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Long-Term Efficacy of Catheter Ablation of Ventricular Tachycardia in Patients With Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy

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Objectives This study sought to evaluate the outcomes of radiofrequency catheter ablation (RFA) of ventricular tachycardia (VT) in arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) patients. Particular focus was placed on defining the single-procedure efficacy over long-term follow-up.

Background ARVD/C is an inherited cardiomyopathy characterized by VT and right ventricular dysfunction. Prior single-center studies have reported conflicting results concerning the efficacy of RFA of VT in ARVD/C patients.

Methods The study population comprised 24 patients (age 36 ± 9 years, 11 male), enrolled in the Johns Hopkins ARVD registry, who underwent 1 or more RFA procedures for treatment of VT. Patients were followed up for 32 ± 36 months (range 1 day to 12 years). Recurrence was defined as the documentation of VT subsequent to the procedure.

Results A total of 48 RFA procedures were performed using 3-dimensional electroanatomical (n = 10) or conventional (n = 38) mapping. Of these procedures, 22 (46%), 15 (31%), and 11 (23%) resulted in elimination of all inducible VTs, clinical VT but not all, and none of the inducible VTs, respectively. Forty (85%) procedures were followed by recurrence. The cumulative VT recurrence-free survival was 75%, 50%, and 25% after 1.5, 5, and 14 months, respectively. The cumulative VT recurrence-free survival did not differ by procedural success, mapping technique, or repetition of procedures. There was 1 procedure-related death.

Conclusions Our study shows a high rate of recurrence in ARVD/C patients undergoing RFA of VT. This likely reflects the fact that ARVD/C is a diffuse cardiomyopathy with progressively evolving electrical substrate. Further studies are needed to define the precise role of RFA of VT in ARVD/C. (J Am Coll Cardiol 2007;50:432–40) © 2007 by the American College of Cardiology Foundation

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is an inherited cardiomyopathy characterized by progressive fibro-fatty replacement of the right ventricular (RV) myocardium (1,2). Recurrent ventricular tachycardia (VT) and sudden cardiac death are clinical hallmarks of the disease (3,4). Scar tissue within the myocardium may be multifocal or diffuse, and provides a substrate for re-entrant VT (5,6). Recent studies have shown that ARVD/C results from mutations in genes encoding desmosomal proteins (7). It has been hypothesized that altered desmosomal proteins impair cell-to-cell adhesion that results in cellular uncoupling and lead to fibro-fatty replacement of myocytes.

Because patients with ARVD/C are at significantly increased risk of sudden death, most patients diagnosed with this disease, especially in the U.S., undergo implantable cardioverter-defibrillator (ICD) implantation. Multiple studies have reported a high rate of appropriate ICD firing

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among patients with ARVD/C (4,8–11). Consequently, adjunctive treatment with antiarrhythmic drug therapy and/or radiofrequency catheter ablation (RFA) is commonly recommended. Several single-center studies have reported conflicting results concerning the acute and long-term efficacy of radiofrequency catheter ablation in patients with ARVD/C (12–18). Interpretation of the results of these studies also is complicated by variable adherence to the International Task Force definition of ARVD/C (19) for enrollment, variable use of repeat ablation procedures, definitions of "success," and marked differences in the duration of follow-up.

The purpose of this study was to investigate the long-term results of catheter ablation of VT performed in ARVD/C patients enrolled in the Johns Hopkins ARVD/C registry. Each of the enrolled patients met the strict criteria for ARVD/C diagnosis as defined by the International Task Force.

Methods

Study population. The Johns Hopkins ARVD registry was established in 1999 with the goal of gaining insights into the diagnosis, genetic basis, and clinical course of patients with known or suspected ARVD/C. All patients included in this registry provided written informed consent to participate in the registry and are contacted at yearly intervals to determine their clinical course. The patient population screened for inclusion in this study was composed of 24 registry participants who met the Task Force Definition of ARVD/C and had undergone 1 or more attempts at RFA. Each patient had previously experienced 1 or more episodes of sustained VT. The study protocol was approved by the Johns Hopkins Medicine Institutional Review Board.

A total of 48 catheter ablation procedures were preformed in the 24 patients included in this report. These procedures were performed in 29 different electrophysiology centers across the U.S. Medical history was elicited by patient interview and a detailed review of the patient's medical records. Therapeutic decisions were made by the treating electrophysiologist in conjunction with each patient. Procedure reports and ICD interrogation reports were obtained directly from the treating electrophysiologists and reviewed at our center.

Electrophysiology study, mapping, and ablation technique. Electrophysiology testing and radiofrequency catheter ablation were performed using standard techniques (20). Clinical VT(s) were defined by several techniques, including a comparison of 12-lead electrocardiographic morphologies of induced and spontaneous VT, and when a 12-lead electrocardiogram of the clinical VT was not available, by comparison of induced and spontaneous VT cycle lengths and/or intracardiac electrogram morphologies. Electroanatomical mapping was used to facilitate ablation during 10 procedures in 6 patients (21,22). All other ablation procedures were performed using conventional mapping and ablation techniques including pace mapping, activation mapping, and entrainment mapping (23).

Standard radiofrequency energy delivered through 4-mm tipped deflectable ablation catheters was used for each of the ablation procedures. Ablation of a particular morphology of VT was considered successful if it could not be induced on repeated stimulation. Procedural success was defined as total when all of the inducible VTs could be successfully mapped and ablated, partial when not all of the inducible VTs were successfully ablated but the clinical VT was successfully ablated, and failure if none of the inducible VTs could be ablated successfully.

Abbreviations and Acronyms

ARVD/C = arrhythmogenic right ventricular dysplasia/cardiomyopathy
ICD = implantable cardioverter-defibrillator
RFA = radiofrequency catheter ablation
RV = right ventricle/ventricular
VT = ventricular tachycardia

Follow-up. Patients were followed up routinely in clinics by their treating electrophysiologists. At the same time, they were contacted at yearly intervals by our center. Implantable cardioverter-defibrillator interrogation reports from patients with ICDs were sent to our center by the patient and/or the treating electrophysiologist. Appropriateness of ICD intervention was defined using the standard criteria (10). The VT recurrence was defined as an appropriate ICD interven-

Table 1 Baseline Characteristics of the Patients

Characteristics	n = 24
Age (yrs) at the time of the first procedure, mean ± SD	36 ± 9
Gender, male	11 (46)
ICD implantation	
Before the first ablation procedure	5 (21)
During follow-up	14 (58)
No ICD	5 (21)
Previously failed antiarrhythmics	
Beta-blockers	8 (33)
Sotalol	5 (21)
Amiodarone	3 (13)
Flecainide	2 (8)
Mexilitine	2 (8)
Calcium channel blockers	2 (8)
Propafenone	2 (8)
Procainamide	1 (4)
Quinidine	1 (4)
Disopyramide	1 (4)
Antiarrhythmics at the time of catheter ablation (n = 48)	
Beta-blockers	15 (32)
Sotalol	11 (23)
Amiodarone	9 (19)
Flecainide	5 (10)
Calcium channel blockers	3 (6)
Mexilitine	2 (4)
Procainamide	1 (2)
Dofetilide	1 (2)

ICD = implantable cardioverter-defibrillator.

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tion or the occurrence of VT subsequent to the ablation procedure as documented by a 12-lead electrocardiogram, an event monitor, or a 24-h Holter monitor. The time to VT recurrence after each ablation procedure was noted. Long-term success was defined as the absence of recurrence of VT over follow-up.

Statistical analysis. Continuous variables are expressed as mean ± SD, and categorical variables as frequency (%). Event was defined as VT recurrence after the ablation procedure. Follow-up time was calculated from the time of procedure and censored at the occurrence of an event, loss of follow-up, or heart transplantation. Kaplan-Meier survival analysis was used to determine the cumulative recurrence-free survival in the study population.

Thirteen of the 24 patients in the study population underwent more than 1 ablation procedure because of VT recurrence subsequent to the initial ablation procedure. To include the subsequent procedures in the survival analysis, a staggered entry approach was used. These individuals who had more than 1 procedure re-entered the survival analysis after their initial recurrence and were followed up until they experienced an event or were censored again. This process was repeated for each time that a new catheter ablation procedure was performed on the same patient. Comparisons in the cumulative event-free survival between patients with total procedural success versus partial procedural success versus procedural failure, patients undergoing mapping of VT using 3-dimensional electroanatomical mapping versus traditional mapping technique, and initial versus repeat ablation procedures were made using the log-rank test.

All statistical analyses were performed using STATA statistical software (version 8.2, 1984, StataCorp, College Station, Texas). A p value of <0.05 was considered statistically significant.

Results

Study population. The study population comprised 24 ARVD/C patients who underwent catheter ablation for VT. Table 1 shows baseline characteristics of the study population. The mean age at their first procedure was 36 ± 9 years. Eleven (46%) of the 24 patients were male. Five (21%) of the patients had an ICD implanted before their first catheter ablation procedure, 14 (58%) had an ICD implanted during follow-up, and 5 (21%) did not have an ICD implanted at the end of follow-up. Table 2 shows the ascertainment of the Task Force criteria in each of the 24 patients. There was no or minimal left ventricular involvement in the patients.

Electrophysiology study, mapping, and ablation. Table 3 shows the electrophysiological details of each of the 48 procedures. Consistent with the entry criteria for this study, all patients had VT induced during baseline electrophysiological testing. More than 1 distinct VT morphology was induced in 37 (77%) of the procedures. Mapping of the VT was performed using 3-dimensional electroanatomical mapping during 10 (21%) of the ablation procedures.

Table 2 Task Force Criteria in the Study Population

No.	Structural	Depolarization	Repolarization	Arrhythmia	Tissue	Family History
1	Major	Major	Minor	Minor	—	None
2	Major	Major	Minor	Minor	—	None
3	Major	Major	Minor	Minor	—	None
4	Minor	Minor	Minor	Minor	—	None
5	Minor	Major	None	Minor	—	None
6	Minor	None	Minor	Minor	Major	None
7	Major	None	None	Minor	Major	None
8	Minor	Minor	None	Minor	None	None
9	Major	Major	Minor	Minor	Major	None
10	Minor	Minor	Minor	Minor	—	None
11	Major	Major	Minor	Minor	—	None
12	Minor	Major	Minor	Minor	—	None
13	Major	Major	Minor	Minor	—	None
14	Minor	Major	Minor	Minor	—	Minor
15	Major	Major	Minor	Minor	—	None
16	Minor	Major	Minor	Minor	—	None
17	Minor	Minor	Minor	Minor	None	None
18	Major	None	Minor	Minor	None	None
19	Major	None	Minor	Minor	Major	None
20	Major	Minor	Minor	Minor	Major	None
21	Minor	Minor	Minor	Minor	—	None
22	Minor	Major	Minor	Minor	Major	None
23	Minor	Minor	Minor	Minor	None	Minor
24	Major	Major	Minor	Minor	—	None

Table 3 Details of Electrophysiology Catheter Ablation Procedure and VT Recurrence

No.	Age (yrs)	Gender	Abl	Mapping	VT Induced	VT Ablated	Clinical VT Ablated	ICD	Rec	Drugs at Ablation	Drugs at Recurrence
1	37	Male	1	Conv	4	4	Yes	No	Yes	None	None
	41		2	Conv	2	1	Yes	No	Yes	None	None
2	41	Female	1	Conv	2	1	Yes	No	No	None	None*
	42		2	Conv	4	1	Yes	Yes	Yes	None	Sot
	47		3	Conv	4	3	Yes	Yes	Yes	Sot	Flec, β-bloc
3	26	Male	1	Conv	Multiple	1	Yes	Yes	Yes	None	Amio, β-bloc
	27		2	Conv	Multiple	1	Yes	Yes	Yes	Coum, Sot	Coum, Sot
	29		3	Conv	Multiple	0	No	Yes	Yes	Amio, β-bloc	Amio, β-bloc
	33		4	3D	2	2	Yes	Yes	Yes	Amio, β-bloc	Amio, β-bloc
4	29	Female	1	Conv	1	1	Yes	No	Yes	None	None
	29		2	Conv	1	1	Yes	No	Yes	None	β-bloc
	30		3	Conv	1	1	Yes	No	Yes	β-bloc	β-bloc
	30		4	3D	1	1	Yes	No	Yes	Amio	Amio, β-bloc
	33		5	Conv	3	3	Yes	Yes	Yes	Flec, β-bloc, CCB	Flec, β-bloc, CCB
5	57	Female	1	Conv	2	1	Yes	No	Yes	CCB	β-bloc
	58		2	Conv	3	0	No	Yes	Yes	β-bloc	β-bloc
6	35	Male	1	Conv	5	1	Yes	Yes	Yes	Met	Met
	35		2	Conv	5	0	No	Yes	Yes	Met	Met
	35		3	Conv	11	2	Yes	Yes	Yes	Met, Mex, Proc	Amio, Met, Mex
	35		4	3D	4	4	Yes	Yes	Yes	β-bloc, Mex	Mex
	35		5	3D	1	1	Yes	Yes	Yes	Mex	Mex
7	38	Female	1	Conv	4	0	No	Yes	Yes	None	β-bloc
8	40	Female	1	Conv	3	3	Yes	No	No	None	None*
	42		2	Conv	1	1	Yes	No	Yes	None	None
	43		3	Conv	2	2	Yes	No	No	Sot	Sot*
9	56	Male	1	Conv	Multiple	1	Yes	Yes	Yes	Amio, β-bloc	Amio, β-bloc
10	22	Male	1	3D	1	1	Yes	No	Yes	None	None
	22		2	3D	3	3	Yes	Yes	No	None	Amio, β-bloc*
11	38	Male	1	Conv	Multiple	6	Yes	Yes	Yes	Flec, Mex	Mex, Proc
	39		2	Conv	5	3	No	Yes	Yes	Mex	Mex, Proc
12	42	Female	1	Conv	1	1	Yes	Yes	Yes	None	None
13	26	Female	1	Conv	3	3	Yes	No	Yes	None	β-bloc
	31		2	3D	Multiple	0	No	Yes	Yes	β-bloc	β-bloc
14	32	Female	1	Conv	3	3	Yes	No	Yes	None	None
	33		2	Conv	2	2	Yes	No	No	None	β-bloc*
15	23		1	Conv	4	4	Yes	Yes	Yes	None	β-bloc
16	32	Male	1	3D	5	3	Yes	Yes	Yes	β-bloc, Flec	β-bloc, Flec
	33		2	3D	6	3	Yes	Yes	Yes	β-bloc, Flec	Amio
	33		3	3D	Multiple	0	No	Yes	NA†	Amio	—
17	39	Male	1	Conv	Multiple	0	No	Yes	Yes	None	None
18	31	Female	1	Conv	1	0	No	Yes	Yes	None	β-bloc
19	42	Female	1	Conv	1	1	Yes	Yes	No	Mex	Mex*
20	45	Male	1	Conv	3	0	No	Yes	Yes	Sot	Sot
21	31	Female	1	Conv	2	2	Yes	No	Yes	None	None
	34		2	Conv	3	1	Yes	Yes	Yes	Sot, β-bloc	Sot, Flec, β-bloc
22	28	Male	1	Conv	2	0	No	No	Yes	Prop	Prop
23	51	Male	1	Conv	3	2	Yes	Yes	Yes	Sot	Sot, Met
24	30	Female	1	Conv	1	1	Yes	No	Yes	None	β-bloc

*Indicates drugs at last follow-up. No recurrence was noted at last contact. †Patient died as a complication of this procedure. Follow-up was not possible.

3D = 3-dimensional electroanatomical; Abl = attempt at ablation; Amio = amiodarone; β-bloc = beta-blocker; CCB = calcium channel blocker; Conv = conventional; Coum = Coumadin; Flec = flecainide; ICD = implantable cardioverter-defibrillator; Met = metoprolol; Mex = mexiletine; Proc = procainamide; Rec = recurrence; Sot = sotalol; VT = ventricular tachycardia.

Radiofrequency energy was applied to ablate the VT in each of these procedures. In 11 (23%) of the 48 procedures, the clinical VT was inducible after ablation, whereas in the remaining 37 (77%) procedures, the clinical VT was successfully ablated and could not be re-induced with programmed electrical stimulation. All of the induced VTs were ablated in 22 (46%) of the 48 procedures. Thus, total procedural success was seen in 46%, partial procedural success in 31%, and procedural failure in 23% of the procedures.

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The only major complication in this patient series was 1 procedure-related death in a 33-year-old male patient (Patient #16, Table 3). He had undergone 2 previous attempts at RFA, which were partially successful. Each of these procedures was followed by recurrent incessant VT. At the third RFA procedure, a highly unstable VT was induced. This patient became severely hypotensive during the procedure. Because of concern for cardiac tamponade, an emergent thoracotomy was performed. No bleeding or cardiac tamponade was present. The patient was resuscitated but died of postoperative pulmonary complications. No perforation was reported in association with this or any other procedure in this group of patients.

Long-term follow-up. The follow-up duration between the first ablation procedure and the last censoring was 32 ± 36 months (range 1 day to 12 years). The time to recurrence after each ablation procedure was 8 ± 10 months (range 1 day to 44 months). The RFA procedure that resulted in death of the patient was not included in the follow-up.

During follow-up, recurrence of VT occurred after 40 (85%) of the 47 RFA procedures. Recurrence during follow-up after at least 1 of the RFA procedures occurred in all but 1 of the 24 patients. Four of these patients developed VT storms during follow-up. Of these patients, 2 were treated with pharmacotherapy with control of their VT storm and 2 underwent repeat RFA procedures. Figure 1 shows the survival analysis demonstrating cumulative VT recurrence-free survival in the entire study population. The cumulative VT recurrence-free survival after a single RFA procedure was 75% at 1.5 month, 50% at 5 months, and 25% at 14 months of follow-up. The cumulative incidence of VT recurrence after a single procedure was 64%, 75%, and 91% at the end of 1, 2, and 3 years. The incidence rate of VT recurrence was 0.88 (95% confidence interval 0.39 to 1.19) episodes per person-year.

There was no significant difference in the cumulative VT recurrence-free survival between patients who had complete procedural success, partial procedural success, and procedural failure (Fig. 2). Similarly, there was no significant difference in the cumulative VT recurrence-free survival between patients in whom a 3-dimensional electroanatomi-

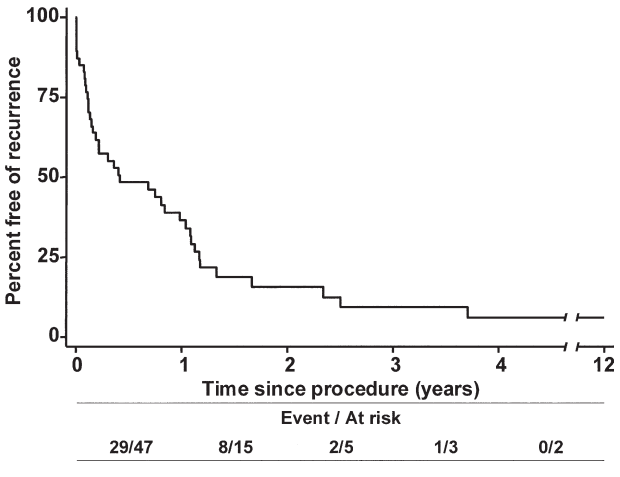

Figure 1 Survival Free of Ventricular Tachycardia Recurrence

Survival analysis showing the overall cumulative ventricular tachycardia recurrence-free survival in the entire study population. The table below the graph represents the number of events during each interval indicated on the X axis and the number of patients at risk at the beginning of that interval.

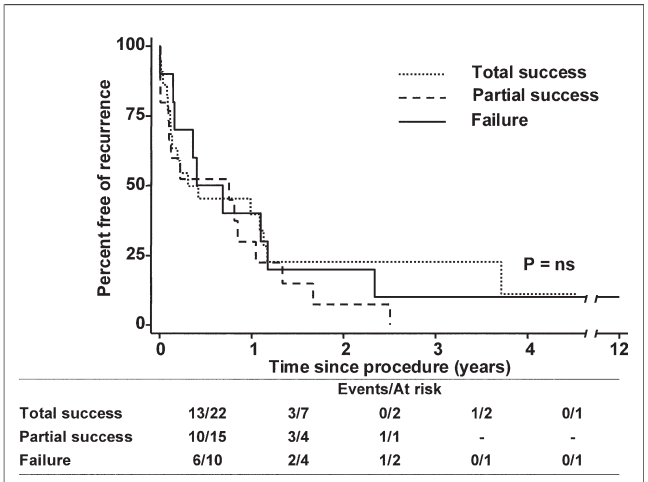

Figure 2 Survival Free of VT Recurrence by Procedural Success

Survival analysis showing the comparison in the cumulative ventricular tachycardia (VT) recurrence-free survival among patients undergoing complete procedural success, partial procedural success, and procedural failure for ablation of VT. The table below the graph represents the number of events during each interval indicated on the X axis and the number of patients at risk at the beginning of that interval.

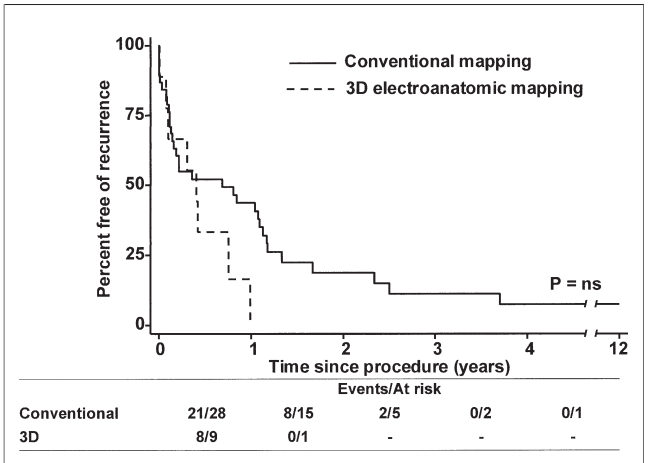

Figure 3 Survival Free of VT Recurrence by Mapping Technique

Survival analysis showing the comparison in the cumulative ventricular tachycardia (VT) recurrence-free survival between patients undergoing the ablation process using 3-dimensional (3D) electroanatomical mapping and combination of the traditional mapping techniques. The table below the graph represents the number of events during each interval indicated on the X axis and the number of patients at risk at the beginning of that interval.

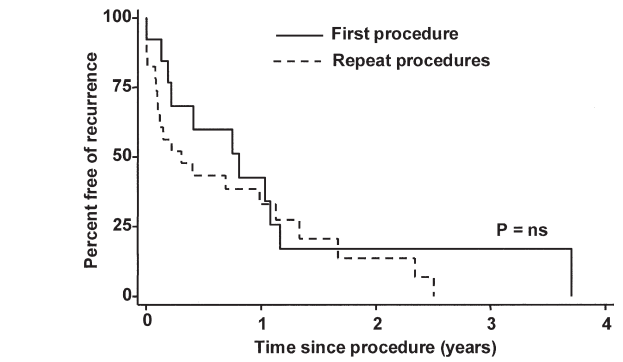

Figure 4 **Survival Free of VT Recurrence by Repetition of RFA Procedure**

Survival analysis showing the comparison in the cumulative ventricular tachycardia (VT) recurrence-free survival between patients undergoing first and subsequent catheter ablation procedures. The table below the graph represents the number of events during each interval indicated on the X axis and the number of patients at risk at the beginning of that interval. RFA = radiofrequency catheter ablation.

cal approach was used and those in whom a traditional approach was used for mapping the VT (Fig. 3). Finally, the cumulative incidence of VT after the repeat procedures did not differ significantly from that after the first procedure (Fig. 4). The incidence rate of VT after the first procedure (1.00, 95% confidence interval 0.56 to 1.82 episodes/year) also was not significantly different from the incidence rate after the subsequent procedures (1.37, 95% confidence interval 0.88 to 2.12 episodes/year) (p = NS). During follow-up, 2 patients underwent heart transplantation because of incessant VT, resulting in repeated ICD interventions.

Discussion

Main findings. Our results show that catheter ablation of VT in patients with ARVD/C is associated with a high rate of recurrence and that acute procedural success is not predictive of freedom from recurrence. Furthermore, the results are unaltered despite the extent of ablation or the performance of repeated attempts at ablation in the same patient. Recurrence rates were similar regardless of whether the initial ablation procedure was defined as total success, partial success, or failure. The use of electroanatomical mapping systems to guide ablation of hemodynamically unstable VTs with a substrate-based ablation strategy did not impact the rate of VT recurrence during follow-up.

ARVD/C. ARVD/C is a complex arrhythmogenic disorder characterized by gradual loss of myocytes and replacement by fatty and fibrous tissue. It leads to dilation of the RV and impaired cardiac function. Progression of ARVD/C is characterized by progressive structural abnormalities of the RV and subsequent signs of heart failure, and the increased frequency and/or severity of ventricular arrhythmias. Sustained ventricular arrhythmias lead to significant mortality in patients with ARVD/C (4,24).

Recent evidence suggests that typical ARVD/C is a disease of the cardiac desmosome. Desmosomes are specialized cadherin-based cell–cell adhesion structures abundant in cardiac muscle and skin epidermis (7). Mutations in 1 or more desmosomal proteins, including desmoglein-2 (25,26), desmoplakin (27–29), desmocollin-2 (30), junctional plakoglobin (31,32), and plakophilin-2 (33–36) have been identified in patients with ARVD/C. Mechanisms by which the affected desmosomes cause myocytes apoptosis, fibrogenesis, and adipogenesis, thus leading to impaired RV function and increased arrhythmogenicity, have been shown in vitro and in animal models (37). The effect of age and exercise on disease progression at the desmosomal level has also been shown in a mouse model (38). These important new developments into the mechanism of ARVD/C help explain the diffuse and progressive nature of ARVD/C. They may also help explain the limited efficacy of catheter ablation reported in this study.

Prior studies. Fontaine et al. (12,13,15) are credited with pioneering the development of catheter ablation for treatment of patients with ARVD/C. They initially used DC shock energy with an approach referred to as fulguration, and more recently have used radiofrequency energy. Their pioneering studies showed that catheter ablation of VT in patients with ARVD/C is feasible, but that repeat ablation procedures are commonly needed to achieve arrhythmia control (15).

There have been 5 prior reports of the outcome of radiofrequency catheter ablation of VT in patients with ARVD/C. In 1998, Ellison et al. (14) reported the acute and long-term outcome of catheter ablation in 5 ARVD/C patients. Of the 19 inducible VTs, 8 were rendered noninducible and 3 were modified to a longer cycle length. During a mean follow-up of 17 months, with 3 of these patients continuing antiarrhythmic therapy, none of these patients had recurrent VT. In 2003, Reithmann et al. (16) reported their experience with VT ablation using an electroanatomical mapping system in 5 patients with ARVD/C. The clinical VT was successfully ablated in 4 of these patients, with 1 patient rendered completely noninducible. During a mean follow-up of 7 ± 3 months, with amiodarone continued in 3 patients, 60% of patients were free of recurrent VT. More recently, there have been 2 studies of catheter ablation of VT in patients with ARVD/C. Both of these studies used an electroanatomical mapping system to allow substrate-based ablation strategy for hemodynamically unstable VT. Marchlinski et al. (18) described their experience with catheter ablation in 19 patients with an RV myopathy who underwent 1 (n = 6) or more (n = 13) attempts at catheter ablation. Acute success, defined as the absence of all inducible VTs, was achieved in 14 (74%) of 19 patients. During a mean follow-up of 27 ± 22 months, 17

(89%) of 19 patients were free of recurrent VT. Whether these patients met Task Force criteria for ARVD/C is unclear. However, it is notable that nearly half of these patients had possible biventricular disease with a left ventricular ejection fraction <45% in 10 (48%) of the 21 patients. It is also unclear whether antiarrhythmic medications were used in this patient population because no details on the use of antiarrhythmic drugs were included in this report. It is also notable that in this series repeat ablation procedures were required in 68% of patients, resulting in a much lower single-procedure efficacy of catheter ablation. Verma et al. (17) reported their experience with catheter ablation in 22 patients with ARVD/C, each of whom had hemodynamically unstable VT. Acute success with no inducible VT at the end of the procedure was achieved in 18 (82%) patients, with VT recurrence rates of 23%, 27%, and 47% at 1, 2, and 3 years, respectively. In this study, patients remained on their antiarrhythmic therapy after the catheter ablation procedure.

Catheter ablation results. The results of this study provide new insights into the acute and long-term efficacy of catheter ablation of VT in patients with ARVD/C. Perhaps the most striking finding is the extremely high rate of recurrent VT after catheter ablation in this patient population, with 75% of patients experiencing a recurrence within 14 months of follow-up. This high rate of recurrence of VT is distinctly different than that reported by Ellison et al. (14) and Marchlinski et al. (18), but somewhat similar to the considerable recurrence rate note in the reports by Reithmann et al. (16) and Verma et al. (17). Reithmann et al. (16) reported a 40% recurrence rate during a mean follow-up of 7 months, and Verma et al. (17) reported a recurrence rate of 47% at 3 years of follow-up.

There are a number of potential explanations for why our incidence of VT during follow-up is higher than in other reports. First, this study reflected the outcomes of a series of ARVD/C patients who underwent catheter ablation in a large number of electrophysiological laboratories throughout the country. In contrast, all prior reports of catheter ablation of VT in patients with ARVD/C have been published by referral institutions with a particular interest in catheter ablation of VT (12–18). This difference is important because the results of this study are more likely to be reflective of the outcomes that can be achieved in widespread clinical practice. Second, this study included only patients who met the strict Task Force criteria for ARVD/C. Earlier studies have generally not used the Task Force criteria for ARVD/C, which were published in 1994, as criteria for enrollment in their studies (19). Of particular note is the recent study by Marchlinski et al. (18). The patients in this series were quite atypical for patients with ARVD/C in that 10 of 21 patients had significant LV dysfunction with an ejection fraction of 45% or less. In contrast, no patient in our series had significant LV dysfunction. Third, this study reported the outcome of all VT ablation procedures. This contrasts distinctly with the report by Marchlinski et al. (18), in which 68% patients underwent a second ablation procedure. This suggests that the long-term single-procedure success rate in this series was <35%. The inclusion of repeat ablation procedures therefore clouds the true rate of recurrence of VT experienced by patients reported in this study. And finally, different ablation strategies were used in patients in this series as compared with those in prior trials. This is particularly true for the 2 most recent series by Marchlinski et al. (18) and Verma et al. (17), who have pioneered the technique of substrate ablation for treatment of unmappable VTs in patients with ARVD/C. Whereas an electroanatomical mapping system was used in only 10 of the 48 ablation procedures in this series, an electroanatomical mapping system was used for all ablation procedures in these 2 recent series. Although use of an electroanatomical approach in our series did not impact long-term efficacy, it is possible that a substrate-based ablation strategy may have higher efficacy than conventional ablation strategies.

Study limitations. Our study has several limitations. First, there might be a significant variability in the performance and the accuracy of these procedures in different centers, and results may not be reflective of any single center. However, in the absence of a prospective multicenter study, in which all treating electrophysiologists are trained to perform procedures using a standard protocol, this is the best alternative for evaluating the true success of these procedures as seen in clinical practice. Second, we did not report the frequency of VT episodes before and after each catheter ablation procedure because not all patients had ICDs implanted for a consistent period before catheter ablation of VT. In many patients, ICD implantation was performed at the time of or subsequent to the initial ablation procedure. And third, the staggered entry survival analysis may have been inadequate to discern the differences in recurrence associated with mapping techniques, procedural success, and repetition of catheter ablation procedures because observations in subgroups created by repetition of the RFA procedure were not independent.

Clinical implications and conclusions. The results of this study, combined with those of prior studies, have several obvious and immediate clinical implications. First, the very high rate of VT recurrence reported in this study and prior studies of catheter ablation of VT in ARVD/C patients makes it clear that catheter ablation of VT in ARVD/C patients cannot and should not be considered curative. Although the precise indications for ICD implantation in ARVD/C are not well established, we recommend ICD implantation for all patients who meet the strict Task Force criteria for ARVD/C (11). Second, the results of this and other studies of catheter ablation of VT in patients with ARVD/C call into question the early use of catheter ablation as an effective antiarrhythmic strategy in these patients. Although there is some anecdotal evidence to suggest that catheter ablation of VT may decrease the frequency of VT episodes and appropriate ICD shocks in this patient population, this has not been well studied. In fact, there have been no large studies that have closely examined the frequency of ICD shocks before and after catheter ablation of

VT in ARVD/C patients. Even if these data were available, the results may reflect the clustering of VT episodes. In this regard, it is notable that a recent study reported that ARVD/C patients with "VT storm" all responded to treatment with antiarrhythmic drugs (39). It is clear that further studies will be needed to determine the clinical role of catheter ablation of VT in patients with ARVD/C. Until these data are available, we would recommend that catheter ablation of VT in patients with ARVD/C only be used as a palliative procedure to reduce the frequency of VT episodes, particularly after failure of 1 or more antiarrhythmic drugs. Moreover, we would recommend that these procedures be performed at centers highly experienced with catheter ablation of ventricular arrhythmias.

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