Catheter Ablation for the Treatment of Electrical Storm in Patients With Implantable Cardioverter-Defibrillators

Short- and Long-Term Outcomes in a Prospective Single-Center Study

Corrado Carbucicchio, MD; Matteo Santamaria, MD; Nicola Trevisi, MD; Giuseppe Maccabelli, MD; Francesco Giraldi, MD; Gaetano Fassini, MD; Stefania Riva, MD; Massimo Moltrasio, MD; Manuela Cireddu, MD; Fabrizio Veglia, PhD; Paolo Della Bella, MD

Background—Electrical storm (ES) caused by recurrent episodes of ventricular tachycardia (VT) can cause sudden death in patients with implantable cardioverter-defibrillators and adversely affects prognosis in survivors. Catheter ablation has been proposed for treating ES, but its long-term effect in a large population has never been verified.

Methods and Results—Ninety-five consecutive patients with coronary artery disease (72 patients), idiopathic dilated cardiomyopathy (10 patients), and arrhythmogenic right ventricular dysplasia/cardiomyopathy (13 patients) undergoing catheter ablation for drug-refractory ES were prospectively evaluated. Short-term efficacy was defined by a complete protocol of programmed electric stimulation and by in-hospital outcome; long-term analysis addressed ES recurrence, cardiac mortality, and VT recurrence. Pleomorphic/nontolerated VTs required electroanatomic and noncontact mapping in 48 and 22 patients, respectively, and percutaneous cardiopulmonary support in 10 patients. An epicardial approach was used in 10 patients. After 1 to 3 procedures, induction of any clinical VT(s) by programmed electrical stimulation was prevented in 85 patients (89%). ES was acutely suppressed in all patients; a minimum period of 7 days with stable rhythm was required before hospital discharge. At a median follow-up of 22 months (range, 1 to 43 months), 87 patients (92%) were free of ES and 63 patients (66%) were free of VT recurrence. Eight of 10 patients with persistent inducibility of clinical VT(s) had ES recurrence; 4 of them died suddenly despite appropriate implantable cardioverter-defibrillator intervention. All together, 11 of 95 patients (12%) died of cardiac-related reasons. In the group of patients presenting with all clinical VTs acutely abolished, no ES recurrence was documented, and cardiac mortality was significantly lower compared with the group of patients showing ≥1 clinical VT still inducible after catheter ablation.

Conclusions—Advanced strategies of catheter ablation applied to a large population of patients are effective in the short-term treatment of ES. By preventing ES recurrence, catheter ablation may play a protective role over the long term and, together with long-term pharmacological therapy, may favorably affect cardiac mortality. **(*Circulation*. 2008;117: 462-469.)**

Key Words: catheter ablation ■ electrical storm ■ cardioverter-defibrillator, implantable ■ tachycardia

The implantable cardioverter-defibrillator (ICD) significantly enhances survival in patients with malignant ventricular tachyarrhythmias, but the recurrence of ventricular tachycardia (VT)/ventricular fibrillation can still be a cause of death.[1–3] More specifically, electrical storm (ES), characterized by very frequent arrhythmic episodes resulting in appropriate ICD shocks,[4] is a frightening event associated with poor short- and long-term prognoses.[5–14] Although radiofrequency catheter ablation (CA) has an established role in the treatment of recurrent VT,[4,15] its value in patients with ES has been investigated only in selected series as a bailout therapy.[16–18]

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In the present study, we prospectively assessed the short-term efficacy of CA when applied extensively in a series of consecutive patients referred for drug-refractory ES. Furthermore, we analyzed the impact of CA outcome on

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From the Arrhythmia Department, Institute of Cardiology, University of Milan, IRCCS–Centro Cardiologico Monzino, Milan, Italy.

Correspondence to Corrado Carbucicchio, Arrhythmia Department, Institute of Cardiology, University of Milan, IRCCS–Centro Cardiologico Monzino, Via Parea, 4, 20138–Milan, Italy. E-mail corrado.carbucicchio@ccfm.it

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Table 1. Baseline Clinical and Demographic Characteristics of the Study Population

Age (mean±SD), y	64±13
Gender, M/F	85/10
LV ejection fraction (mean±SD), %	36±11
NYHA class (mean±SD)	2.9±1.1
Underlying heart disease, %	
CAD	72 (76)
IDCM	10 (11)
ARVD	13 (14)
Medications, %	
Amiodarone	89 (94)
β-Blockers	92 (97)
ACE inhibitors or ARBs	81 (85)
Sotalol	5 (5)
Class I antiarrhythmic drugs	6 (6)
VT episodes per patient per day (mean±SD), n	16±8
ICD shocks per patient per day (mean±SD), n	14±8
Time from implant to ES (mean±SD), mo	14±8
Spontaneous VT cycle (mean±SD), ms	381±62
Spontaneous VT pleomorphism, %	36 (38)

ACE indicates angiotensin-converting enzyme; ARBs, angiotensin receptor blockers. n=95.

long-term arrhythmia recurrence and on patient survival to support its earlier and wider use in the treatment of ES.

Methods

Patient Population

Ninety-five consecutive patients (85 men; mean age, 64±13 years) undergoing CA for ES at our institution between January 2003 and December 2005 were enrolled in the study (Table 1). ES was defined as the occurrence of ≥3 episodes of VT separated by >5 minutes during a 24-hour period, each resulting in an appropriate shock by the ICD.[4] Patients were selected from the 305 patients with structural heart disease undergoing CA for any type of VT during the same period; 65 patients (68%) were referred from other institutions. Seventy-two patients (76%) had coronary artery disease (CAD), 10 (10%) had idiopathic dilated cardiomyopathy (IDCM), and 13 (14%) had arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C). Patients had ES despite chronic antiarrhythmic drug treatment, including amiodarone since ≥5 months (89 patients, 94%) (350±120 mg/d during a 11±5-month period) and β-blockers (92 patients, 97%) at maximal tolerated doses. Patients with acute ischemia, drug intoxication, and electrolyte imbalance were excluded. Coronary angiography was performed in 60 of 95 patients (63%) in whom myocardial ischemia was suspected. In all cases, coronary revascularization was excluded on the basis of the absence of stenosis >50% in any coronary vessel tributary of viable myocardium identified by nuclear imaging techniques.

Patients were monitored continuously by a 12-lead ECG system so that all presenting VT episodes were recorded and the corresponding ECG morphologies were defined as clinical. Spontaneous VT pleomorphism, defined by the presence of ECGs recorded at different times showing different VT bundle-branch-block patterns in V_1 or a QRS axis on the frontal plane differing by ≥45°,[19] was documented in 36 of 95 patients (38%). Seventeen patients (18%) had already undergone previous CA (16±6 months before) for VT episodes but not for ES. Mean number of VT episodes per day per patient was 16±8 and mean number of ICD shocks was 14±8 per day per patient over a mean 3.9±3.6-day period.

As a result of recurrent VTs causing >20 shocks per day, 50 patients (group 1) developed cardiogenic shock defined by prolonged phases (>3 hours) of severe hypotension (≤70 mm Hg) persisting beyond the temporary resumption of regular rhythm despite continuous infusion of pressor agents. They required prompt admission to the intensive care unit and underwent CA within 24 hours because of their life-threatening status. The clinical characteristics and short- and long-term outcome of group 1 were compared with those of the remaining study population (45 patients, group 2).

Table 2. Electrophysiological and Procedural Characteristics of the Study Population

Induced VT cycle (mean±SD), ms	365±77
Pleomorphic VT induced, n (%)	66 (69)
Nontolerated VT induced, n (%)	67 (71)
Median VTs induced per patient (range), n	2 (1–5)
CA acute result, n (%)	
Complete success (class A)	68 (72)
Partial success (class B)	17 (18)
Failure (class C)	10 (11)
Combined endocardial/epicardial CA, n (%)	10 (11)
Nonconventional mapping system, n (%)	65 (68)
Noncontact mapping	17 (23)
Electroanatomic mapping	43 (45)
Noncontact mapping+electroanatomic mapping	5 (5)
Cardiopulmonary support, n (%)	10 (11)
Fluoroscopy time (mean±SD), min	52±17
Total procedure time (mean±SD), min	260±70

n=95.

Mapping and Ablation Strategy

Written informed consent was obtained from all patients. The procedure was performed under deep sedation with direct arterial blood pressure and O_2 saturation monitoring. Quadripolar catheters were placed in the right atrium and at the right ventricular apex. Mapping and ablation were performed by an irrigated-tip catheter (Navistar or Celsius Thermocool, Biosense Webster, Inc, Diamond Bar, Calif; Sprinklr, Medtronic Inc, Minneapolis, Minn) introduced into the right ventricle (RV) or left ventricle (LV) by a venous or a retrograde-transaortic/transseptal approach, respectively. RV mapping was performed in 17; LV mapping was performed in 85 patients; and 7 patients underwent combined RV/LV mapping and ablation. Data were recorded on a multichannel electrophysiological system (Cardiolab IT, GE Healthcare Inc, Milwaukee, Wis). Intravenous antiarrhythmic therapy was withheld before CA. If VT was not ongoing, a programmed stimulation protocol from multiple RV/LV sites at the 600-, 500-, and 400-ms drive cycle with up to 3 extrastimuli was applied to induce VT(s).

Ablation lesions were obtained by the delivery of radiofrequency current (EP Technologies Inc, San Jose, Calif) between the distal electrode of the mapping catheter and a cutaneous adhesive electrode. At each ablation point, power started at 30 W with progressive titration up to 40 W based on temperature values not exceeding 43°C with an irrigation rate of 20 to 30 mL/min. Power output was decreased if any impedance drop of >10 Ω was observed. Sequential point lesions were created by pulses lasting 90 to 180 seconds each; loss of capture (10 mA at 2 ms) and electrogram abatement were preliminarily considered the expression of a local lesion. The mapping and ablation strategy was defined by the operators on the basis of their personal evaluation of the characteristics of each patient; in 65 patients (68%), nonconventional mapping methods were used to treat multiple and/or nontolerated VTs (Table 2). The target for ablation of monomorphic tolerated VTs was identified during activation mapping by isolated diastolic electrograms and confirmed by entrainment with concealed fusion.

The electroanatomic mapping system (CARTO, Biosense Webster, Inc)[20] was used to guide mapping in 48 patients. In 40 patients

with post–myocardial infarction VT, the infarct area was defined during sinus rhythm by electrograms with an amplitude ≤1.5 mV; dense scars were defined by electrograms with an amplitude ≤0.5 mV. Once the map was completed, amplitude scale was adjusted (0.2 to 0.5 mV), setting the value for scar at ≤0.2 mV to identify conducting channels within the scar area. They were defined as corridors of continuous electrograms differentiated from the surrounding scar tissue by a higher amplitude, bounded by 2 scar areas or 1 scar area and the mitral annulus and connected to normal myocardium by at least 2 sites.[21,22] Conducting channels were identified in 22 of 40 patients (55%). Their involvement in the reentry circuit was validated by entrainment mapping in 12 patients, whereas in 10 patients with unstable VTs, pace mapping maneuvers were applied. In these patients, pace mapping could support only the involvement of the conducting channel on the basis of the long "stimulus-to-QRS" interval and on the 12-lead ECG match. In addition, activation mapping and entrainment maneuvers or pace mapping only, depending on VT tolerance, was used to define the location of any isthmus of slow conduction. Sequential lesions were created to transect any isthmus and to connect the lowest-amplitude signals areas to healthy endocardium across the borders of abnormal endocardium; otherwise, the infarct area was completely encircled.[21–25] When a conducting channel was identified, the lesion was first placed to transect the conducting channel because it was considered the most appropriate target for ablation. A similar mapping and ablation strategy was used in 6 patients with IDCM. In these patients, linear ablation was guided by electroanatomic mapping, and any isthmus of slow conduction that could be validated by activation and entrainment mapping was targeted by radiofrequency application. Conducting channels within an area of scar were validated and transected on the electroanatomic map in 3 patients. Two patients affected by ARVD/C underwent electroanatomic mapping. In these patients, multiple linear lesions were created to connect scar areas located in the proximal RV outflow tract and in the lateral peritricuspid region to a valve continuity supported by pace mapping maneuvers. In both patients, additional lesions were placed to encircle multiple areas of abnormal endocardium in the inferolateral free wall on the basis of anatomic criteria.

In 10 patients (6 IDCM, 4 CAD) with persistent inducibility and early recurrence of clinical VT(s) supported by the endocardial mapping data, electroanatomic epicardial mapping[26] was performed during a subsequent procedure and revealed the presence of extensive areas with low-amplitude (<1.5-mV), fragmented electrograms occurring late after QRS during sinus rhythm. As for the endocardial mapping procedure, once scar and near-scar areas were defined, the isthmus of slow conduction was identified by activation and entrainment techniques in the case of tolerated VT. In the case of nontolerated epicardial VTs (4 patients), ablation was performed on the basis of the electroanatomic mapping supported by pace mapping to determine the site of origin of the VT and to minimize radiofrequency delivery. Coronary angiography was performed to avoid radiofrequency current delivery at sites ≤5 mm from an epicardial vessel, and pacing at the ablation sites was undertaken to check for left phrenic nerve stimulation.

According to the operator's preference, CA was guided by noncontact mapping (ESI 3000, St Jude Medical, St Paul, Minn)[27] in 13 patients with ARVD/C and in 9 patients with CAD. This was placed in the RV outflow tract (n=10), near the RV apex (n=3), or as close as possible to the LV apex (n=9). After reconstruction of the cardiac chamber, areas of low-amplitude potentials were searched during sinus rhythm. Offline analysis of a single VT cycle was obtained to identify the exit point and the diastolic pathway guided by the unipolar virtual electrograms and by the color-coded isopotential map. A linear ablation was drawn across the diastolic pathway. If only the exit point was localized, it was encircled by a linear lesion. The area treated by ablation was 2.5 to 3.0 cm^2 on the 3-dimensional map.[28]

Cardiopulmonary support[29,30] was used in 10 patients in group 1 because of the inability to maintain even short periods of regular rhythm. Arterial (15F) and venous (17F) cannulas were positioned at the distal abdominal aorta and at the right atrial-inferior vena cava junction, respectively, and connected to a centrifugal nonocclusive pump (Bio-Medicus Perfusion System, Medtronic Minneapolis, Minn) in series with a membrane oxygenator and a heat exchanger able to achieve blood flow rates up to 5 L/min. After the induction of any sustained nontolerated VT, cardiopulmonary support was activated to provide an average arterial pressure of ≥70 mm Hg. Conventional activation mapping of each VT was performed to identify the ablation site. The overall duration of the cardiopulmonary support never exceeded 180 minutes.

Systemic anticoagulation was achieved by intravenous heparin in left-sided procedures with a target activation clotting time of 250 to 300 seconds. In the case of noncontact mapping, activation clotting time was maintained between 300 and 350 seconds as recommended.

After CA, a complete stimulation protocol at the 600-, 500-, and 400-ms drive cycle through triple extrastimuli from multiple RV/LV sites was effected in all patients, including those presenting with incessant VT. Any induced nonclinical VT was the target for further ablation, and the entire stimulation protocol was repeated subsequently. The end point was the noninducibility of any sustained VT.

Programmed stimulation was used to assess the acute result of CA, defined by the inducibility of clinical and nonclinical VTs. Nonclinical VTs were defined as those VTs presenting different morphology from any spontaneous episode documented by continuous 12-lead ECG monitoring or from any previous episode occurring within the ES presentation. Different morphologies were identified by the criteria used to define pleomorphism.[19] Prevention of inducibility of any VT was defined as complete success (class A); ablation of the clinical VT(s) with persistent inducibility of ≥1 nonclinical sustained VTs was defined as partial success (class B). The inability to prevent reinduction of ≥1 clinical VT(s) was considered a failure (class C). Because of early in-hospital VT recurrence, CA was repeated in 18 patients (19%). The acute success rate of CA is reported for each session. Long-term results refer to the period after the last procedure.

Follow-Up

After CA, patients were monitored in hospital for at least 7 days. At discharge, amiodarone (89 patients), sotalol (5 patients), and class 1 antiarrhythmic drugs (6 patients) were maintained as before ES presentation. Oral anticoagulation treatment was continued for at least 6 to 8 weeks in all patients undergoing left CA. Follow-up was obtained in the ICD outpatient clinic every 2 months or whenever an arrhythmic event was suspected.

Study End Points

The primary end point was ES recurrence. Secondary end points were cardiac death (CD), sudden cardiac death (SCD; defined as death resulting from malignant ventricular arrhythmias occurring within 1 hour of the onset of symptoms), and VT recurrence.

Statistical Analysis

Descriptive statistics are reported as mean and SD (or median and range for skewed distributions) for continuous variables and as absolute frequencies and percentages for categorical variables. Between-group comparisons were performed with the unpaired Student t test, the Mann-Whitney U test, the χ^2 test, or Fisher's exact test as appropriate, and the Bonferroni stepdown (Holm) correction for multiple comparison was subsequently applied. The univariate effect of predictor variables (age, gender, ejection fraction, New York Heart Association [NYHA] class, underlying heart disease, induction of nontolerated VT, and induction of pleomorphic VT) on the incidence of the end points was analyzed by Kaplan-Meier event-free survival estimates. Differences between strata were assessed by log-rank test. Multivariate analysis, adjusted for the relevant confounders (age, gender, ejection fraction, NYHA class, underlying heart disease, induction of nontolerated VT, induction of pleomorphic VT, and acute CA results when appropriate), was performed by Cox proportional-hazards model, with hazard ratios (HRs) and 95% CIs reported. When the HRs could not be estimated, we adjusted by Kaplan-Meier analysis, stratifying for each confounder. All

Table 3. Long-Term Outcome According to Acute Results of CA

	ES Recurrence	VT Recurrence	SCD	CD
Complete success (class A) (n=68), n (%)	0/68	11/68 (16)	0/68	6/68 (9)
Partial success (class B) (n=17), n (%)	0/17	11/17 (65)	0/17	1/17 (6)
Failure (class C) (n=10), n (%)	8/10 (80)	10/10 (100)	4/10 (40)	4/10 (40)

tests were 2 sided, and a value of $P<0.05$ was considered statistically significant. Statistical analysis was performed with SAS statistical package version 8.02 (SAS Institute, Cary, NC).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Short-Term Results of Catheter Ablation

After the first procedure, 62 patients had a class A result; 19 and 14 had class B and C results, respectively (Table 2). Because of the recurrence of in-hospital VT episodes, 12 patients (in either class B or C) underwent a second procedure, leading to 68 class A, 15 class B, and 12 class C results. The third session was performed in 6 class C patients, achieving clinical VT suppression in 2. Complete success (class A) was obtained in 68 (72%), partial success (class B) in 17 (18%), and failure (class C) in 10 patients (11%). In the class C group, ≥1 clinical VTs could be terminated, but ≥1 of them remained inducible at programmed electric stimulation. At multivariate analysis adjusted for the relevant confounders, IDCM was the only independent predictor of acute failure of the procedure (odds ratio, 7.42; 95% CI, 1.8 to 29.9; $P=0.005$, class C versus A or B). After CA treatment, ES was suppressed in all patients, as proved by the presence of stable rhythm during the minimum period of 7 days of in-hospital monitoring.

Long-Term Outcome of CA

At a median follow-up of 22 months (range, 1 to 43 months; mean, 22±13 months), 15 of 95 patients (16%) died, 11 as a result of cardiac causes (12%): 4 of SCD and 7 of refractory heart failure (Table 3). The recurrence of intractable ES was the cause of SCD in the 4 patients resulting from electromechanical dissociation and presented within 3 months from CA. Altogether, ES recurred in 8 patients (8%) at 5±7 months (median, 2.5 months; range, 1 to 20 months), with ES recurring in 6 patients within 3 months. Survivors underwent heart transplantation (2 patients) or LV aneurysmectomy (2 patients) at the time of ES recurrence. The estimated cumulative ES-free survival was 94% (95% CI, 89 to 99), 92% (95% CI, 86 to 98), and 90% (95% CI, 84 to 96) at the 3-, 22-, and 43-month follow-up, respectively. Kaplan-Meier event-free survival estimates are shown in Figure 1.

Paroxysmal VT recurred in 32 patients (34%). Overall, 87 patients (92%) remained free of ES, and 63 (66%) remained free of any VT. In patients receiving amiodarone, at the end of the follow-up, the mean daily dose per patient decreased from 350 to 225 mg/d. Amiodarone was withdrawn in 10 patients because of serious side effects, whereas it was continued at maximal tolerated doses in 18 patients with VT recurrences. Sotalol and class 1 antiarrhythmic drugs were maintained as at discharge.

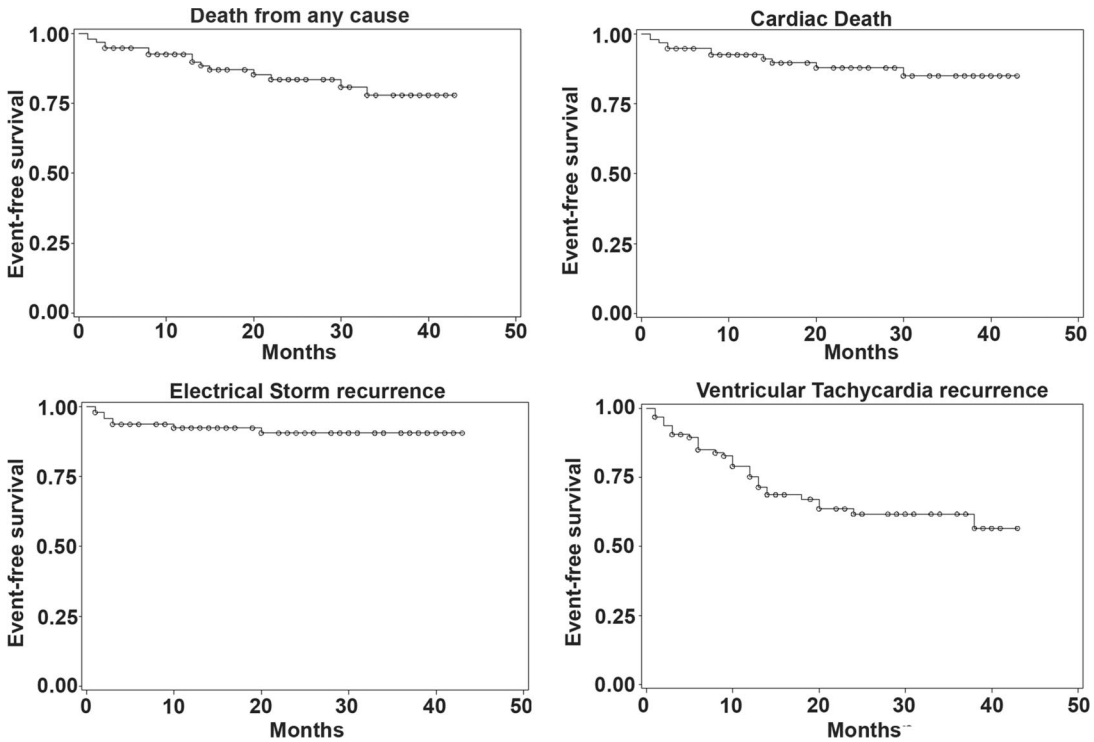

Figure 1. Kaplan-Meier event-free survival estimates in patient population during follow up.

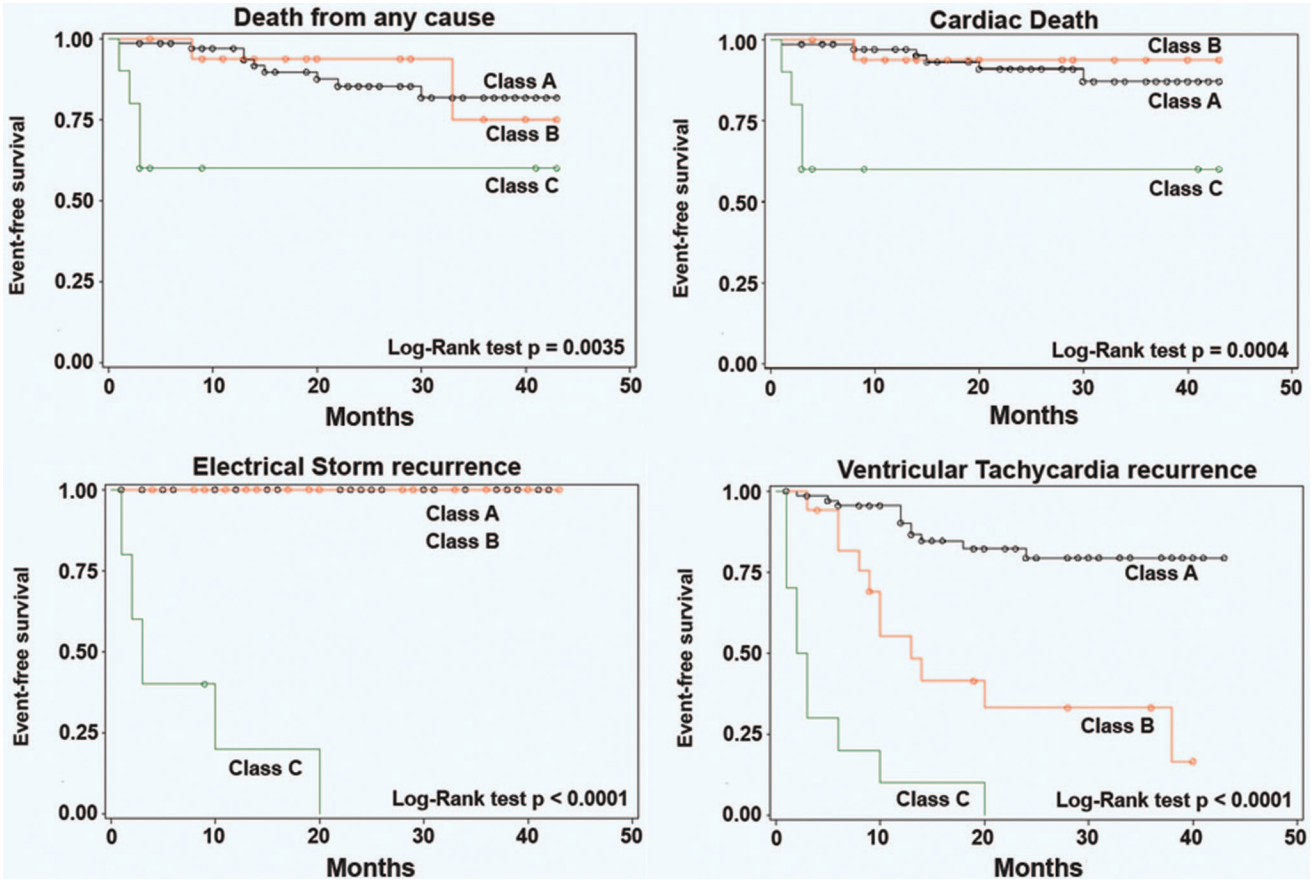

Figure 2. Kaplan-Meier event-free survival estimates according to acute CA results during follow up. Class A indicates CA success; class B, CA partial success; and class C, CA failure.

Predictors of Long-Term Outcome After Catheter Ablation

Class C result was strongly associated with ES recurrence ($P<0.0001$) and SCD ($P<0.0001$) on univariate analysis. The incidence of both CD and SCD was significantly higher in patients with ES recurrence (50% versus 8%, respectively, $P=0.02$; and 50% versus 0%, respectively, $P<0.0001$). The Cox multivariate model was not applicable for ES and SCD because both types of events occurred only in class C. Stratification analysis showed that a confounding effect by IDCM or ejection fraction <30% was unlikely. ES recurrence and SCD also were associated with IDCM (75% versus 8%; $P=0.018$), whereas all other variables showed no significant association.

Kaplan-Meier event-free survival estimates according to acute results of CA are shown in Figure 2. In the multivariate Cox regression model, CD was significantly and independently predicted by class C result (HR, 15.23; 95% CI, 2.0 to 112.8; $P=0.008$ versus class A or B:), IDCM (HR, 13.69; 95% CI, 2.4 to 75.6; $P=0.003$ versus non-IDCM), and age (HR, 1.15; 95% CI, 1.0 to 1.2; $P=0.004$ for each 1-year increase) (Table 4). No significant difference was found between class A and B ($P=0.66$). VT recurrence was predicted by class C (HR, 42.4; 95% CI, 13.4 to 134.0; $P<0.0001$ versus class A) and class B (HR, 6.8; 95% CI, 2.6 to 17.7; $P<0.0001$ versus class A) results, IDCM (HR, 5.8; 95% CI, 2.0 to 17.1; $P=0.0013$ versus non-IDCM), and ejection fraction (HR, 1.5; 95% CI, 1.0 to 2.4; $P=0.041$ for 10% unit increment). There was no significant difference between ARVD/C and CAD patients.

Group 1 Versus Group 2: CA Short- and Long-Term Outcome

In group 1 patients, CA was performed for intractable ES causing cardiogenic shock (Table 5). At multivariate analysis, the only independent factor significantly associated with group 1 was NYHA class (odds ratio, 35.1; 95% CI, 7.7 to 159 for 1-unit increment). Despite the use of cardiopulmonary support in 10 patients (20%) and nonconventional mapping in 48 (96%), group 1 had a higher percentage of class C result compared with group 2 (16% versus 4%); moreover, all group 1 patients presented with subsequent ES recurrence after a failed procedure. In Bonferroni stepdown

Table 4. Multivariate Cox Regression Model for Cardiac Mortality

Variables	*P*	HR	95% CI
Gender (male vs female)	0.124	7.28	0.58–91.14
Age (for each 1-y increase)	0.004	1.15	1.04–1.25
IDCM vs non-IDCM	0.003	13.69	2.47–75.64
LV ejection fraction (for 10% unit increment)	0.05	0.40	0.15–0.99
NYHA class (for 1-step increment)	0.77	0.86	0.31–2.37
Nontolerated vs tolerated VT	0.11	6.75	0.66–69.60
Pleomorphic vs monomorphic VT	0.58	0.55	0.06–4.64
Acute failure of CA (class C vs A or B)	0.008	15.23	2.05–112.83

Table 5. Group 1 Versus Group 2

Variables	Group 1 (n=50)	Group 2 (n=45)	*P*	Holm-Adjusted *P*
Follow-up, median (range), mo	22 (1–43)	20 (4–43)	0.59	0.741
Age (mean±SD), y	65±12	61±14	0.283	0.741
Gender, M/F	44/6	41/4	0.74	0.741
CAD, n (%)	40 (80)	32 (71)		
IDCM, n (%)	7 (14)	3 (7)	0.039	0.312
ARVD/C, n (%)	3 (6)	10 (22)		
LV ejection fraction (mean±SD), %	31±10	38±11	0.043	0.312
NYHA class (mean±SD)	3.7±0.3	2.0±0.8	0.0001	0.0012
Nonconventional mapping, n (%)	48 (96)	17 (38)	0.0001	0.0012
Cardiopulmonary support, n (%)	10 (20)	0 (0)	0.001	0.01
CA acute results, n (%)				
Class A	32 (64)	36 (80)		
Class B	10 (20)	7 (15)	0.127	0.714
Class C	8 (16)	2 (4)		
VT recurrence, n (%)	19 (38)	13 (29)	0.247	0.82
ES recurrence, n (%)	8 (16)	0 (0)	0.005	0.045
SCD, n (%)	4 (8)	0 (0)	0.119	0.714

analysis corrected for multiple comparison, group 1 ES recurrence rate was significantly higher compared with group 2 ($P=0.045$).

Procedural Complications

There were no procedure-related deaths. Periprocedural complications were transient ischemic attack (n=2), femoral artery false aneurysm (n=2), and moderate pericardial effusion (n=4) not requiring drainage because of the absence of any sign of ventricular filling impairment.

Discussion

This study examines the largest consecutive series of ICD patients undergoing CA for drug-refractory ES related to a variety of cardiac disease. The data show that CA is acutely an effective treatment of ES in most patients in whom the complete suppression of all clinical VTs was achieved. The protective role of CA over the long term is suggested by the evidence of a complete prevention of ES recurrence in this part of our population, which may have contributed to improved survival.

Nature and Size of the Problem

The incidence of ES ranges from 10% to 40% in secondary prevention and averages 3.5% among primary prevention patients.[5–14] No data are reported on the short-term mortality rate related to this event in ICD recipients. Over the long term, scientific evidence from large population studies indicates that CD is significantly affected in patients surviving ES.[8–10] Moreover, ES has been recognized as an important predictor of subsequent CD independently of ejection fraction and other main prognostic variables.[2,8–11] This indicates that the occurrence of ES directly affects patient prognosis and leads to the hypothesize that CA, by preventing ES recurrence, may exert a beneficial role in the prevention of CD. Isolated episodes of VT have been considered devoid of predictive value.[8,9,11]

Feasibility of CA Targeting ES

Successful treatment of ES in the setting of acute myocardial ischemia was reported by Bänsch et al[16] in 4 patients with repetitive polymorphic VT in whom CA acted as a focal treatment targeting monomorphic premature beats triggering ES. A single catheter-based ablation procedure enabled Silva et al[17] to effectively treat 12 of 15 patients with ES caused by recurrent hemodynamically tolerated VT(s) and various cardiac diseases. A substrate modification strategy using electroanatomic mapping was successfully reported by Schreieck et al[18] as a bailout therapy in 4 patients with intractable unmappable postischemic VT. Our study extends the notion of short- and long-term efficacy of CA to a large cohort of patients with various underlying cardiac diseases, thus reproducing a good sample of the overall population suffering from ES.

Clinical Outcome Based on Procedure Results

All patients had a favorable short-term clinical outcome once the treatment with CA was completed, with no ES recurrence during the immediate postprocedural period to hospital discharge. Solid electrophysiological evidence of the effective treatment of the presenting VT(s) was achieved in 85 of 95 patients (89%; class A and B); a transient effect of CA causing short-term stabilization also was observed in the remaining 10 patients in whom, however, ≥1 clinical VTs were still inducible (class C). In this group, CA acted only as a temporary bailout therapy in an emergency clinical setting but proved ineffective in long-term ES prevention. The results of programmed stimulation effectively predicted long-term outcome in that all class A and B patients were free of ES recurrence during follow-up; therefore, suppression of the presenting VT(s) seems to be a reasonable marker of ES recurrence prevention. According to previous experience,[19,31,32] the VT recurrence rate was significantly reduced only in those patients in whom all (clinical and nonclinical) VTs had been suppressed (class A).

Impact on Overall Prognosis

ES has been recognized as an independent predictor of total death and CD.[2,8–11] The high mortality rate in patients suffering from ES might be related to progressive deterioration of cardiac function resulting from the direct cell injury effect caused by frequent shocks[33,34]; additionally, prolonged exposure to low-output states may further compromise cardiac contractility and impair renal and hepatic function.[35] In our population, a direct effect of CA on the prevention of ES has been suggested by the evidence that ES recurred only in the case of acute failure of the procedure; on other hand, survival rates were significantly higher among patients who had undergone CA successfully. Therefore, the favorable impact on CD may be related in part to the prevention of ES; in fact, 4 of 8 patients with ES recurrence died because of the recurrent event, whereas the 4 survivors required an immediate surgical treatment.

The hypothesis of a beneficial effect of CA is further supported by the comparative analysis of long-term mortality rates of historical controls with ES not treated by CA.[2,8–10] These are represented by various populations of patients with significant structural heart disease, primary and secondary indication to ICD implantation, and depressed LV ejection fraction, comparable to ours. In these studies, the ES recurrence rate was not reported; the estimates of CD rate were 27% at 20 months,[9] 54% at 24 months,[2] and between 38% and 54% at 31 to 33 months[8,10] compared with 12% at a median period of 22 months in our overall study population. Among patients unsuccessfully treated by CA, the incidence of CD rate (40%) in our study population approximated that of historical controls.

Role of Clinical Presentation: Group 1 Versus Group 2

Because of the extremely severe arrhythmia pattern causing cardiogenic shock, CA had to be performed as an emergency procedure in more than half of the patients. The requirement for intensive assistance and the short delay from admission to procedure underline the need for specific clinical pathways. Even in this high-risk group, CA allowed recovery of stable rhythm and subsequent stabilization in the absence of major complications, but the electrophysiological prediction of failure documented in 10 patients was reflected by the high ES recurrence and CD-related rate. Alternative therapeutic options (ventricular assist devices, cardiac transplantation) should therefore be considered before hospital discharge in these selected patients after CA fails.

Characteristics of Patients and Need for Advanced Methods of Mapping

Monomorphic VT was prevalent at clinical presentation, but the variability of hemodynamic tolerance and the evidence of multiple VT morphologies required the implementation of advanced strategies of mapping and ablation. In most patients, adequate periods of sinus rhythm allowed the use of nonconventional mapping techniques to define the arrhythmogenic substrate. Not infrequently, however, because of iterative nontolerated arrhythmias, cardiopulmonary support was needed to accomplish the procedure.

In IDCM patients, CA was less effective compared with patients with CAD and ARVD/C. Given the limitation of the small group of patients, this may be due in part to the higher incidence of an intramyocardial/epicardial location of the critical isthmus sustaining VT.[36] This may impair the efficacy of endocardial CA, suggesting that a combined endoepicardial approach might be considered a first-line strategy.

Study Limitations

This study was a prospective analysis of the short- and long-term outcome in patients with ES treated by CA, not a controlled randomized trial comparing CA with other forms of treatment for ES. Therefore, the study cannot unequivocally prove that CA is superior to other therapies to enhance survival in patients with ES. Similarly, the observation that failure of CA portents a worse prognosis also could reflect a more advanced cardiac disease in these patients.

Conclusions

This is the largest clinical experience evaluating the potential benefit of CA for the treatment of ES in patients with ICD receiving chronic antiarrhythmic drugs. Data indicate that CA can be applied to a broad population of patients suffering from ES and that it may favorably affect cardiac mortality, mainly through the long-term prevention of ES recurrence. This study lays the foundations for further studies and a wider use of CA for the treatment of ES.

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Disclosures

Dr Della Bella is a consultant for Biosense Webster and St Jude Medical. The other authors report no conflicts.

References

1. Pacifico A, Ferlic LL, Cedillo-Salazar FR, Nasir N, Doyle TK, Henry PD. Shocks as predictors of survival in patients with implantable cardioverter-defibrillators. *J Am Coll Cardiol*. 1999;34:204–210.
2. Bänsch D, Böcker D, Brunn J, MD, Weber M, Breithardt G, Block M. Clusters of ventricular tachycardias signify impaired survival in patients with idiopathic dilated cardiomyopathy and implantable cardioverter defibrillators. *J Am Coll Cardiol*. 2000;36:566–573.
3. Mitchell LB, Pineda A, Titus JL, MD, Bartosch PM, Benditt DG. Sudden death in patients with implantable cardioverter defibrillators: the importance of post-shock electromechanical dissociation. *J Am Coll Cardiol*. 2002;39:1323–1328.
4. Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, Gregoratos G, Klein G, Moss AJ, Myerburg RJ, Priori SG, Quinones MA, Roden DM, Silka MJ, Tracy C. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *J Am Coll Cardiol*. 2006;48:247–346.
5. Villacastin J, Almedral J, Arenal A, Albertos J, Ormaetxe J, Peinado R, Bueno H, Merino JL, Pastor A, Medina O, Tercedor L, Jimenez F, Delcan JL. Incidence and clinical significance of multiple consecutive, appropriate, high-energy discharges in patients with implanted cardioverter-defibrillators. *Circulation*. 1996;93:753–762.
6. Credner SC, Klingenheben T, Mauss O, Sticherling C, Hohnloser SH. Electrical storm in patients with implantable cardioverter-defibrillators: incidence, management and prognostic implications. *J Am Coll Cardiol*. 1998;32:1909–1915.
7. Greene M, Newman D, Geist M, Paquette M, Heng D, Dorian P. Is electrical storm in ICD patients the sign of a dying heart? Outcome of patients with clusters of ventricular tachyarrhythmias. *Europace*. 2000;2:263–269.
8. Exner DV, Pinski SL, Wyse G, Renfroe EG, Follmann D, Gold M, Beckman KJ, Coromilas J, Lancaster S, Hallstrom AP, for the AVID Investigators. Electrical storm presages non sudden death: the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial. *Circulation*. 2001;103:2066–2071.
9. Verma A, Kilicaslan F, Marrouche NF, Minor S, Khan M, Wazni O, Burkhardt JD, Belden WA, Cummings JE, Abdul-Karim A, Saliba W,

Schweikert RA, Tchou JP, Martin DO, Natale A. Prevalence, predictors, and mortality significance of the causative arrhythmia in patients with electrical storm. *J Cardiovasc Electrophysiol*. 2004;15:1265–1270.
10. Gatzoulis KA, Andronikopoulos GK, Apostolopoulos T, Sotiropoulos E, Zervopoulos G, Antoniou J, Brili S, Stefanadis CI. Electrical storm is an independent predictor of adverse long-term outcome in the era of implantable defibrillator therapy. *Europace*. 2005;7:184–192.
11. Sesselberg HW, Huang DT, Zareba W, Andrews M, McNitt S, McClintic B, Daubert JP, Moss AJ. Storms of ventricular tachycardia/fibrillation in MADIT II patients. *Heart Rhythm*. 2005;2:S205. Abstract.
12. Arya A, Haghjoo M, Reza Dehghani M, Fazelifar AF, Nikoo MH, Bagherzadeh A, Sadr-Ameli MA. Prevalence and predictors of electrical storm in patients with implantable cardioverter-defibrillator. *Am J Cardiol*. 2006;97:389–392.
13. Brigadeau F, Kouakam C, Didier K, Marquié C, Duhame A, Mizon-Gérard Frédérique, Lacroix D, Kacet S. Clinical predictors and prognostic significance of electrical storm in patients with implantable cardioverter defibrillators. *Eur Heart J*. 2006;27:700–707.
14. Hohnloser SH, Al-Khalidi HR, Pratt CM, Brum JM, Tatla D, Tchou P, Dorian P. Electrical storm in patients with an implantable defibrillator: incidence, features, and preventive therapy: insights from a randomized trial. *Eur Heart J*. 2006;27:3027–3032.
15. Strickberger SA, Ching Man K, Daoud EG, Rajiva G, Brinkman K, Hasse Carol, Bogun F, Knight BP, Weiss R, Bahu M, Morady F. A prospective evaluation of catheter ablation of ventricular tachycardia as adjuvant therapy in patients with coronary artery disease and an implantable cardioverter-defibrillator. *Circulation*. 1997;96:1525–1531.
16. Bänsch D, Ouyang 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. Silva RM, Mont L, Nava S, Rojel U, Matas M, Brugada J. Radiofrequency catheter ablation for arrhythmic storm in patients with an implantable cardioverter defibrillator. *Pacing Clin Electrophysiol*. 2004;27:971–975.
18. Schreieck J, Zrenner B, Deisenhofer I, Schmitt C. Rescue ablation of electrical storm in patients with ischemic cardiomyopathy: a potential-guided ablation approach by modifying substrate of intractable, unmappable ventricular tachycardias. *Heart Rhythm*. 2005;2:10–14.
19. 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.
20. Gepstein L, Hayam G, Ben-Haim SA. A novel method for nonfluoroscopic catheter-based electroanatomical mapping of the heart: in vitro and in vivo accuracy results. *Circulation*. 1997;95:1611–1622.
21. Arenal A, del Castillo S, Gonzalez-Torrecilla E, Atienza F, Ortiz M, Jimenez J, Puchol A, Garcia J, Almendral J. Tachycardia-related channel in the scar tissue in patients with sustained monomorphic ventricular tachycardias: influence of the voltage scar definition. *Circulation*. 2004;110:2568–2574.
22. Hsia HH, Lin D, Sauer WH, Callans DJ, Marchlinski FE. Anatomic characterization of endocardial substrate for hemodynamically stable reentrant ventricular tachycardia: identification of endocardial conducting channels. *Heart Rhythm*. 2006;3:503–512.
23. Marchlinski FE, Callans DJ, Gottlieb CD, Zado E. Linear ablation lesions for control of unmappable ventricular tachycardia in patients with ischemic and nonischemic cardiomyopathy. *Circulation*. 2000;101:1288–1296.
24. 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.
25. Kottkamp H, Wetzel U, Schirdewahn P, Dorszewski A, Gerds-Li JH, Carbucicchio C, Kobza R, Hindricks G. Catheter ablation of ventricular tachycardia in remote myocardial infarction: substrate description guiding placement of individual linear lesions targeting non inducibility. *J Cardiovasc Electrophysiol*. 2003;14:675–681.
26. Sosa E, Scanavacca M, d'Avila A, Pilleggi F. A new technique to perform epicardial mapping in the electrophysiology laboratory. *J Cardiovasc Electrophysiol*. 1996;7:531–536.
27. Schilling RJ, Peters NS, Davies DW. Feasibility of a non-contact catheter for endocardial mapping of human ventricular tachycardia. *Circulation*. 1999;99:2543–2552.
28. Della Bella P, Pappalardo A, Riva S, Tondo C, Fassini G, Trevisi N. Non-contact mapping to guide catheter ablation of untolerated ventricular tachycardia. *Eur Heart J*. 2002;23:742–752.
29. Fassini G, Della Bella P, Trevisi N, Tondo C, Riva S, Carbucicchio C, Bartorelli A. Long term safety and outcome of hemodynamically-supported catheter ablation for the treatment of untolerated ventricular tachycardia. *Pacing Clin Electrophysiol*. 2002;25:533. Abstract.
30. Kurusz M, Zwischenberger JB. Percutaneous cardiopulmonary bypass for cardiac emergency. *Perfusion*. 2002;17:269–277.
31. Della Bella P, De Ponti R, Salerno-Uriarte JA, Tondo C, Klersy C, Carbucicchio C, Storti C, Riva S, Longobardi M. Catheter ablation and antiarrhythmic drugs for hemodynamically tolerated post-infarction ventricular tachycardia: long-term outcome in relation to acute electrophysiological findings. *Eur Heart J*. 2002;23:414–424.
32. Rothman SA, Hsia HH, Cossu SF, Chmielewski IL, Buxton AE, Miller JM. Radiofrequency catheter ablation of post-infarction ventricular tachycardia: long-term success and the significance of inducible non-clinical arrhythmias. *Circulation*. 1997;96:3499–3508.
33. Jones DL, Narayanan N. Defibrillation depresses heart sarcoplasmic reticulum calcium pump: a mechanism of postshock disfunction. *Am J Physiol*. 1998;274:H-98–H-105.
34. Wilson CM, Allen JD, Bridges JB, Adgey AAJ. Death and damage caused by multiple direct current shocks: studies in an animal model. *Eur Heart J*. 1988;9:1257–1265.
35. Chalvidan T, Deharo JC, Dieuzaide P, Defaye P, Djiane P. Near fatal electrical storm in a patient equipped with an implantable cardioverter defibrillator for Brugada syndrome. *Pacing Clin Electrophysiol*. 2000;23:410–412.
36. Soejima K, Stevenson WG, Sapp JL, Selwyn AP, Couper G, Epstein LM. Endocardial and epicardial radiofrequency ablation of ventricular tachycardia associated with dilated cardiomyopathy: the importance of low-voltage scars. *J Am Coll Cardiol*. 2004;43:1834–1842.

CLINICAL PERSPECTIVE

Multiple shocks resulting from repetitive episodes of ventricular tachycardia, known as electrical storm (ES), occur in 10% to 20% of patients with implantable cardioverter-defibrillators. This frightening clinical emergency also predicts an increased risk of subsequent cardiac death among survivors. This case series assesses the role of catheter ablation in controlling ES and the subsequent long-term incidence of recurrent ventricular tachycardia and cardiac mortality. Ninety-five patients with structural heart disease undergoing catheter ablation for drug-refractory ES were prospectively evaluated. Advanced strategies of mapping and ablation were used in most patients. After 1 to 3 procedures, ES was suppressed in all patients. Programmed electrical stimulation showed that all inducible clinical ventricular tachycardias were abolished in 89% of patients. At a median follow-up of 22 months, 92% of patients were free of ES; 8 patients had recurrent ES, 4 of whom died despite implantable cardioverter-defibrillator intervention. The total cardiac mortality rate was 12%, which compares favorably with the reported late mortality rates for patients who suffer ES. Acute results of catheter ablation predicted the absence of ES recurrence and correlated with reduced cardiac mortality. These observations support the early use of catheter ablation as adjunctive therapy for the treatment of ES. This experience lays the foundation for further studies to determine whether controlling ES with catheter ablation improves long-term survival.