Odds Ratio (95% Confidence Interval)
Successful follow-up	329 (98.8%)	118 (100%)	211 (98.1%)	0.14	
Follow-up duration, d	572 (446;774)	572 (442;775)	572 (446;770)	0.96	
Total death	42 (12.8%)	6 (5.1%)	36 (17.1%)		
Cardiac death	16 (38.1%)	1 (16.7%)	15 (41.7%)		
Noncardiac death	3 (7.1%)	1 (16.7%)	2 (5.6%)		
Unknown	23 (54.8%)	4 (66.7%)	19 (52.7%)		
Stroke/TIA (nonfatal)	1 (0.3%)	0 (0.0%)	1 (0.5%)		
MI (nonfatal)	1 (0.3%)	0 (0.0%)	1 (0.5%)		
MACE (death, MI)	43 (13.1%)	6 (5.1%)	37 (17.5%)		
MACCE (death, MI, stroke)	44 (13.4%)	6 (5.1%)	38 (18.0%)		
Events among survivors	n=287	n=112	n=175		
Resuscitation	3/264 (1.1%)	1/102 (1.0%)	2/162 (1.2%)	0.85	1.26 (0.11–14.10)
Revascularization	9/265 (3.4%)	0/102 (0.0%)	9/163 (5.5%)	0.016	
VT recurrence	102/278 (36.7%)	41/108 (38.0%)	61/170 (35.9%)	0.73	0.91 (0.56–1.51)
Recurrent VT Ablation	48/278 (17.3%)	21/108 (19.4%)	27/170 (15.9%)	0.44	0.78 (0.42–1.47)
Rehospitalization	148/263 (56.3%)	47/101 (46.5%)	101/162 (62.3%)	0.012	1.90 (1.15–3.15)
Cardiac cause	113 (76.4%)	33 (70.2%)	80 (79.2%)		
Noncardiac cause	35 (23.6%)	14 (29.8%)	21 (20.8%)		

Number (percentage) of patients or median with quartiles are shown. MACE indicates major adverse cardiac events; MACCE, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; SHD, structural heart disease; SNH, structurally normal heart; TIA, transient ischemic attack; VT, ventricular tachycardia.

Table 6. Predictors of Mortality and Nonfatal VT Recurrence Using Regression Modeling at Follow-Up

Variable	Total Mortality		Nonfatal Recurrence	
	Crude Hazard Ratio (95% Confidence Interval)	Adjusted Hazard Ratio (95% Confidence Interval)	Crude Odds Ratio (95% Confidence Interval)*	Adjusted Odds Ratio (95% Confidence Interval)*
Age >60 y	6.49 (2.54–16.60)	5.56 (2.08–14.86)	1.14 (0.70–1.86)	1.31 (0.76–2.28)
SHD	5.21 (1.85–14.67)	1.47 (0.46–4.72)	0.90 (0.55–1.49)	0.84 (0.48–1.47)
Incessant VT	4.25 (1.87–9.66)	2.99 (1.27–7.07)	0.60 (0.19–1.92)	NS
Known LVEF ≤30%	4.37 (2.27–8.44)	2.53 (1.21–5.31)	1.12 (0.62–2.03)	NS
Procedural failure	2.12 (0.89–5.07)	3.16 (1.28–7.75)	4.76 (1.78–12.75)	4.89 (1.81–13.19)
Use of Class I AADs at discharge	1.88 (0.79–4.49)	2.56 (1.05–6.26)	2.12 (0.94–4.82)	NS
Use of Class III AADs at discharge	4.17 (2.14–8.12)	2.26 (1.12–4.57)	1.04 (0.61–1.79)	NS

AADs indicates anti-arrhythmic drugs; LVEF, left ventricular ejection fraction; NS, not significant; SHD, structural heart disease; VT, ventricular tachycardia.
*Calculated in proportional odds model including logarithm of follow-up time.

4.76 [1.78–12.75]) and adjusted analysis (OR adjusted for SHD and age 4.89 [1.81–13.19]). Nonsignificant factors included age >60 years old (OR 1.14 [0.70–1.86]), SHD (OR 0.90 [0.55–1.49]), incessant VT (OR 0.60 [0.19–1.92]), LVEF ≤30% (OR 1.12 [0.62–2.03]), and the use of Class III AADs at discharge (OR 1.04 [0.61–1.79]) (Table 6).

Predictors of Nonfatal VT Recurrence in Patients With SHD Versus SNH

In a separate analysis of VT recurrence in patients with SHD and SNH, procedural failure was the only statistically significant predictor of nonfatal VT recurrence after catheter ablation in patients with SHD in unadjusted (OR 3.37 [0.94–12.04]) and adjusted analysis (OR 3.44 [0.96–12.32]) as well as in patients with SNH in unadjusted (OR 7.52 [1.49–37.89]) and adjusted analysis (OR 7.92 [1.53–40.83]) (Table 7).

Discussion

We present the first multicenter, prospective German registry of a large group of patients referred for first-time ablation of VT to evaluate the safety and efficacy of catheter ablation for the treatment of VT in a real-world scenario. To the best of our knowledge, there has to date not been another German registry including such a large study population.

Main Findings

The results of this study demonstrate that there are substantial differences in patient and arrhythmia characteristics between patient groups referred for ablation of VT. These differences can lead to different ablation approaches used, as well as differences in the procedural, acute, and longer-term patient outcomes. This registry also identified certain predictors of mortality and nonfatal recurrence that may help guide cardiologists to decide how to best manage individual patients.

Patient and Arrhythmia Characteristics

Our study identified that the overall distribution of patients referred for catheter ablation of VT was at a ratio of 2:1 for SHD:SNH patients. Those with SNH were younger, with lower CHA_2DS_2-VASc risk scores. SNH patients were less likely to have VTs that were hemodynamically unstable, that were

Table 7. Predictors of Nonfatal VT Recurrence Using Regression Modeling at Follow-Up

Variable	SHD		SNH	
	Crude Odds Ratio (95% Confidence Interval)	Adjusted Odds Ratio (95% Confidence Interval)	Crude Odds Ratio (95% Confidence Interval)	Adjusted Odds Ratio (95% Confidence Interval)
Age >60 y	1.12 (0.58–2.18)	1.18 (0.60–2.31)	1.44 (0.58–3.58)	1.60 (0.62–4.09)
Procedural failure	3.37 (0.94–12.04)	3.44 (0.96–12.32)	7.52 (1.49–37.89)	7.92 (1.53–40.83)

SHD indicates structural heart disease; SNH, structurally normal heart; VT, ventricular tachycardia.

incessant, and were less likely to have required prior resuscitation. They had more drug-responsive arrhythmias. This collection of characteristics would be consistent with the pathologies that may cause SNH VT.[21] Ventricular arrhythmias such as those originating from the right ventricular outflow tract were seen more often in this group, and these arrhythmias have been previously shown to be associated with a younger population.[22–24] In fact, right ventricular outflow tract VT can follow a benign course.[25] In patients with SHD, the underlying pathologies such as IHD, valvular heart disease, and cardiomyopathies lead to a much more complex substrate.[26–28] These patients are more likely to have cardiovascular risk factors, are often more unstable, have more incessant arrhythmias, and are less likely to be responsive to AADs.[29,30] It was also seen in this registry that these patients predominantly had VTs with origins in the LV.

In addition, the subgroup of patients with IHD were older, had higher CHA_2DS_2-VASc risk scores, worse NYHA functional class, and lower LVEFs, in line with the acquired nature of the disease.

All patients with primary electrical diseases such as Brugada syndrome, long QT syndrome, and arrhythmogenic right ventricular cardiomyopathy were excluded in this study. This decision was made because the underlying pathology of these primary electrical diseases is distinct from other causes of VT, which leads to different disease progression as well as different treatment approaches.[31–35]

Procedural, Acute, and Long-Term Outcomes

Ablation success requires detailed mapping and adequate radiofrequency lesion formation. In keeping with the cause of VTs in SNH and SHD patients, SNH patients underwent more ablations performed only using conventional approaches. This group of patients more often had focal ablation, and the length of the procedures, radiofrequency applications, and fluoroscopy time and doses were significantly shorter compared with ablation in SHD patients. Although the rate of unsuccessful ablation was the same in both groups, there were more patients who had partial success in the SHD group. This reflects that SHD patients are more likely to have complex substrates, and electrophysiologists are more likely to be limited by procedural factors, such as time, radiofrequency application, and fluoroscopy exposure.[10,28,36,37] Patients with IHD were also less likely to have epicardial disease, which is in line with the predominantly endocardial substrate from coronary artery stenosis/occlusion.[38–40] However, they are more likely to receive substrate modification/linear ablation, and had more ablation success. This is likely secondary to these patients more frequently having substrates with clear coronary artery distribution.[13,40] The comparable recurrence rate in the SHD and SNH group might be explained by the fact that a 3D mapping system was only used in about every second patient with SNH. In addition, some patients in the SNH group might have had an undiagnosed SHD.[21] Since this is a registry study, no standardized workup was required before enrollment. However, routine workup before a VT ablation procedure at that time in Germany included at least a transthoracic echocardiogram and a coronary angiogram in most patients. Furthermore, ablation techniques and catheters have improved in the past few years, very likely resulting in better ablation outcome currently.[41–43]

The overall 12-month mortality rate at follow-up was 8.8%. The mortality rate for patients with SHD was 12.2%, which is in line with other studies[36,44–46] and was similar in the nIHD and IHD group. The 12-month mortality rate in the Multicenter Thermocool Ventricular Tachycardia Ablation Trial was 18%.[30] Interestingly, the mortality rate in the SNH group was 2.6%, which is higher than in previous reports. In a study by Ventura et al, for instance, the mortality rate during 10 years of follow-up after right ventricular outflow tract–VT ablation was only 5%.[47] This low mortality rate might be explained by the younger patient population in the latter group (50.5 ± 15 versus 39 ± 13 years). This surprisingly high mortality rate in our study may indicate that VTs in patients without SHD might not be as benign as previously thought.[22] There was no difference periprocedurally in the rates of MACE, MACCE, and major complications between the 2 groups, as well as in the subgroup of patients with and without IHD. However, at 12-month follow-up, patients with SHD experienced significantly more MACE, MACCE, and major complications. There were also more patients requiring resuscitation in the SHD group, although there were no differences between patients with or without IHD in regard to MACE, MACCE, and major complications.

In a subgroup analysis of patients' outcome after successful versus partially successful procedures, recurrence rates during hospital stay were higher after partial success, but recurrence rate during follow-up was similar. This outcome suggests that partial success with noninducibility of the clinical VT may be a reasonable end point.

In regard to medical treatment, more patients with SHD received Class III AADs on discharge and more patients with SNH received Class I AADs. This is because of the high prevalence of IHD in SHD patients. As expected, patients with IHD also received more β-blockers and angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, and antiplatelet/anticoagulation therapy. At 12 months, more patients in the SNH group ceased medications; however, medications were generally maintained in the SHD group.

All this leads to longer hospital stays for patients with SHD, with more re-admissions within the follow-up period. In line

with previous studies, at the end of the follow-up period, there were no differences in the rate of nonfatal VT recurrence between the 2 groups, with an overall recurrence rate of 36.7%. Calkins et al reported a recurrence rate of 46% during 243±153 days of follow-up.[37]

Predictors of Mortality and Nonfatal VT Recurrence

The end point of this study was to identify predictors of mortality and nonfatal VT recurrence. After multivariate logistic regression modeling, predictors of mortality were the following: age >60 years old, incessant VT, LVEF ≤30%, procedural failure, and use of Class I and III AADs at discharge. The only predictor of nonfatal VT recurrence was procedural failure. Because of the vast age difference, in this study SHD was not a predictor of mortality or nonfatal VT recurrence after adjustment, which is surprising given the more complex nature of the diseases. However, the variables predicting mortality were seen significantly more often in the group with SHD, as well as in the subgroup of patients with IHD. For SHD as for SNH, procedural failure independently predicted VT recurrence. In SHD, procedural failure predicts mortality; in SNH the number of events is too small to allow for a meaningful analysis of predictors. In our study, procedural failure was the only predictor for both mortality and nonfatal VT recurrence; however, its frequency was not different between the 2 groups.

Limitations

Firstly, although prospective, participation in this study is voluntary for both the patient and the operator. Therefore, patients who were not able to consent (eg, intubated patients) could not be included in this registry. In addition, more experienced operators might have been more likely to participate in this registry. In addition, some procedures with a very high complication risk might not have been included in this registry. Therefore, the success rate might be overestimated and the complication rate underestimated.

Secondly, this is a registry study, and all database studies have inherent limitations in regard to follow-up and completeness of data collection. In addition, the follow-up data are based on telephone interview, and not specifically on the outpatient follow-up with the treating physician. However, these data reflect more real-world data than data from clinical trials.

Thirdly, although this is the largest German registry of VT ablations to date, the total study population is moderate. Therefore, the number of patients with MACE was low, and overall mortality and nonfatal VT recurrence percentages were 12.5% and 36.7%, respectively. This leads to limitation in the number of significant variables that could be identified for predictors of mortality and nonfatal VT recurrence. However, because VT ablation is often associated with high mortality and nonfatal VT recurrence, recruitment may be restricted.

Fourthly, the variety of SHD was widespread, with the majority of patients having IHD. Although a subgroup analysis of patients with and without IHD was performed, the pathologies are very different in the different causes for SHD. However, because 75.6% of SHD patients had IHD, it is unlikely that the major findings of this study would be altered.

Fifthly, our study did not include a baseline ECG. Data on prevalence of atrial fibrillation, which is associated with an increased mortality and incidence of stroke, are insufficient.

Clinical Implications

We know that management of VT in patients with SHD is often complex, and that mortality and nonfatal VT recurrence is frequent, even with optimal medical therapy and ICD implantation. Given the recent data demonstrating that inappropriate and even appropriate ICD discharges are detrimental to patients' morbidity and mortality, this study showed that catheter ablation of VT can prevent recurrence at 12 months in 63.3% of all patients. Outcome during follow-up was similar after partially successful and successful procedures. These data suggest that noninducibility of the clinical VT is a reasonable procedural end point for VT ablation. A mortality rate of 17% in the SHD and 4.4% in the SNH group highlights the importance of intensified treatment and close follow-up in those patients. In addition, as the only predictor for nonfatal VT recurrence was procedural failure, this suggests that persistence to eliminate VTs during the procedure is important for long-term mortality and nonfatal VT recurrence. This highlights the importance of further improvement of ablation techniques such as scar homogenization, elimination of local abnormal ventricular activities, substrate isolation, or technologies such as contact force guided ablation that have the potential to improve the outcome.

Conclusion

Our prospective multicenter German registry study identified that an older age, incessant VT, procedural failure, highly impaired LVEF, and use of Class III AADs at discharge were independent predictors of mortality, and procedural failure turned out to be the sole independent predictor for nonfatal VT recurrence. This further emphasizes the importance of a successful ablation procedure with successful elimination of the clinical arrhythmia to reduce long-term mortality and nonfatal VT recurrence.

Sources of Funding

The 1-year follow-up and a previous publication were partially supported by unrestricted grants from Medtronic, Biosense Webster, and Biotronik.

Disclosures

None.

References

1. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med*. 2002;346:877–883.
2. Schron EB, Exner DV, Yao Q, Jenkins LS, Steinberg JS, Cook JR, Kutalek SP, Friedman PL, Bubien RS, Page RL, Powell J. Quality of life in the antiarrhythmics versus implantable defibrillators trial: impact of therapy and influence of adverse symptoms and defibrillator shocks. *Circulation*. 2002;105:589–594.
3. Irvine J, Dorian P, Baker B, O'Brien BJ, Roberts R, Gent M, Newman D, Connolly SJ. Quality of life in the Canadian Implantable Defibrillator Study (CIDS). *Am Heart J*. 2002;144:282–289.
4. Poole JE, Johnson GW, Hellkamp AS, Anderson J, Callans DJ, Raitt MH, Reddy RK, Marchlinski FE, Yee R, Guarnieri T, Talajic M, Wilber DJ, Fishbein DP, Packer DL, Mark DB, Lee KL, Bardy GH. Prognostic importance of defibrillator shocks in patients with heart failure. *N Engl J Med*. 2008;359:1009–1017.
5. Steinberg JS, Martins J, Sadanandan S, Goldner B, Menchavez E, Domanski M, Russo A, Tullo N, Hallstrom A; AVID Investigators. Antiarrhythmic drug use in the implantable defibrillator arm of the Antiarrhythmics Versus Implantable Defibrillators (AVID) Study. *Am Heart J*. 2001;142:520–529.
6. Connolly SJ, Dorian P, Roberts RS, Gent M, Bailin S, Fain ES, Thorpe K, Champagne J, Talajic M, Coutu B, Gronefeld GC, Hohnloser SH; Optimal Pharmacological Therapy in Cardioverter Defibrillator Patients (OPTIC) Investigators. Comparison of beta-blockers, amiodarone plus beta-blockers, or sotalol for prevention of shocks from implantable cardioverter defibrillators: the OPTIC Study: a randomized trial. *JAMA*. 2006;295:165.
7. Pacifico A, Hohnloser SH, Williams JH, Tao B, Saksena S, Henry PD, Prystowsky EN. Prevention of implantable-defibrillator shocks by treatment with sotalol. d, l-Sotalol Implantable Cardioverter-Defibrillator Study Group. *N Engl J Med*. 1999;340:1855–1862.
8. Antz M, Berodt K, Bänsch D, Ernst S, Chun KJ, Satomi K, Schmidt B, Boczor S, Ouyang F, Kuck K-H. Catheter-ablation of ventricular tachycardia in patients with coronary artery disease: influence of the endocardial substrate size on clinical outcome. *Clin Res Cardiol*. 2008;97:110–117.
9. Volkmer M, Ouyang F, Deger F, Ernst S, Goya M, Bänsch D, Berodt K, Kuck K-H, Antz M. Substrate mapping vs. tachycardia mapping using CARTO in patients with coronary artery disease and ventricular tachycardia: impact on outcome of catheter ablation. *Europace*. 2006;8:968–976.
10. Segal OR, Chow AWC, Markides V, Schilling RJ, Peters NS, Davies DW. Long-term results after ablation of infarct-related ventricular tachycardia. *Heart Rhythm*. 2005;2:474–482.
11. Kottkamp H, Hindricks G, Chen X, Brunn J, Willems S, Haverkamp W, Block M, Breithardt G, Borggrefe M. Radiofrequency catheter ablation of sustained ventricular tachycardia in idiopathic dilated cardiomyopathy. *Circulation*. 1995;92:1159–1168.
12. Coggins DL, Lee RJ, Sweeney J, Chein WW, Van Hare G, Epstein L, Gonzalez R, Griffin JC, Lesh MD, Scheinman MM. Radiofrequency catheter ablation as a cure for idiopathic tachycardia of both left and right ventricular origin. *J Am Coll Cardiol*. 1994;23:1333–1341.
13. Kottkamp H, Wetzel U, Schirdewahn P, Dorszewski A, Gerds-Li J-H, Carbucicchio C, Kobza R, Hindricks G. Catheter ablation of ventricular tachycardia in remote myocardial infarction: substrate description guiding placement of individual linear lesions targeting noninducibility. *J Cardiovasc Electrophysiol*. 2003;14:675–681.
14. Della Bella P, Riva S, Fassini G, Giraldi F, Berti M, Klersy C, Trevisi N. Incidence and significance of pleomorphism in patients with postmyocardial infarction ventricular tachycardia. Acute and long-term outcome of radiofrequency catheter ablation. *Eur Heart J*. 2004;25:1127–1138.
15. Soejima K, Stevenson WG, Maisel WH, Sapp JL, Epstein LM. Electrically unexcitable scar mapping based on pacing threshold for identification of the reentry circuit isthmus: feasibility for guiding ventricular tachycardia ablation. *Circulation*. 2002;106:1678–1683.
16. Bansch D, Oyang F, Antz M, Arentz T, Weber R, Val-Mejias JE, Ernst S, Kuck K-H. Successful catheter ablation of electrical storm after myocardial infarction. *Circulation*. 2003;108:3011–3016.
17. Aliot EM, Stevenson WG, Almendral-Garrote JM, Bogun F, Calkins CH, Delacretaz E, Della Bella P, Hindricks G, Jaïs P, Josephson ME, Kautzner J, Kay GN, Kuck K-H, Lerman BB, Marchlinski F, Reddy V, Schalij M-J, Schilling R, Soejima K, Wilber D; European Heart Rhythm Association (EHRA); Registered Branch of the European Society of Cardiology (ESC); Heart Rhythm Society (HRS); American College of Cardiology (ACC); American Heart Association (AHA). EHRA/HRS expert consensus on catheter ablation of ventricular arrhythmias. *Heart Rhythm*. 2009;6:886–933.
18. Tilz RR, Makimoto H, Lin T, Rillig A, Deiss S, Wissner E, Mathew S, Metzner A, Rausch P, Kuck K-H, Ouyang F. Electrical isolation of a substrate after myocardial infarction: a novel ablation strategy for unmappable ventricular tachycardias—feasibility and clinical outcome. *Europace*. 2014;16:1040–1052.
19. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary. *J Am Coll Cardiol*. 2014;64:2246–2280.
20. Camm AJ, Kirchhof P, Lip GYH, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Al-Attar N, Hindricks G, Prendergast B, Heidbuchel H, Alfieri O, Angelini A, Atar D, Colonna P, De Caterina R, De Sutter J, Goette A, Gorenek B, Heldal M, Hohloser SH, Kolh P, Le Heuzey JY, Ponikowski P, Rutten FH; ESC Committee for Practice Guidelines. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Europace*. 2010;12:1360–1420.
21. Jewell N. Correspondences between regression models for complex binary outcomes and those for structured multivariate survival analyses. UC Berkeley Div Biostat Work Pap Ser. 2005.
22. Deal BJ, Miller SM, Scagliotti D, Prechel D, Gallastegui JL, Hariman RJ. Ventricular tachycardia in a young population without overt heart disease. *Circulation*. 1986;73:1111–1118.
23. Kim RJ, Iwai S, Markowitz SM, Shah BK, Stein KM, Lerman BB. Clinical and electrophysiological spectrum of idiopathic ventricular outflow tract arrhythmias. *J Am Coll Cardiol*. 2007;49:2035–2043.
24. Ouyang F, Mathew S, Wu S, Kamioka M, Metzner A, Xue Y, Ju W, Yang B, Zhan X, Rillig A, Lin T, Rausch P, Deiss S, Lemes C, Tonnis T, Wissner E, Tilz RR, Kuck K-H, Chen M. Ventricular arrhythmias arising from the left ventricular outflow tract below the aortic sinus cusps: mapping and catheter ablation via transseptal approach and electrocardiographic characteristics. *Circ Arrhythm Electrophysiol*. 2014;7:445–455.
25. Ouyang F, Fotuhi P, Ho SY, Hebe J, Volkmer M, Goya M, Burns M, Antz M, Ernst S, Cappato R, Kuck KH. Repetitive monomorphic ventricular tachycardia originating from the aortic sinus cusp: electrocardiographic characterization for guiding catheter ablation. *J Am Coll Cardiol*. 2002;39:500–508.
26. Buxton AE, Waxman HL, Marchlinski FE, Simson MB, Cassidy D, Josephson ME. Right ventricular tachycardia: clinical and electrophysiologic characteristics. *Circulation*. 1983;68:917–927.
27. Stevenson WG, Khan H, Sager P, Saxon LA, Middlekauff HR, Natterson PD, Wiener I. Identification of reentry circuit sites during catheter mapping and radiofrequency ablation of ventricular tachycardia late after myocardial infarction. *Circulation*. 1993;88:1647–1670.
28. Betensky BP, Marchlinski FE. Outcomes of catheter ablation of ventricular tachycardia in the setting of structural heart disease. *Curr Cardiol Rep*. 2016;18:68.
29. Soejima K, Suzuki M, Maisel WH, Brunckhorst CB, Delacretaz E, Blier L, Tung S, Khan H, Stevenson WG. Catheter ablation in patients with multiple and unstable ventricular tachycardias after myocardial infarction: short ablation lines guided by reentry circuit isthmuses and sinus rhythm mapping. *Circulation*. 2001;104:664–669.
30. Rothman SA, Hsia HH, Cossú SF, Chmielewski IL, Buxton AE, Miller JM. Radiofrequency catheter ablation of postinfarction ventricular tachycardia: long-term success and the significance of inducible nonclinical arrhythmias. *Circulation*. 1997;96:3499–3508.
31. Stevenson WG, Wilber DJ, Natale A, Jackman WM, Marchlinski FE, Talbert T, Gonzalez MD, Worley SJ, Daoud EG, Hwang C, Schuger C, Bump TE, Jazayeri M, Tomassoni GF, Kopelman HA, Soejima K, Nakagawa H; Multicenter Thermocool VT Ablation Trial Investigators. Irrigated radiofrequency catheter ablation guided by electroanatomic mapping for recurrent ventricular tachycardia after myocardial infarction: the multicenter thermocool ventricular tachycardia ablation trial. *Circulation*. 2008;118:2773–2782.
32. Nademanee K, Veerakul G, Chandanamattha P, Chaothawee L, Ariyachaipanich A, Jirasirirojanakorn K, Likittanasombat K, Bhuripanyo K,

Ngarmukos T. Prevention of ventricular fibrillation episodes in Brugada syndrome by catheter ablation over the anterior right ventricular outflow tract epicardium. *Circulation*. 2011;123:1270–1279.

33. Knecht S, Sacher F, Wright M, Hocini M, Nogami A, Arentz T, Petit B, Franck R, De Chillou C, Lamaison D, Farré J, Lavergne T, Verbeet T, Nault I, Matsuo S, Leroux L, Weerasooriya R, Cauchemez B, Lellouche N, Derval N, Narayan SM, Jaïs P, Clementy J, Haïssaguerre M. Long-term follow-up of idiopathic ventricular fibrillation ablation. *J Am Coll Cardiol*. 2009;54:522–528.
34. Haissaguerre M, Extramiana F, Hocini M, Cauchemez B, Jaïs P, Cabrera JA, Farré J, Farre G, Leenhardt A, Sanders P, Scavée C, Hsu L-F, Weerasooriya R, Shah DC, Frank R, Maury P, Delay M, Garrigue S, Clémenty J. Mapping and ablation of ventricular fibrillation associated with long-QT and Brugada syndromes. *Circulation*. 2003;108:925–928.
35. Dalal D, Jain R, Tandri H, Dong J, Eid SM, Prakasa K, Tichnell C, James C, Abraham T, Russell SD, Sinha S, Judge DP, Bluemke DA, Marine JE, Calkins H. Long-term efficacy of catheter ablation of ventricular tachycardia in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy. *J Am Coll Cardiol*. 2007;50:432–440.
36. Garcia FC, Bazan V, Zado ES, Ren J-F, Marchlinski FE. Epicardial substrate and outcome with epicardial ablation of ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy/dysplasia. *Circulation*. 2009;120:366–375.
37. Calkins H, Epstein A, Packer D, Arria AM, Hummel J, Gilligan DM, Trusso J, Carlson M, Luceri R, Kopelman H, Wilber D, Wharton JM, Stevenson W. Catheter ablation of ventricular tachycardia in patients with structural heart disease using cooled radiofrequency energy: results of a prospective multicenter study. Cooled RF Multi Center Investigators Group. *J Am Coll Cardiol*. 2000;35:1905–1914.
38. Di Biase L, Santangeli P, Burkhardt DJ, Bai R, Mohanty P, Carbucicchio C, Dello Russo A, Casella M, Mohanty S, Pump A, Hongo R, Beheiry S, Pelargonio G, Santarelli P, Zucchetti M, Horton R, Sanchez JE, Elayi CS, Lakkireddy D, Tondo C, Natale A. Endo-epicardial homogenization of the scar versus limited substrate ablation for the treatment of electrical storms in patients with ischemic cardiomyopathy. *J Am Coll Cardiol*. 2012;60:132–141.
39. Hsia HH, Callans DJ, Marchlinski FE. Characterization of endocardial electrophysiological substrate in patients with nonischemic cardiomyopathy and monomorphic ventricular tachycardia. *Circulation*. 2003;108:704–711.
40. Nakahara S, Tung R, Ramirez RJ, Michowitz Y, Vaseghi M, Buch E, Gima J, Wiener I, Mahajan A, Boyle NG, Shivkumar K. Characterization of the arrhythmogenic substrate in ischemic and nonischemic cardiomyopathy. Implications for catheter ablation of hemodynamically unstable ventricular tachycardia. *J Am Coll Cardiol*. 2010;55:2355–2365.
41. Klein H, Karp RB, Kouchoukos NT, Zorn GL, James TN, Waldo AL. Intraoperative electrophysiologic mapping of the ventricles during sinus rhythm in patients with a previous myocardial infarction. Identification of the electrophysiologic substrate of ventricular arrhythmias. *Circulation*. 1982;66:847–853.
42. Marchlinski FE, Haffajee CI, Beshai JF, Dickfeld T-ML, Gonzalez MD, Hsia HH, Schuger CD, Beckman KJ, Bogun FM, Pollak SJ, Bhandari AK. Long-term success of irrigated radiofrequency catheter ablation of sustained ventricular tachycardia. *J Am Coll Cardiol*. 2016;67:674–683.
43. Jais P, Maury P, Khairy P, Sacher F, Nault I, Komatsu Y, Hocini M, Forclaz A, Jadidi AS, Weerasooryia R, Shah A, Derval N, Cochet H, Knecht S, Miyazaki S, Linton N, Rivard L, Wright M, Wilton SB, Scherr D, Pascale P, Roten L, Pederson M, Bordachar P, Laurent F, Kim SJ, Ritter P, Clementy J, Haïssaguerre M. Elimination of local abnormal ventricular activities: a new end point for substrate modification in patients with scar-related ventricular tachycardia. *Circulation*. 2012;125:2184–2196.
44. Tilz RR, Makimoto H, Lin T, Rillig A, Metzner A, Mathew S, Deiss S, Wissner E, Rausch P, Kamioka M, Heeger C, Kuck K-H, Ouyang F. In vivo left-ventricular contact force analysis: comparison of antegrade transseptal with retrograde transaortic mapping strategies and correlation of impedance and electrical amplitude with contact force. *Europace*. 2014;16:1387–1395.
45. Kuck K-H, Schaumann A, Eckardt L, Willems S, Ventura R, Delacrétaz E, Pitschner H-F, Kautzner J, Schumacher B, Hansen PS; VTACH study group. Catheter ablation of stable ventricular tachycardia before defibrillator implantation in patients with coronary heart disease (VTACH): a multicentre randomised controlled trial. *Lancet*. 2010;375:31–40.
46. Tanner H, Hindricks G, Volkmer M, Furniss S, Kühlkamp V, Lacroix D, DE Chillou C, Almendral J, Caponi D, Kuck KH, Kottkamp H. Catheter ablation of recurrent scar-related ventricular tachycardia using electroanatomical mapping and irrigated ablation technology: results of the prospective multicenter Euro-VT-study. *J Cardiovasc Electrophysiol*. 2010;21:47–53.
47. Ventura R, Steven D, Klemm HU, Lutomsky B, Müllerleile K, Rostock T, Servatius H, Risius T, Meinertz T, Kuck K-H, Willems S. Decennial follow-up in patients with recurrent tachycardia originating from the right ventricular outflow tract: electrophysiologic characteristics and response to treatment. *Eur Heart J*. 2007;28:2338–2345.