Catheter Ablation of Ventricular Tachycardia in Nonischemic Heart Disease

Michifumi Tokuda, MD; Usha B. Tedrow, MD, MSc; Pipin Kojodjojo, MD, PhD; Keiichi Inada, MD, PhD; Bruce A. Koplan, MD, MPH; Gregory F. Michaud, MD; Roy M. John, MD, PhD; Laurence M. Epstein, MD; William G. Stevenson, MD

Background—Catheter ablation of ventricular tachycardia (VT) in nonischemic heart diseases can be challenging, and outcomes across different diseases are incompletely defined. The aim of this study was to describe the outcomes after catheter ablation for nonischemic VT in a large cohort and to compare the electrophysiological findings and outcomes according to the type of underlying disease.

Methods and Results—Of the 891 consecutive patients undergoing catheter ablation for ventricular arrhythmias, 226 patients (52±14 years; 79% men) with sustained VT due to nonischemic heart disease were included. The primary end point was all-cause death or heart transplantation. Secondary end points were a composite of death, heart transplantation, or readmission because of VT recurrence within 1 year of discharge. Underlying heart diseases were dilated cardiomyopathy in 119 (53%), valvular heart disease in 34 (15%), arrhythmogenic right ventricular cardiomyopathy in 37 (16%), congenital heart disease in 16 (7%), cardiac sarcoidosis in 13 (6%), and hypertrophic cardiomyopathy in 7 (3%) patients. After ablation, inability to induce any VT was achieved in 55%, and another 20% had inducible VTs modified. Major complications occurred in 5%. Arrhythmogenic right ventricular cardiomyopathy had better outcomes than dilated cardiomyopathy for primary (P=0.002) and secondary end points (P=0.004). Sarcoidosis had worse outcome than dilated cardiomyopathy for secondary end point (P=0.002). At 1 year after the last ablation (a mean of 1.4±0.6 procedures, 1–4), freedom from death, heart transplantation, and readmission for VT recurrence were achieved in 173 (77%) patients.

Conclusions—In patients with recurrent VT due to nonischemic heart disease, catheter ablation is often useful, although the outcome varies according to the nature of the underlying heart disease. (Circ Arrhythm Electrophysiol. 2012;5:992-1000.)

Key Words: cardiomyopathy ■ catheter ablation ■ morbidity ■ mortality ■ ventricular tachycardia

Ventricular tachycardia (VT) is a marker for increased mortality and reduces quality of life in patients who have implanted defibrillators and heart disease.1 Evidence that catheter ablation can reduce VT episodes in ischemic heart disease has been reported in case series and several multicenter trials.2 In patients with nonischemic heart disease, sustained monomorphic VT is also usually due to scar-related reentry, with a minority due to bundle branch reentry or having a focal origin.3,4 Catheter ablation outcomes in this population are derived from only a small number of single-center reports, in a relatively small number of patients. Acute success in eliminating inducible VT has varied from 55% to 89% with VT recurrence of 16% to 63%.2,5-9 The aim of this study was to clarify the outcomes of VT ablation for patients with different forms of nonischemic heart disease.

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From the Cardiovascular Division, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA.

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Correspondence to Michifumi Tokuda, MD, Cardiovascular Division, Brigham and Women’s Hospital, 75 Francis St, Boston, MA 02115. E-mail tokudam@gmail.com

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cardiac involvement. Patients with prior valvular surgery only were classified as valvular heart disease. Clinical VT, sustained VT, and unmappable VT were defined according to the European Heart Rhythm Association/Heart Rhythm Society Expert Consensus on VT ablation. Each patient gave written informed consent. Studies and data collection were performed according to protocols approved by the Human Research Committee of Brigham and Women’s Hospital.

Electrophysiological Study

Ventricular mapping and ablation were performed with saline-irrigated or saline-nonirrigated tip catheters as previously described. Electroanatomical mapping was performed with the CARTO mapping system (Biosense Webster, Diamond Bar, CA). Bipolar electrograms were band-pass filtered from 30 to 500 Hz and digitally recorded along with a 12-lead surface ECG using the Cardiolab EP system (General Electric Healthcare, Buckinghamshire, UK). VT was induced with up to 3 extrastimuli and burst pacing from 2 right ventricular sites. Isoproterenol was used if VT was exercise related and usually required in ARVC.

Briefly, hemodynamically tolerated VTs were mapped and ablated during VT. Target sites for ablation were sites with an isolated mid-diastolic potential, where pacing entrained the VT with concealed fusion and a postsystolic interval within 30 ms and a stimulus-to-QRS interval <70% of the VT cycle length.

Electroanatomic mapping for unstable, unmappable VTs was performed during sinus rhythm. Areas of scar were identified based on a bipolar electrogram amplitude of <1.5 mV. Ablation targeted presumptive channels and exits within the low-voltage area as identified from a paced QRS morphology similar to the VT QRS morphology, wide fractionated potentials, or isolated late potentials during sinus or paced rhythm where pacing captured, particularly if the stimulus-to-QRS interval was >40 ms, consistent with abnormal conduction. Furthermore, when these sites were adjacent to a valve annulus or region of electrically unexcitable scar, ablation lesions were extended to the unexcitable area in the hope of dividing reentry circuit paths.

When possible, we assessed electrograms and entrainment at the initial sites of interest, with initiation of a short episode of VT. This was particularly attempted when initial substrate ablation failed to abolish inducible VT. If no low-voltage area was identified, ablation was attempted at the likely exit region identified as sites with presystolic electrograms during VT or where pace mapping resembled the VT QRS.
VT Ablation
A total of 2.7±2.1 different monomorphic VTs per patient were induced during procedure (Table 2). Bundle branch reentry was recognized in 19 (8%) patients. Low-voltage areas consistent with scar were usually observed in the RV in ARVC and sarcoid patients, but left ventricular scar was detected in 4 of 37 (11%) patients with ARVC and 6 of 13 (46%) patients with sarcoidosis. A transseptal approach was performed in 21 of 159 (13%) patients who required left ventricular access. Epicardial mapping was performed in 60 (27%) patients, and 52 (23%) received epicardial ablation. All 60 patients had prior endocardial mapping and failed endocardial ablation, which had occurred at another institution in 43 patients. In 11 patients, our first attempt was epicardial mapping, but all had a history of prior failed endocardial ablation at another institution. In the remaining 49 patients, we attempted endocardial...
mapping first but then proceeded to epicardial mapping either at a later procedure (2 patients) or during the same procedure (47 patients). Comparing the first 6 years of the study period to the second 6 years (before versus after January 2005), use of epicardial ablation increased from 13% to 28% of patients, \(P=0.01\). In two thirds of patients, at least 1 induced VT was not mappable. In 63 (28%) patients, only substrate-guided ablation was performed because of hemodynamically unstable VT or inability to reliably induce a clinical or presumptive clinical VT. In 5 patients, transcoronary ethanol ablation was performed after failed radiofrequency catheter ablation.

After ablation, no VT was inducible in 124 patients (55%), at least 1 clinical VT was not inducible with other VTs still inducible in 46 patients (20%), and clinical VTs were still inducible in 34 (15%) patients. In the remaining 22 (10%) patients, VT inducibility was not assessed after ablation because it was felt to place the patient at unnecessary risk of hemodynamic or respiratory compromise. During the index hospitalization, 18 patients required a second ablation procedure because of early VT recurrence a median of 2 days after first procedure.

**Complications**

Major complications, defined as those resulting in permanent injury or requiring intervention for treatment, occurred in 12 (5%) patients during initial hospitalization (Table 3). Three were clearly related to epicardial access or ablation. Epicardial bleeding >80 mL occurred in 2 cases (bleeding stopped spontaneously or after reversal of heparin anticoagulation; no patient required blood transfusion or surgery). One patient had a small myocardial infarction 2 weeks after epicardial ablation as a result of damage to a right ventricular branch of the right coronary artery that gave rise to the distal portion of the posterior descending coronary artery. Ventricular perforation occurred during endocardial mapping and ablation in 4 patients, of which 3 of them required emergent surgical repair. Two (0.9%) patients died within 30 days, 1 due to uncontrollably VT after failed ablation and the other from sepsis related to surgical pulmonary valve replacement performed after catheter ablation, unrelated to the ablation procedure.

**Outcome**

Kaplan-Meier curves of the primary and secondary end points are shown in Figure 1. During 4.4±3.3 years of follow-up, 66 (29%) patients reached the primary end point: death in 50 (21%) and heart transplant in 16 (7%). In 71 (31%) patients, the secondary end point was reached, including 23 (10%) deaths, 8 (3%) heart transplants, and 40 (18%) hospitalizations for VT recurrence within 1 year of discharge. Of 40 patients hospitalized for VT, 13 met the definition for VT storm of ≥3 episodes within 24 hours. In multivariable Cox proportional hazards analysis, lower LVEF, New York Heart Association class ≥III, greater number of induced VTs, and renal insufficiency were independent predictors of the primary end point (Table 4). Age, lower LVEF, and renal insufficiency were associated with the secondary end point (Table 5). Acute ablation failure or no attempted VT induction after ablation was not a predictor of the primary or secondary outcome end point (Tables 4 and 5). After excluding the 22 patients who did not have attempted VT induction after ablation, absence of inducible VT after ablation still failed to predict the primary (hazard ratio, 0.926; 95% CI, 0.519–1.650; \(P=0.794\)) or secondary end point (hazard

<table>
<thead>
<tr>
<th>Table 3. Major Complications Related to Endocardial and Epicardial Ablation</th>
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<tbody>
<tr>
<td>Complication</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Endocardial pop with pericardial effusion</td>
</tr>
<tr>
<td>Heart block</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
</tr>
<tr>
<td>Related to epicardial access or ablation</td>
</tr>
<tr>
<td>Pericardial bleeding &gt;80 mL</td>
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<tr>
<td>Coronary artery injury</td>
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Table 4. Multivariable Analysis for the Primary End Point

<table>
<thead>
<tr>
<th></th>
<th>P Value</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.119</td>
<td>1.016</td>
<td>0.996–1.037</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.004</td>
<td>0.968</td>
<td>0.947–0.989</td>
</tr>
<tr>
<td>NYHA class ≥III</td>
<td>&lt;0.001</td>
<td>2.998</td>
<td>1.705–5.272</td>
</tr>
<tr>
<td>No. of VTs induced</td>
<td>0.006</td>
<td>1.168</td>
<td>1.045–1.305</td>
</tr>
<tr>
<td>Acute ablation failure or not tested</td>
<td>0.282</td>
<td>1.366</td>
<td>0.792–2.357</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>0.003</td>
<td>2.330</td>
<td>1.333–4.075</td>
</tr>
</tbody>
</table>

LVEF indicates left ventricular ejection fraction; NYHA, New York Heart Association; VT, ventricular tachycardia.

data for patients who had epicardial ablation, after failing endocardial ablation, were different from those who had only endocardial ablation (P=0.85) (Figure 2).

Repeat Ablation Procedures

During follow-up after the index hospitalization, repeat ablation procedures were performed in 62 patients. Epicardial ablation, transcoronary ethanol ablation, and surgical ablation were performed in 23, 9, and 3 patients, respectively. Thus, considering all ablation procedures in the 226 patients, epicardial ablation, transcoronary ethanol ablation, and surgical ablation were required in 76 (34%), 17 (8%), and 4 (2%) patients, respectively. Finally, 1 year after the discharge from the last ablation procedure (a mean of 1.4±0.6 procedures, 1–4), freedom from death, heart transplantation, and readmission for VT recurrence were achieved in 173 (77%) patients. Kaplan-Meier curves of VT recurrence requiring hospitalization after the index ablation procedure at our center or after the last ablation procedure are shown in Figure 3.

Differences Among Types of Cardiomyopathies

The DCM group was chosen as a reference group. Comparisons between the DCM and other groups are shown in Tables 1 and 2. DCM patients had lower LVEF than other groups. Patients with sarcoidosis had a larger number of induced VTs than those with DCM (P<0.01). Ablation abolished all inducible VTs more often in patients with ARVC than in those with DCM (P<0.01).

The outcomes after initial hospitalization differed according to the type of nonischemic heart disease (Figures 4 and 5). For the primary end point, patients with ARVC had better outcomes than those with DCM (P=0.04). In contrast, patients with cardiac sarcoidosis had worse outcomes than those with DCM (P=0.002). VT recurrences requiring hospitalization differed according to the type of nonischemic heart disease (overall log-rank P=0.04; Figure 6). Patients with sarcoidosis had greater risk of VT recurrence requiring hospitalization than those with DCM (P=0.007).

In 119 patients who were classified as DCM, 13 patients had a suspected cause of DCM: doxorubicin-induced in 3, postmyocarditis in 3, postpartum in 2, muscular dystrophy in 3, hemochromatosis in 1, and alcohol-related in 1 patient, respectively. The remaining 106 patients without obvious causes were classified as idiopathic DCM. The outcomes

Table 5. Multivariable Analysis for the Secondary End Point

<table>
<thead>
<tr>
<th></th>
<th>P Value</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.015</td>
<td>0.977</td>
<td>0.959–0.996</td>
</tr>
<tr>
<td>LVEF</td>
<td>&lt;0.001</td>
<td>0.964</td>
<td>0.948–0.981</td>
</tr>
<tr>
<td>NYHA class ≥III</td>
<td>0.987</td>
<td>1.005</td>
<td>0.582–1.735</td>
</tr>
<tr>
<td>Number of VTs induced</td>
<td>0.293</td>
<td>1.058</td>
<td>0.952–1.176</td>
</tr>
<tr>
<td>Acute ablation failure or not tested</td>
<td>0.931</td>
<td>0.977</td>
<td>0.569–1.677</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>0.003</td>
<td>2.274</td>
<td>1.325–3.901</td>
</tr>
</tbody>
</table>

LVEF indicates left ventricular ejection fraction; NYHA, New York Heart Association; VT, ventricular tachycardia.

Figure 2. Kaplan-Meier curves showing the secondary end point, freedom from death, heart transplant, or hospitalization for ventricular tachycardia recurrence in patients with (gray line) or without epicardial ablation (black line).

Figure 3. Kaplan-Meier curves showing freedom from VT recurrence requiring hospitalization after the initial procedure at our institution and after the last ablation procedure at our institution. Follow-up started at discharge from the ablation hospitalization.
appeared similar between idiopathic DCM and nonidiopathic DCM patients for both primary ($P=0.31$) and secondary end points ($P=0.39$). Familial DCM was defined as the presence of DCM in $\geq 2$ family members. In 106 patients with idiopathic DCM, familial DCM was identified in 19 (18%). Outcomes appeared similar between those DCM patients with and without a family history ($P=0.27$ for primary end point and $P=0.71$ for secondary end point), but the number of patients is small.

**Discussion**

**Study Results**

Our single-center study characterizes the clinical outcomes associated with catheter ablation for VT due to nonischemic heart disease in a large cohort of consecutive patients. To our knowledge, this is the largest study of VT ablation for nonischemic heart disease and the first study to compare the electrophysiological findings and outcomes of catheter ablation procedures for ventricular arrhythmias according to the type of underlying heart disease in this population.

In this cohort of patients with recurrent VT referred for catheter ablation, the prevalence of DCM, ARVC, cardiac sarcoidosis, and HCM are 54%, 15%, 5%, and 3%, respectively. These ratios are in approximate agreement with the estimated prevalence of these diseases in the general population: 1:2500 for DCM, 1:5000 for ARVC, 1:20,000 for cardiac sarcoidosis, but with fewer HCM patients, for whom the prevalence is

**Figure 4.** Kaplan-Meier curves of primary end point according to the type of heart disease is shown (overall log-rank $P=0.02$). Each curve is compared with the curve of dilated cardiomyopathy (DCM). The patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) had significantly better outcomes than those with DCM ($P=0.002$). In pairwise comparison, Bonferroni-adjusted $P<0.05/5$ was considered significant. HCM indicates hypertrophic cardiomyopathy.

**Figure 5.** Kaplan-Meier curves of the secondary end point, death, transplantation, or hospitalization for ventricular tachycardia recurrence according to the type of heart disease are shown (overall log-rank $P=0.01$). The patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) had better ($P=0.004$) and the patients with sarcoidosis had worse ($P=0.002$) outcome than those with dilated cardiomyopathy (DCM). In pairwise comparison, Bonferroni-adjusted $P<0.05/5$ was considered significant. HCM indicates hypertrophic cardiomyopathy.
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disease, it seems likely that progression of the underlying myo-
sant VT or electrical storm, which is likely to improve survival
we observed that catheter ablation is often able to control inces-
that included many of our patients.36 During early childhood, 30% to 50% require surgery.35 Ventricular scars from ventriculotomy or patches create the
substrate for scar-related reentry. VT ablation outcomes were relatively favorable in this group, consistent with a prior report that included many of our patients.36

Study Limitations
This study has several limitations. Several forms of nonischemic heart disease causing VT are rare, and sample sizes in subgroups are small, precluding statistical comparisons. However, these data comprise the largest series of such patients treated with catheter ablation for recurrent monomorphic VT. This was a retrospective study, and selection biases undoubtedly determine who is referred for VT ablation. Very ill, end-stage heart failure patients are less likely to be considered for ablation. In the present study, isolated VT recurrences that did not result in hospitalization were not included as an end point. Detection of these events in our referral population can be problematic, and isolated VT recurrences may not preclude good long-term control and clinical benefit.

Conclusions
This relatively large series demonstrates that in patients with recurrent VT due to nonischemic heart disease catheter ablation...
is often useful and that the outcome of catheter ablation varies according to the nature of the underlying cardiomyopathy.

Disclosures

Usha Tedrow receives research grants supported by St Jude Medical and Biosense Webster. Pipin Kojodjojo was funded by a British Heart Foundation Travel Fellowship (FS/09/047). William Stevenson is a coholder of a patent for needle ablation consigned to Brigham and Women’s Hospital. The other authors have no conflicts to report.

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**CLINICAL PERSPECTIVE**

Outcomes of catheter ablation of ventricular tachycardia (VT) in patients with nonischemic heart disease are not fully defined as ablation therapy has evolved. This comparatively large series of 226 (mean age, 52 years; 79% men) patients of catheter ablation for VT due to nonischemic heart disease further compares electrophysiological findings and outcomes according to the type of heart disease. Epicardial mapping was performed in 27% of patients. Ablation abolished all inducible monomorphic VT in 55% of patients, and another 20% had inducible VTs modified. Major complications occurred in 5%, and 30-day mortality was 0.9%. One year after discharge from last ablation procedure (a mean of 1.4±0.6 procedures, 1–4), freedom from death, heart transplantation, and readmission for VT recurrence were achieved in 173 (77%) patients. Compared with patients with nonischemic dilated cardiomyopathy, patients with arrhythmogenic RV cardiomyopathy had better outcomes and patients with sarcoidosis had worse outcomes. In patients with recurrent VT due to nonischemic heart disease, catheter ablation is often useful. The outcome varies according to the nature of the underlying heart disease.
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Supplemental Table 1.
Multivariable Analysis for the primary endpoint after excluding the 22 patients who did not have attempted VT induction after ablation

<table>
<thead>
<tr>
<th>Factor</th>
<th>P</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.063</td>
<td>1.022</td>
<td>0.999-1.045</td>
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<tr>
<td>LVEF</td>
<td>0.025</td>
<td>0.974</td>
<td>0.951-0.997</td>
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<td>NYHA class ≥ III</td>
<td>&lt;0.001</td>
<td>3.290</td>
<td>1.780-6.084</td>
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<td>Number of VTs induced</td>
<td>0.001</td>
<td>1.219</td>
<td>1.082-1.372</td>
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<tr>
<td>Acute Ablation Failure</td>
<td>0.794</td>
<td>0.926</td>
<td>0.519-1.650</td>
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<tr>
<td>Renal insufficiency</td>
<td>0.015</td>
<td>2.164</td>
<td>1.161-4.035</td>
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</table>

LVEF indicates left ventricular ejection fraction, NYHA: New York Heart Association, and VT: ventricular tachycardia
Supplemental Table 2. Multivariable Analysis for the secondary endpoint after excluding the 22 patients who did not have attempted VT induction after ablation

<table>
<thead>
<tr>
<th></th>
<th>P</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
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<td>Age</td>
<td>0.009</td>
<td>0.974</td>
<td>0.954-0.993</td>
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<tr>
<td>LVEF</td>
<td>&lt;0.001</td>
<td>0.967</td>
<td>0.950-0.985</td>
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<td>NYHA class ≥ III</td>
<td>0.668</td>
<td>1.140</td>
<td>0.627-2.072</td>
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<tr>
<td>Number of VTs induced</td>
<td>0.220</td>
<td>1.072</td>
<td>0.959-1.197</td>
</tr>
<tr>
<td>Acute Ablation Failure</td>
<td>0.410</td>
<td>0.786</td>
<td>0.443-1.394</td>
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<tr>
<td>Renal insufficiency</td>
<td>0.001</td>
<td>2.597</td>
<td>1.451-4.647</td>
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LVEF indicates left ventricular ejection fraction, NYHA: New York Heart Association, and VT: ventricular tachycardia