Catheter Ablation of Ventricular Tachycardia in Patients With Structural Heart Disease Using Cooled Radiofrequency Energy

Results of a Prospective Multicenter Study

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OBJECTIVES	The purpose of this multicenter study was to evaluate the safety and efficacy of a radiofrequency (RF) catheter ablation system with internal saline irrigation.
BACKGROUND	Catheter ablation of ventricular tachycardia (VT) associated with structural heart disease is more difficult than ablation of idiopathic VT. The larger size of responsible reentrant circuits contributes to the difficulty in achieving an adequate ablation lesion with conventional techniques. Recently, cooling of the ablation electrode by saline irrigation has been shown to increase RF lesion size.
METHODS	The patient population included 146 patients who participated in the Cooled RF Ablation System clinical trial and underwent an attempt at ablation of VT occurring in the presence of structural heart disease. The duration of follow-up was 243 ± 153 days.
RESULTS	Catheter ablation was acutely successful, as defined by elimination of all mappable VTs, in 106 patients (75%). In 59 patients (41%), no VT of any type was inducible after ablation. Twelve patients (8%) experienced a major complication. After catheter ablation, 66 patients (46%) developed one or more episodes of a sustained ventricular arrhythmia.
CONCLUSIONS	The results of this study demonstrate that catheter ablation of all mappable forms of sustained VT can be performed with high initial success and a moderate incidence of major complications (8%). (J Am Coll Cardiol 2000;35:1905–14) © 2000 by the American College of Cardiology

Since the introduction of radiofrequency (RF) catheter ablation into clinical use in the early 1990s, a number of studies have evaluated its safety and effectiveness in the treatment of ventricular tachycardia (VT) occurring either in the presence or absence of structural heart disease (1–13). Catheter ablation of idiopathic VT in the absence of structural heart disease was rapidly determined to be a safe and effective procedure and has gained widespread acceptance. In contrast, the safety and efficacy of catheter ablation of VT associated with structural heart disease remainscontroversial. Previous studies have included relatively small numbers of highly selected patients, often representing the experience of a single institution. Variations in patient selection, mapping and ablation methods and definitions of success make evaluation of the risk/benefit ratio difficult. There have been no multicenter or randomized trials.

It is generally recognized that ablation of VT associated with structural heart disease is more difficult than ablation of idiopathic VT. The relatively larger size of responsible reentrant circuits, and the fact that they can be located deep to the endocardium, often contribute to difficulty in achieving an adequate ablation lesion. Recently, cooling of the ablation electrode by saline irrigation has been shown to increase RF lesion size by 30% to 50% in animal models (14,15). The purpose of this prospective multicenter study was to evaluate the safety and efficacy of a RF catheter ablation system with internal saline irrigation. The relation

Abbreviations and Acronyms	
ECG	= electrocardiogram
EF	= ejection fraction
EP	= electrophysiology
ICD	= implantable cardioverter defibrillator
RF	= radiofrequency
VT	= ventricular tachycardia

Figure 1. Schematic drawing showing the cooled RF ablation catheter. Cooling is achieved by circulating saline through the ablation electrode.

between acute procedural success, long-term success, and clinical and electrophysiology (EP) variables were also defined.

METHODS

Patient population. The patient population included 146 consecutive patients who participated in the Cooled RF Ablation System (Cardiac Pathways, Sunnyvale, California) clinical trial. The patients underwent an attempt at ablation of VT occurring in the presence of structural heart disease at 1 of 18 institutions between September 1995 and December 1997. This trial was designed to study the effectiveness of an ablation system incorporating internal saline irrigation. Patients were initially recruited for the study if they fulfilled the following criteria: 1) documented sustained monomorphic VT with two or more episodes in the two months before enrollment; 2) spontaneous VT that was hemodynamically stable; 3) VT due to ischemic heart disease; 4) an implantable cardioverter defibrillator (ICD) device with electrogram storage; and 5) failure of at least two antiarrhythmic agents. At the onset of the study, patients were randomized 1:1 between ablation and continued antiarrhythmic therapy. As the study progressed, the enrollment criteria were altered to facilitate enrollment, including elimination of randomization and the requirement for an ICD. A subgroup of patients was enrolled on a compassionate use basis. Among the 146 patients included in this report were four subgroups of patients. The first was comprised of 63 patients who were randomized to catheter ablation. The second was comprised of 17 patients who were randomized to medical therapy and underwent catheter ablation after failure of medical therapy. The third was comprised of 13 patients who received ablation under compassionate use. The final subgroup was comprised of 53 patients who were enrolled in the study after the randomization arm of the study was discontinued. During the course of the study, a total of 171 ablation procedures was performed in these patients. Twenty-five patients underwent two ablation procedures either because of failure of an initial attempt (n = 14) or after an arrhythmia recurrence (n = 11).

Patient evaluation, EP testing and catheter ablation. Before the ablation procedure, each patient gave written informed consent according to a protocol approved by the Institutional Review Board. A history and physical examination, electrocardiogram (ECG), echocardiogram and neurologic examination by a neurologist were also obtained. Each patient underwent an EP test with the intent to perform an ablation procedure using Cooled RF energy. The inducibility of VT was assessed by programmed electrical stimulation with one to three extra stimuli at two sites. Ablation was performed with an investigational 7Fr quadripolar electrode catheter with 2-5-2-mm interelectrode spacing and a deflectable 4-mm electrode tip (Cardiac Pathways Corporation Cooled RF catheter) (Fig. 1). Before the ablation catheter was positioned in the left ventricle, heparin was administered to achieve an activated clotting time >250 s.
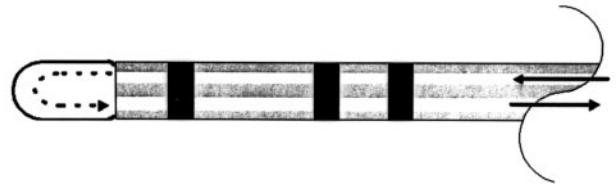
The four predefined criteria that were used to select target sites included concealed entrainment, identification of an isolated mid-diastolic potential, identification of the earliest presystolic endocardial activation during VT and pace mapping. Investigators were instructed to deliver RF energy at sites demonstrating concealed entrainment or a mid-diastolic potential whenever possible. Pace mapping was used to identify target sites only if alternative criteria were not met. When an appropriate target site was identified, up to 50 W of RF energy was delivered at 500 kHz (Cardiac Pathways Model 8002 or 8004 RF Generator and integrated Cooled Ablation Pump System; Cardiac Pathways). Saline was infused through the catheter at 0.6 ml/s before and during energy delivery. RF energy was then delivered for 60 to 180 s in the power control mode. Power output was automatically shut down if the impedance exceeded 250 Ω or if the electrode temperature exceeds 65°C. The energy output was initially set at 25 W but was generally increased incrementally during the RF application to achieve an increase in the electrode temperature from <31°C to between 40°C and 50°C.

The predetermined end point of the ablation procedures was the elimination of all VTs that were associated with sufficient hemodynamic stability to allow mapping to be performed (mappable VTs). Thirty minutes after the successful application of RF energy, programmed stimulation was repeated. Before discharge, patients underwent a repeat echocardiogram, as well as a second neurological examination. The cycle length, bundle branch block configuration and axis of each VT was recorded. Ventricular tachycardias that in the investigators judgement had occurred spontaneously were designated as a "clinical VT."

Clinical follow-up. Each patient was evaluated 1, 3, 6, 9, 12, and 24 months after ablation. According to the study protocol, patients were to be continued on the type of antiarrhythmic therapy they had received before ablation for at least the first three months after hospital discharge. The mean duration of clinical follow-up was 243 ± 153 days.

Outcomes. There were three end points of the study: acute success, long-term success and safety. Acute success was defined as absence of inducible, mappable VT at the end of the ablation procedure. This was a strict criteria; if three mappable VTs were identified and only two were ablated, the procedure was classified as a failure. Long-term success was defined as the absence of any spontaneous sustained VT during follow-up. By this definition, failures included patients with arrhythmias that had not been targeted for ablation, including polymorphic VT and unmappable rapid VT. Data on patients who experienced neither recurrence nor death were censored at the last follow-up. Safety was assessed in terms of the procedure-related adverse event rate. Complications were classified as major or minor. Major complications were defined as those that resulted in permanent injury or death, required an intervention for treatment or prolonged the duration of hospitalization. All other adverse events were classified as minor.

During the course of the trial, several studies demonstrated the efficacy of ICDs for preventing sudden death. Therapy that achieved a reduction in spontaneous episodes of arrhythmia, reducing the frequency of ICD shocks, became recognized as beneficial (9). Therefore, an additional outcome measure, clinical success, defined as a >75% reduction in spontaneous VT episodes during follow-up as compared with the two months before ablation, was also assessed.

Data analysis and statistical methods. The covariates of interest in the study fell into three broad groups. The first group of covariates was related to demographic and baseline characteristics and included patient's age and gender, study subgroup to which patient belonged, volume of procedures performed at the ablation center, cause of VT and ejection fraction (EF). The second group of covariates was related to arrhythmia history and included whether the patient had ever undergone a previous ablation, number of VT episodes in the two months before the ablation procedure, whether amiodarone therapy failed, the number of clinical VTs >300 ms, whether a clinical VT was induced, whether the patient had only one slow VT >300 ms and whether the patient was implanted with an ICD at discharge postablation. The third group of covariates was related to preablation diagnostic EP assessments and included such measures as number of inducible VTs and number of VTs with a cycle length <300 ms.

Patients for whom the catheter ablation procedure was an acute and/or long-term success were compared with those for whom the procedure was a failure, as defined above, with respect to these characteristics. All significance tests were two-sided, with alpha = 0.05 level of confidence. Significant differences in proportions of success by patient group were assessed by examining the chi-square statistics from two-by-two tables. Covariates that were significantly associated with procedure success in two-by-two tables were then examined in a logistic regression framework. An unadjusted odds ratio corresponding to each covariate was estimated first from a univariable regression. Thereafter, an adjusted odds ratio for each covariate was estimated after controlling for baseline and demographic characteristics deemed likely to confound any analysis of the association between the covariate and procedure success. The significance of the regression parameter corresponding to each covariate was assessed by both the -2-log-likelihood (-2LL) statistic, a likelihood ratio test to determine the improvement in model goodness-of-fit with the addition of the covariate to the baseline model, as well as the Wald statistic, a test to determine the significance of each regression parameter compared with its expected standard normal distribution.

Long-term success (i.e., time to VT recurrence and time to death) was also examined in a survival analysis framework. Time-to-event survival curves were graphed for different patient subgroups using the Kaplan-Meier estimation technique. Thereafter, Cox proportional hazards models were fitted to assess which factors were associated with risk of recurrence and risk of death. In a fashion similar to the logistic regression analyses above, characteristics that appeared to distinguish survivorship curves were then assessed in a proportional hazards regression framework. An unadjusted hazards ratio corresponding to each covariate was estimated first from a univariable regression. Thereafter, an adjusted hazards ratio for each covariate was estimated after controlling for baseline and demographic characteristics deemed likely to confound any analysis of the association between the covariate and long-term success. The significance of the regression parameter corresponding to each covariate was assessed by both the -2LL statistic as well as the Wald statistic.

RESULTS

Patient characteristics. The clinical characteristics and electrophysiologic features of the 146 patients included in this study are shown in Table 1. Structural heart disease was present in all patients, with ischemic heart disease present in 119 (82%). The mean left ventricular EF was 31 ± 13%. One hundred seven patients (73%) had an EF ≤ 35%. All patients in this study had failed prior antiarrhythmic therapy with 2.5 ± 1.5 drugs, including amiodarone therapy in 58 patients (40%). The number of VT episodes in the preceding two months was 25 ± 31. Fifty-eight patients (40%) had inducible rapid VTs with a cycle length shorter than 300 ms. One hundred six patients had an ICD implanted before their ablation procedure. An additional nine patients

Table 1. Patient Characteristics

Demographic	n (%)
Age (mean years, SD)	65, 12.6
30–65	67 (46%)
>65	79 (54%)
Gender (% male)	134 (92%)
Ischemic heart disease	119 (82%)
Ejection fraction (mean, SD)	31, 13
0–20	41 (28%)
21–35	66 (45%)
36+	39 (27%)
Group	
Crossover	17 (12%)
Randomized to ablation	63 (43%)
Compassionate use	15 (10%)
Nonrandomized	51 (35%)
Center (n, % patients enrolled)	
High	60 (41%)
Medium	41 (28%)
Low	45 (31%)
Arrhythmia history	
Prior ablation	32 (22%)
Failed amiodarone	58 (40%)
Number prior VT episodes	
0 to 2	27 (19%)
3 to 8	67 (46%)
10 to 99	42 (29%)
100 +	10 (7%)
Only 1 VT, CL >300 ms	33 (23%)
Clinical VT induced	126 (89)
Number of VTs CL >300	
0 to 1	55 (39%)
≥2	87 (61%)
ICD at entry	106 (71%)
ICD at discharge	115 (79%)
Number failed AA drugs (mean, SD)	2.5, 1.5
EP findings	
Induced VTs (mean, SD)	3 (2.1)
VT CL ≤300	0.7 ± 0.6
VTs >300	2.4, 1.9
Noninducible	1 (0.7%)
With 1 VT induced	37 (25%)
With 2 VTs induced	35 (25%)
With >2 VTs induced	70 (49%)

ICD = implantable cardioverter defibrillator; VT = ventricular tachycardia.

Table 2. Multivariable Model for Ablation of All VTs

Predictor	Adjusted OR	p Value
Age (65+ years)	0.69	0.34
Gender (male)	0.61	0.5
EF (<35%)	0.72	0.42
Failed amiodarone	0.44	0.03
≥2 inducible VTs, CL >300	0.46	0.04

The adjusted odds ratio represents the increase (>1.0), or decrease (<1.0) in the odds of having acute success associated with the presence of a specific variable, assuming that all other variables in the model are equal. The odds of success are defined as the probability of success/1− probability of success.

tients. The duration of the procedure was 288 ± 160 min, with 56 ± 42 min of fluoroscopy.

Based on an intention-to-treat analysis, catheter ablation was acutely successful, as defined prospectively by elimination of all mappable VTs in 106 patients (75%). Acute efficacy was not determined in three patients. In 59 patients (41%), no VT of any type, mappable or unmappable, was inducible after the ablation procedure. The results of univariable analysis revealed that the likelihood of acute success, defined as abolition of mappable VTs, was not influenced by any of the variables that we examined including age, gender, VT cause, EF, prior ablation attempt, failure of amiodarone, the number of induced VTs or the number of clinical episodes of VT. The only two variables that were associated with successful ablation of all induced VTs were prior failure of amiodarone and the number of induced VTs with a cycle length >300 ms. Ablation of all VTs was less likely in patients who had previously failed amiodarone or who had multiple (greater than two morphologies) or relatively slow (cycle length >300 ms) VTs. In multivariable analysis after controlling for age, gender and EF, the results remained essentially unchanged (Table 2). For success defined as ablation of mappable VTs, no variable or combination of variable in multivariate analysis was predictive. No difference was observed in the power of RF applications (36 ± 8 vs. 36 ± 8 W, p = 0.64), the duration of RF applications (63 ± 43 vs. 55 ± 27 s, p = 0.16) or the electrode temperature (46± 12 vs. 47 ± 12°C, p = 0.58) between patients with and without acute success. The number of delivered RF applications was greater in patients in whom catheter ablation failed (16 ± 14 vs. 12 ± 8, p < 0.01).

Complications. A procedure-related major complication occurred during or after the ablation procedure in 12 patients (8%) and a minor complication developed in 9 patients (6%). Four of the major complications led to a patient death (2.7%). The type and distribution of complications are shown in Table 3. The most significant complications were four strokes or transient ischemic attacks, four episodes of pericardial tamponade, inadvertent complete heart block in two patients, one myocardial infarction and aortic valve injury in one patient. Among the four patients

received an ICD before hospital discharge. Thus, 119 patients (79%) had an ICD implanted.

Acute success of catheter ablation. During EP testing, 3 ± 2 VT morphologies were induced, including the patients' clinical VT in 126 patients (89%). The number of RF applications was 12 ± 10. The maximum power delivered was 35 ± 9 W, with a mean duration of RF applications of 63 ± 41 s. One patient received no RF applications because an acceptable site for ablation was not identified. Two ablation sessions were required in 14 pa-

Table 3. Procedure-related Complications

Complication Type	No. of Patients	No. of Deaths
Major complications		
Stroke/TIA	4 (2.7%)	1
Complete AV block	2 (1.4%)	0
Tamponade	4 (2.7%)	1
Valve injury	1 (0.7%)	1
Myocardial infarction	1 (0.7%)	1
Femoral artery laceration	1 (0.7%)	0
No. of patients with a major complication	12 (8%)	4 (2.7%)
Other complications		
Aortic dissection (distal)	1 (0.7%)	
Defibrillation skin burn	1 (0.7%)	
Anxiety and stress	1 (0.7%)	
Peroneal nerve palsy (transient)	1 (0.7%)	
Loss of pulses in extremity (transient)	1 (0.7%)	
Pseudoaneurysm (no treatment required)	1 (0.7%)	
Transient left leg numbness	1 (0.7%)	
Slurred speech due to sedation	1 (0.7%)	
Visual blurring (transient)	1 (0.7%)	
Other AV block*	0 (0%)	
No. of patients with a minor complication	9 (6%)	

*Transient AV block, 1° or 2° AV block.
AV = arterio-ventricular.

Figure 2. Kaplan-Meier curve showing freedom from arrhythmia recurrence among patients who underwent ablation of VT.

with pericardial tamponade, only one appeared to be temporally related to delivery of RF energy. This patient had right ventricular dysplasia. Ablation at a site located on the free wall aspect of the right ventricular outflow tract was associated with pericardial tamponade, which required surgical repair because a pericardiocentesis was precluded due to an ICD patch. A "pop" was not reported in association with this RF application. Paired echocardiographic analysis revealed no change in ventricular function before and after ablation (31 ± 13 vs. 30 ± 13, $p > 0.1$).

There were four procedure-related deaths. The first patient was a 63-year-old man with ischemic heart disease. Thirty minutes after successful ablation of VT, the patient became hypotensive. Catheterization revealed a 99% occlusion of the left main coronary artery most consistent with a coronary embolus. Despite an angioplasty with initial clinical improvement, the patient's condition deteriorated, and he died of cardiogenic shock. Upon review of ACT levels, it was evident that despite receiving heparin, the ACT remained subtherapeutic. The second patient was a 72-year-old man with a severe ischemic cardiomyopathy who developed acute pericardial tamponade. A transeptal approach was used to advance the ablation catheter into the left ventricle. After delivery of three RF energy applications, the patient became hypotensive. A pericardiocentesis was performed followed by surgical repair of a perforation in the left atrial appendage. The patient initially recovered but devel-

oped pneumonia and progressive heart failure resulting in death one week later. The third patient was a 49-year-old man with an ischemic cardiomyopathy. The patient underwent a successful ablation, but suffered a cerebrovascular accident that progressed to herniation and death. The fourth procedure-related death was in a 74-year-old man with an ischemic cardiomyopathy (EF = 15%), moderate mitral regurgitation and mild aortic insufficiency. An echocardiogram obtained after two ablation procedures 48 h apart demonstrated increased aortic regurgitation. The patient subsequently underwent a previously planned coronary artery bypass graft; aortic valve replacement and mitral annuloplasty were also performed. At surgery, the aortic valve was noted to be friable with a tear attributed to catheter injury. The patient died from cardiogenic shock on the day after surgery.

Arrhythmia recurrence. Consistent with the study protocol, the majority of patients in this study were discharged on the same antiarrhythmic therapy they were receiving before ablation. Antiarrhythmic drug therapy at the time of hospital discharge consisted of amiodarone in 42% of patients, sotolol in 12% of patients and a type 1 antiarrhythmic agent in 12% of patients. Although it was recommended that patients continue on the antiarrhythmic therapy they received before catheter ablation for at least the first three months after hospital discharge, the use of antiarrhythmic therapy decreased with time. At three months of follow-up, 33% of patients were treated with amiodarone, 11% were treated with a class 1 antiarrhythmic agent and 12% were treated with sotolol. At the time of last follow-up, the use of these three types of antiarrhythmic agents had decreased to 30%, 5% and 10%, respectively.

After catheter ablation, 66 (46%) of the 146 patients developed one or more episodes of a sustained ventricular arrhythmia during 243 ± 153 days of follow-up. The median time to VT recurrence was 24 days (range 1 to 309

Table 4. Multivariate Logistic Regression Model: Recurrence and Survival

Predictor	Adjusted Odds Ratio	p Value
Long–term survival		
Age (65+ years)	0.31	0.02
Gender (male)	3.9	0.06
EF (<35)	0.41	0.16
≥2 VTs CL >300	0.23	0.02
Clinical success		
Age (65+ years)	1.02	0.96
Gender (male)	1.21	0.83
EF (<35%)	1.24	0.71
Failed Amiodarone (yes)	0.43	0.09
Clinical VT induced (yes)	4.57	0.03
No VT recurrence		
Age (65+ years)	0.41	0.02
Gender (male)	1.37	0.67
EF (<35%)	2.32	0.06
VT episodes post (3+)	0.23	0.02
ICD at discharge (yes)	0.08	0.002

CL = cycle length (ms); EF = ejection fraction; ICD = implantable cardioverter defibrillator; VT = ventricular tachycardia.

Figure 3. Kaplan-Meier curve showing freedom from arrhythmia recurrence among patients who underwent catheter ablation of VT subclassified by whether the patient was discharged with or without an ICD.
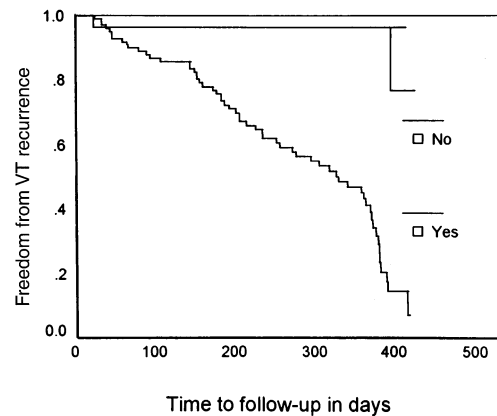
days). The one-year recurrence rate by the Kaplan-Meier method was 56% (Fig. 2). In univariable analysis, three variables were predictive of absence of recurrence of a sustained ventricular arrhythmia during follow-up: 1) age >65 years; 2) at least three episodes of VT in the two months before ablation and 3) the absence of an ICD at hospital discharge (p < 0.05). Interestingly, acute success was not predictive of clinical success. Ventricular tachycardia recurred in 44% of patients who had no inducible VT at the end of the procedure and in 46% of patients who had any VT inducible at the end of the procedure.

Table 4 shows the results of multivariate logistic regression analysis. The three variables identified as jointly predictive of freedom from VT recurrence were: 1) age, 2) at least three episodes of VT in the two months before ablation and 3) the presence of an ICD at discharge. A Cox proportional hazards multivariate regression analysis identified the number of VT episodes in the two months before ablation, and the presence of an ICD at hospital discharge to be jointly predictive of the time to arrhythmia recurrence (Table 5, Figs. 2 and 3).

A measure of clinical success (≥75% reduction in the VT frequency in the two months after ablation) was assessed among the 122 patients who were followed for at least two months. Clinical success was observed in 99 patients (81%) of patients. Only the presence of an inducible VT identified as a clinical VT was identified as a predictor of clinical success (Tables 5 and 6). A trend was also observed suggesting a greater likelihood of clinical success among those who had not previously failed treatment with amiodarone. The results of programmed stimulation at the end of the procedure (acute success or failure) were not predictive of clinical success.

Long-term survival. Twenty-six patients died either in the periprocedural period (n = 4, see above) or during follow-up. Of the 22 nonprocedure related deaths, 2 were attributed to noncardiac causes (e.g., cancer, COPD), 16 were classified as cardiac nonarrhythmic (e.g., pump failure) and 4 were presumed due to a ventricular arrhythmia. Total survival was estimated by the Kaplan-Meier method. Overall, 75% of patients were alive at one year of follow-up (Fig. 4).

When separate logistic regression models were used to assess the odds of survival during follow-up, the only two variables that were identified were younger age and the presence of fewer than two types of inducible sustained VT

Table 5. Multivariate Cox Proportional Hazards Models for Prediction of Time to Recurrence

Predictor	Adjusted Odds Ratio	p Value
Age (65+ years)	1.67	0.06
Gender (male)	1.18	0.74
Ejection fraction (>35%)	1.38	0.24
Prior VT episodes (>2)	2.37	0.05
ICD at discharge	7.14	0.001

Abbreviations are defined in Table 4 legend.

Table 6. Multivariate Cox Proportional Hazards Models for Prediction of Time to Death

Predictor	Adjusted Odds Ratio	p Value
Age (65+ years)	2.37	0.04
Gender (male)	0.44	0.14
VT cause (ischemic)	0.46	0.10
Ejection fraction (>36%)	0.35	0.06
Number of VTs CL >300	3.52	0.02

Abbreviations are defined in Table 4 legend.
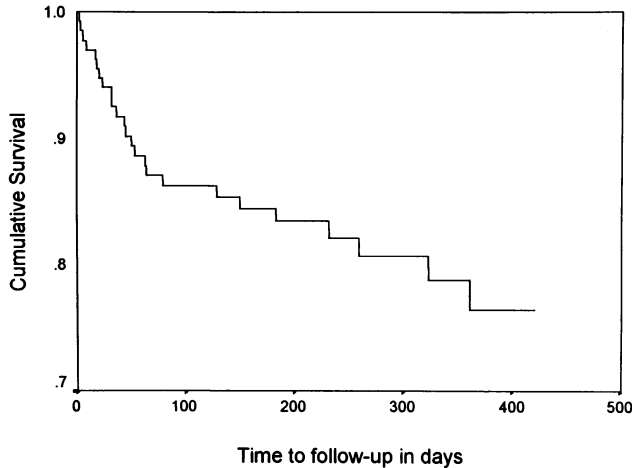
Figure 4. Kaplan-Meier curve showing patient survival after ablation of VT.

with a cycle length >300 ms before ablation. Table 4 shows the results of multivariate logistic regression analysis for prediction of survival. Patient age and the presence of less than two types of inducible sustained VT with a cycle length >300 ms before ablation were identified. Figure 4 shows a Kaplan-Meier curve showing the time to death. A Cox proportional hazards multivariate regression analysis also identified age and multiple morphologies of relatively slow sustained VT (cycle length >300 ms) as predictive of death. A trend was also shown suggesting a greater mortality among those with an EF ≤35% (Table 6).

DISCUSSION

Main findings. The present study is the first prospective multicenter trial to evaluate the safety and efficacy of catheter ablation of VT and to report the use of an internally cooled RF ablation system in humans. The results of this study demonstrate that catheter ablation of all mappable forms of sustained VT, in patients with very frequent episodes of VT and severely impaired ventricular function, can be performed with high immediate success (75%), and a moderate incidence of major complications (8%). Fifty-four percent of patients were rendered free of VT during follow-up. As appropriate for the initial evaluation of a new technology, this study enrolled only patients with arrhythmias that were refractory to antiarrhythmic therapy. The definitions of success were strict. The presence of any inducible VT that was mappable was considered a procedural failure, even if other morphologies of VT were successfully abolished. During follow-up, recurrence of any sustained VT was counted as a recurrence, even if the arrhythmia was not one that had been targeted for ablation. Thus, a patient undergoing catheter ablation of recurrent slow VT who had an ICD discharge due to polymorphic VT during follow-up was classified as having a recurrence. This definition was chosen as to eliminate any possibility of

bias on the part of the investigators given that the classification of VTs as "clinical" versus "nonclinical" are highly subjective.

Cooled RF ablation. Ventricular tachycardia associated with structural heart disease is often due to reentry through regions of myocardial scar. The relatively larger size of reentry circuits and the fact that they can be located deep to the endocardium is felt to be responsible, at least in part, for the greater difficulty and lower efficacy of catheter ablation as compared with ablation of supraventricular tachycardias and idiopathic VT (16,17). Surgical ablation of VT often requires removal or laser coagulation of 2 to >40 cm^2 of tissue (18). With conventional RF ablation, application of RF energy is limited when excessive heat transfer to the ablation electrode results in formation of an insulating coagulum on the electrode surface, preventing further energy delivery. Individual RF lesions are generally less than 1 cm in diameter. Cooling of the ablation electrode by saline irrigation has been shown to allow production of larger RF lesions in animal models, presumably by allowing greater energy delivery before coagulum formation (14,15,19). This is the first large-scale evaluation of this technology in humans.

The potential for greater lesion size is expected to increase the likelihood of successful ablation. This study did not compare cooled RF ablation with standard RF ablation; therefore, the relative efficacy remains unclear. In several recent studies of standard RF ablation, the VT recurrences during follow-up have ranged from 16% to 45% (6,8–11). These trials often selected patients for one "clinical" morphology of VT (6,11). In some studies, only recurrences of the VT that was targeted for ablation were considered arrhythmia recurrences. Rothman et al. (8) recently reported their experience with catheter ablation of VT in 35 patients with ischemic heart disease and VT that was sufficiently stable to allow adequate mapping to be performed. Catheter ablation was successful in eliminating all VTs in 11 patients and was successful in eliminating the "clinical VT" in 31 patients. Thus, based on an intention-to-treat analysis as was used in the present study, 75% of patients had their clinical VT successfully ablated and 26% of patients were rendered completely noninducible. The recurrence rate at 24 months was 34%. In a similar series of 52 patients, ablation of all inducible VTs was achieved in 40% of patients; the recurrence rate at three years was 33% (10). Differences in patient selection make comparisons difficult.

The potential for greater lesion size may also introduce the potential for increasing complications related to myocardial damage. The 8% incidence of major complications in this study is more than twofold higher than the 3% incidence of major complications reported during ablation of supraventricular arrhythmias (20). The data reported in the Multicenter European Radiofrequency Survey (MERFS) and the NASPE survey may provide a better benchmark with which to compare the complication rate

reported in this trial (21,22). Among the 320 patients who underwent catheter ablation of VT in the MERFS registry, the major complication rate was 7.5%, which is remarkably similar to the 8% complication major rate reported in the present study. However, the incidence of certain major complications was greater in the present study than was reported based on the MERFS data (cerebrovascular event, 2.7% vs. 1.3%; cardiac tamponade, 2.7% vs. 0.3%; and death, 2.7% vs. 0.3%). Scheinman (22) reported a major complication rate of 2.3% among the 844 patients undergoing VT ablation enrolled in the NASPE survey, including six instances of pericardial tamponade and three systemic emboli. These differences in complication rates most likely large differences in study design. In addition, both the MERFS registry and the NASPE survey enrolled patients who were undergoing catheter ablation of either idiopathic or nonidiopathic VT, whereas the present study enrolled only patients undergoing catheter ablation of VT in the setting of structural heart disease. Therefore, the complication rates are not directly comparable. In other recent series of VT ablation, the incidence of complications has ranged from 5% to 12% (6,8–11). During cooled RF ablation, the potential exists for achieving temperatures of 100°C deep to the endocardium. Studies in in vitro and in vivo models have shown that steam formation can cause rupture of overlying myocardial tissue either into the myocardial cavity or outward to the pericardium (14,15,19). It is reassuring, therefore, that in the present series only one patient, who had right ventricular dysplasia and was undergoing ablation of the free wall of the outflow tract, developed pericardial tamponade during an application of RF energy. It is also reassuring to note that no change in ventricular function was observed after catheter ablation. The 11% incidence of death due to heart failure during follow-up is also similar to that in other series of patients with ventricular arrhythmias and does not suggest excessive myocardial damage (10,11).

Factors affecting ablation success and recurrence. Successful ablation of VT requires both accurate mapping of the VT circuit as well as creation of a lesion of sufficient size. The primary end point of this study, which was prospectively defined as successful ablation of all forms of mappable VT, was accomplished in 75% of patients. No clinical variables were predictive of this definition of acute success, and similar acute success rates were achieved in patients with ischemic and nonischemic heart disease. The inability of any variable to predict acute success may reflect the importance of the skill of the operator, which was not included in this analysis. The absence of any difference in delivered power and electrode temperature during successful versus failed procedures likely reflects the critical importance of mapping to the overall ablation success. A secondary acute end point of this study was successful ablation of all VTs. This was accomplished less frequently, in 41% of patients, because faster VTs that are not mappable often coexist with slow VTs in these patients. The two variables, which were predictive of an inability to ablate VTs, were prior amiodarone failure and the presence of multiple relatively slow VTs (cycle length >300 ms). Forty-six percent of patients experienced a recurrence after their ablation procedure. This apparently high recurrence rate can be understood, in part, based on the fact that 40% of patients had rapid VTs induced before the ablation procedure that were hemodynamically unstable and were therefore not targeted. It is also important to note that a development of "recurrence" was defined as the development of any type of sustained VT during follow-up. Surprisingly, acute success was not predictive of arrhythmia recurrence during follow-up. Acute success was defined by programmed stimulation at the end of the ablation procedure. Over the ensuing days to weeks, there is further healing of ablation lesions, with resolution of some of the initial injury in some cases and, occasionally, expansion in others, accounting for the 8% recurrence rate after successful ablation of an accessory pathway (20). It appears that the likelihood of arrhythmia recurrence after VT ablation is higher, possibly related to resolution of some of the acute injury. This problem may be magnified when a relatively large ablation lesion is required to interrupt a reentry circuit. Although we attempted to maintain a stable antiarrhythmic regimen after ablation, changes are inevitable given the frequency of side effects of these drugs and that many patients had multiple trials of drug therapy before ablation. The two variables that were predictive of arrhythmia recurrence were the number of VT episodes before ablation and the presence of an ICD at discharge. Whereas only 10% of those patients discharged without an ICD developed a recurrence, more than 50% of those patients discharged with an ICD had a recurrent episode. Patients with a persistently inducible VT and worse ventricular function may have been more likely to receive an ICD, even if ablation of all mappable was achieved.

Survival. The one-year survival rate after catheter ablation was 75%. The two factors identified by multivariate analysis as independent predictors of increased risk of death included age over 65 years, and multiple morphologies of slow inducible sustained VT. There was also a strong trend showing a relationship between worse survival and impaired ventricular function (p = 0.06). It is not surprising that increased age and greater impairment of ventricular function predict mortality. However, the predictive value of multiple morphologies of slow VT has not previously been reported. Given that nearly 80% of patients in this series were discharged with ICDs and that 73% of deaths were related to heart failure, it seems likely that multiple VTs may be associated with a larger scar, worse ventricular function and greater risk of death from pump failure.

Comparison with prior reports. A number of studies have been published that have reported the results of catheter ablation of nonidiopathic VT. The majority of these studies have been confined to patients with isch-

emic heart disease (5–12). Rothman et al. (8) recently reported their experience with catheter ablation of VT in 35 of 42 patients with ischemic heart disease who were determined to have VT that was sufficiently stable to allow adequate mapping to be performed. Catheter ablation was successful in eliminating all VTs in 11 patients and was successful in eliminating the "clinical VT" in 31 patients. Thus, based on an intention-to-treat analysis as was used in the present study, 74% of patients had their clinical VT successfully ablated and 26% of patients were rendered completely noninducible. The recurrence rate at 24 months was 34%. The largest series of patients undergoing RF ablation of nonidiopathic VT published to date, by Gonska et al. (11), reported an acute success rate of 74% among 72 patients with one configuration of monomorphic VT in the setting of ischemic heart disease. Similar results have been reported by others in clinical series involving 21 or fewer patients (5–7). Scheinman reported a 66% success rate among the 257 patients undergoing ablation of VT in the setting of ischemic heart disease who were enrolled in the NASPE survey (22). There is considerably less experience with catheter ablation of VT in the setting of nonischemic heart disease. The only series published to data, by Kottkamp et al. (13), involved eight patients with recurrent VT in the setting of a dilated cardiomyopathy. Six of nine targeted VTs were successfully ablated and three of nine patients were rendered noninducible. During follow up, one patient died suddenly, five developed recurrent VT and two patients remained free of recurrent arrhythmias. The success rate for ablation of VT associated with cardiomyopathy in the NASPE survey was 68% (22).

It is difficult to directly compare the results of the present study with the findings of these prior reports for a number of reasons. First, this study is the first prospective multicenter trial of catheter ablation of nonidiopathic VT that has ever been performed. Second, this study involved a larger number of patients and enrolled patients with and without ischemic heart disease. Third, the definitions of acute success and long-term success have varied between trials. And finally, catheter ablation in the clinical trial was performed with an ablation system that incorporated internal cooling whereas prior studies have employed conventional RF ablation techniques. This study was not designed to compare the safety and efficacy of catheter ablation of nonidiopathic VT using cooled RF energy versus conventional RF ablation techniques. Because of these significant differences in study design, it is impossible to directly compare the results of this trial with prior reports. Nonetheless, it is notable that the acute success rate reported in this trial is not significantly different from prior reports and that the recurrence and complication rates are somewhat greater. Although we feel that these differences reflect the prospective multicenter design of this trial and the prospectively defined definitions of acute and long-term success used in this trial, it is possible that these findings reflect the absence of an intrinsic advantage of cooled RF ablation as compared with conventional RF ablation techniques. Hopefully, future trials will be performed to directly compare these two energy sources.

Study limitations. There are several limitations that should be considered when interpreting the results of this study. This study was a prospective multicenter clinical trial that evaluated the safety and efficacy of catheter ablation of nonidiopathic VT using the Cooled RF Ablation system. However, it should be recognized that the number of patients enrolled at participating institutions ranged from 3 to 32. Therefore, it is possible that the relatively low efficacy and high incidence of complications may in part be attributable to an unequal distribution of mapping/ablation skills at participating centers. Although additional important information could have been learned if patients were randomized to undergo catheter ablation of VT with either the Cooled RF Ablation System or standard RF ablation, this study design was not used. A second limitation of this study was that the type of structural heart disease present in study patients was classified by the investigator as to whether they did or did not have ischemic heart disease. The types of nonischemic cardiomyopathies were not broken down further. Although this represents a limitation of this article, the great majority of patients in this study had ischemic heart disease (82%). It is unlikely that the major findings of this study would have been significantly altered by a further subclassification of the 18% of patients with nonischemic heart disease according to the types of nonischemic cardiomyopathy that were present.

Clinical implications. Management of VT associated with structural heart disease is often difficult. Recurrences are frequent despite antiarrhythmic therapy. Implantable cardioverter defibrillators offer excellent protection from sudden death, but do not prevent episodes of arrhythmia. Management of frequent VT recurrences has become an important problem in caring for patients with ICDs. This study further defines the efficacy and risks of catheter ablation for patients with recurrent episodes of VT. Prevention of further spontaneous episodes of VT was achieved in 54% of patients. This efficacy must be balanced against the risk of procedure complications including stroke (2.7%) and death (2.7%).

APPENDIX: COOLED RF INVESTIGATORS AND INSTITUTIONS

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