Ventricular Tachycardia Ablation in Severe Heart Failure
An International Ventricular Tachycardia Ablation Center Collaboration Analysis

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Background—Ventricular tachycardia (VT) radiofrequency ablation has been associated with reduced VT recurrence and mortality, although it is typically not considered among New York Heart Association class IV (NYHA IV) heart failure patients. We compared characteristics and VT radiofrequency ablation outcomes of those with and without NYHA IV in the International VT Ablation Center Collaboration.

Methods and Results—NYHA II–IV patients undergoing VT radiofrequency ablation at 12 international centers were included. Clinical variables, VT recurrence, and mortality were analyzed by NYHA IV status using Kaplan–Meier analysis and Cox proportional hazard models. There were significant differences between NYHA IV (n=111) and NYHA II and III (n=1254) patients: NYHA IV had lower left ventricular ejection fraction; more had diabetes mellitus, kidney disease, cardiac resynchronization implantable cardioverter–defibrillator, and VT storm despite greater antiarrhythmic drug use (P<0.01). NYHA IV subjects required more hemodynamic support, were inducible for more and slower VTs, and were less likely to undergo final programmed stimulation. There was no significant difference in acute complications. In-hospital deaths, recurrent VT, and 1-year mortality were higher in the NYHA IV group, in the context of greater baseline comorbidities. Importantly, NYHA IV patients without recurrent VT had similar survival compared with NYHA II and III patients with recurrent VT (68% versus 73%). Early VT recurrence (≤30 days) was significantly associated with mortality, especially in NYHA IV patients.

Conclusions—Despite greater baseline comorbidities, VT radiofrequency ablation can be safely performed among NYHA IV patients. Early VT recurrence is significantly associated with subsequent mortality regardless of NYHA status. Elimination of recurrent VT in NYHA IV patients may reduce mortality to a level comparable to NYHA II and III with arrhythmia recurrence.

Key Words: catheter ablation □ heart failure □ tachycardia, ventricular

Ventricular tachycardia (VT) ablation among patients with structural heart disease has evolved from a procedure of last resort to one that is recommended as first-line therapy in certain patients. Still, ablation is often deferred even after implantable cardioverter–defibrillator (ICD) therapies have been delivered because of perceived risks and efficacy concerns. Patients with heart failure (HF) and New York Heart Association class IV (NYHA IV) functional status represent a special population for whom this procedure is often deferred because of elevated risk, even though significant benefit may be derived. Despite this potential benefit, there are limited data in this patient population because of safety concerns and exclusion from industry-sponsored clinical research evaluating catheter ablation of ventricular arrhythmias (VT/ventricular fibrillation [VF]).

During the past decade, there have been advances in the ability to minimize hemodynamic instability during catheter ablation, including improved methods for substrate-based...
VT Ablation in Severe Heart Failure

WHAT IS KNOWN
- Catheter ablation of VT is an effective treatment for VT, and lack of recurrent VT after ablation has been associated with improved survival.
- VT ablation is often avoided among patients with NYHA IV HF because of a perception of prohibitively high risk/benefit ratio.

WHAT THE STUDY ADDS
- VT ablation can be performed safely among patients with advanced HF, and lack of recurrent VT among these patients is associated with improved survival.
- Early recurrence of VT after ablation in NYHA IV patients is strongly associated with subsequent mortality and should prompt consideration for advanced HF therapies.

ablation. In addition, use of percutaneous left ventricular assist devices (LVADs) during ablation, in selected cases, has helped to minimize hemodynamic compromise. Not only has the need for repeated VT induction and activation mapping been minimized with contemporary approaches, but freedom from VT recurrence and outcomes have improved.

We sought to assess the safety and efficacy of VT ablation in patients with NYHA IV HF and ventricular arrhythmias refractory to medical therapy among a contemporary group of patients included in the cohort established by the International VT Ablation Center Collaborative Group (IVTCC).3

Methods

Study Cohort
We retrospectively analyzed data collected by the IVTCC to evaluate the safety and efficacy of VT ablation in patients with NYHA IV HF and structural heart disease. Details of this shared database have been previously reported. Briefly, patients with structural heart disease and refractory VT undergoing catheter ablation between 2002 and 2013 among 12 international, tertiary-care sites specializing in VT management were included. Data collection and analysis were approved by the institutional review board of each participating center, and all subjects gave informed consent. For this study, only patients with NYHA II–IV HF with left ventricular ejection fraction <50% were included, and characteristics between NYHA IV and NYHA II and III were examined.

NYHA Classification
Investigators contributing to the IVTCC database assigned NYHA functional class to each subject included in the database using standard classifications. NYHA I patients were those with no limitation of physical activity. NYHA II comprised those with slight physical activity limitation but comfortable at rest. Patients with NYHA III HF had marked limitation of any physical activity but were asymptomatic at rest. Patients with NYHA IV HF were those with dyspnea at rest, inability to perform any physical activity without HF symptoms, and were often inotrope dependent.

Ablation and Procedural Data Collection
Details of ablation procedures performed and data collected have been previously reported. Contemporary approaches for substrate-based ablation guided by electroanatomic mapping, pace-mapping, and, when feasible, activation and entrainment mapping were performed across all centers. Specific techniques used were case and operator dependent, including epicardial access and ablation and use of hemodynamic support devices (extracorporeal membrane oxygenation, Impella [Abiomed, Inc, Danvers, MA], TandemHeart [CardiacAssist, Pittsburgh, PA] or intra-aortic balloon counterpulsation). Acute ablation success was defined as noninducibility of sustained, monomorphic VT with programmed stimulation after ablation and was performed unless hemodynamic instability or other patient safety risk was present.

Follow-up and End Points
All subjects included in the IVTCC database were followed in the outpatient setting to assess for recurrent VT, transplant, and mortality. Outpatient assessments included device interrogations and office visits. Recurrent VT/VF was defined as spontaneous recurrence lasting ≥30 seconds and documented by telemetry, ECG, or device recording, or any appropriate ICD therapy, including antiarrhythmia pacing. The date of VT recurrence, cardiac transplant, or death was noted in addition to the last follow-up date. Twelve-month survival in patients was assessed in those with and those without recurrence of VT, based on NYHA II–IV classification. Baseline, procedural, and outcome differences between NYHA IV and NYHA II and III patients were compared. Risk factors for recurrence of VT and mortality were further analyzed among NYHA IV patients.

Statistical Analyses
Continuous data are expressed as mean±SD, and categorical data are expressed as number (%). Two-sided Student t test was used for comparison of continuous variables; the Wilcoxon rank-sum test was used for nonparametric comparative testing. Pearson χ2 test was used for comparison of proportions. Cox proportional hazard analysis was used to evaluate significant univariable and multivariable correlates for time to ventricular arrhythmia recurrence and mortality, and results are reported as hazard ratio (95% confidence interval). In addition, VT recurrence as a time-dependent covariate was used to analyze the association between VT recurrence and early VT recurrence (≤30 days after ablation) with mortality in unadjusted and multivariable analyses. Characteristics included in the multivariable model included those that were significant in univariable analysis (P<0.1) and those that were felt to be otherwise clinically relevant (age and left ventricular ejection fraction). Kaplan–Meier survival analysis was performed to estimate survival among patients with NYHA IV versus NYHA II and III HF and (1) VT recurrence after ablation, with time to death assessed from time of recurrence and (2) lack of VT recurrence, with time to death assessed from time of ablation. Landmark analysis was additionally performed to compare survival between NYHA IV and NYHA II and III cohorts based on early VT recurrence, after excluding those who had died before day 30 or those without early recurrence with <1-year follow-up. Comparisons were performed using the log-rank test. Statistical analyses were performed using the IBM SPSS (version 24.0, New York) statistical software program, and statistical significance was defined as a 2-sided P<0.05.

Results

Patient Characteristics
There were a total of 2061 patients with structural heart disease who underwent VT ablation among 12 centers in the IVTCC. Of those, 698 had NYHA I functional status and were not included in this study because of lack of clinical HF. There were 1365 patients included in the present analysis, 111 who had NYHA IV HF (Table 1). Mean age was 64±12 years, and left ventricular ejection fraction was 30±11%. The majority were male (88%) and had ischemic cardiomyopathy (59%). VT storm or incessant VT was present in 38%, and 77% had been treated with at least 1 antiarrhythmic drug before ablation.
There were notable differences in baseline characteristics between patients with NYHA II and III and NYHA IV HF presenting for VT ablation (Table 1). Comorbidities were greater among patients with NYHA IV HF, with significantly higher prevalence of diabetes mellitus, chronic kidney disease, and hyperlipidemia. Left ventricular ejection fraction was significantly worse among patients with NYHA IV compared with those with NYHA II and III HF (30±11% versus 21±7%; \( P<0.001 \)).

There were significantly more NYHA IV HF patients who had cardiac resynchronization therapy--defibrillators (CRT-Ds), and they were more likely to present with VT storm or incessant VT, as well as with multiple ICD shocks not meeting criteria for storm. These presentations were more frequent despite greater use of antiarrhythmic drugs, especially amiodarone (82% versus 60%; \( P<0.001 \)). Sotalol was used less often (82% versus 60%; \( P=0.009 \)), although there was also significantly greater use of other \( \beta \)-blockers in the NYHA IV group. There were no differences observed in age, sex, or cause of heart disease.

### Table 1. Baseline Characteristics by NYHA Classification

<table>
<thead>
<tr>
<th>Variable</th>
<th>NYHA II and III (n=1254)</th>
<th>NYHA IV (n=111)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64±12</td>
<td>65±11</td>
<td>0.317</td>
</tr>
<tr>
<td>Male sex</td>
<td>1113 (89)</td>
<td>95 (86)</td>
<td>0.350</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>741 (59)</td>
<td>68 (61)</td>
<td>0.688</td>
</tr>
<tr>
<td>LVEF</td>
<td>30±11</td>
<td>21±7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>663 (53)</td>
<td>57 (61)</td>
<td>0.132</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>695 (55)</td>
<td>59 (69)</td>
<td>0.018</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>357 (32)</td>
<td>39 (40)</td>
<td>0.116</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>280 (22)</td>
<td>45 (42)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>432 (34)</td>
<td>58 (52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VT storm/Incessant VT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICD shocks</td>
<td>750 (60)</td>
<td>75 (72)</td>
<td>0.016</td>
</tr>
<tr>
<td>Syncope</td>
<td>114 (9)</td>
<td>8 (19)</td>
<td>0.055</td>
</tr>
<tr>
<td>Previous ablation</td>
<td>478 (38)</td>
<td>40 (36)</td>
<td>0.685</td>
</tr>
<tr>
<td>Previous cardiothoracic surgery</td>
<td>409 (34)</td>
<td>36 (33)</td>
<td>0.916</td>
</tr>
<tr>
<td>Use of antiarrhythmic drug</td>
<td>959 (81)</td>
<td>96 (91)</td>
<td>0.008</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>706 (60)</td>
<td>86 (82)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sotalol</td>
<td>139 (12)</td>
<td>4 (4)</td>
<td>0.009</td>
</tr>
<tr>
<td>( \geq 2 )</td>
<td>239 (20)</td>
<td>27 (26)</td>
<td>0.209</td>
</tr>
<tr>
<td>( \beta )-Blocker</td>
<td>1022 (83)</td>
<td>99 (90)</td>
<td>0.046</td>
</tr>
</tbody>
</table>

Continuous variables are reported as mean±SD, unless specified. Categorical variables are reported as n (%). CRT indicates cardiac resynchronization therapy; ICD, implantable cardioverter–defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; and VT, ventricular tachycardia.

### Procedural Characteristics Based on NYHA Classification

There also were notable differences observed during VT ablation procedures between NYHA IV and NYHA II and III patients (Table 2). There was a significantly greater use of hemodynamic cardiac support devices among patients with NYHA IV compared with NYHA II and III HF (22% versus 7%; \( P<0.001 \)). There was no difference in the proportion undergoing epicardial access and mapping, but more of the NYHA IV patients required cardiothoracic surgical assistance to obtain epicardial access. There was a trend toward greater number of VTs induced among the advanced HF patients, and VT cycle lengths were significantly slower than in the NYHA II and III group (376±90 versus 351±87 ms, fastest, and 458±110 versus 420±110 ms, slowest). Programmed electric stimulation after ablation was more often deferred among NYHA IV patients; however, among those undergoing final programmed electric stimulation, there was no significant difference observed in rates of inducible clinical/targeted VT (79% versus 82%; \( P=0.521 \)). When examining baseline and procedural differences among the minority of patients in each group with nonischemic cardiomyopathy (NICM), based on NYHA IV versus NYHA II and III HF, there were no significant differences noted, included among the following (NICM NYHA II and III versus NICM NYHA IV, respectively): epicardial ablation (46% versus 54%; \( P=1.000 \)), procedure time (297 versus 269 minutes; \( P=0.211 \)), or acute noninducibility after ablation (55% versus 42%; \( P=0.114 \)).

Despite significant differences in baseline and procedural characteristics, the acute complication rate between groups did not differ significantly (7% among NYHA II and III versus 10% in NYHA IV; \( P=0.246 \)). The most common complications included the following, with frequencies listed for NYHA II and III versus NYHA IV, respectively: vascular access or access-related bleeding in 31 (2.5%) versus 2 (1.8%); pericardial effusion leading to pericardiocentesis in 27 (2.2%) versus 3 (2.7%); or surgical repair in 3 (0.2%) versus 0; thromboembolic events in 6 (0.5%) versus 3 (2.7%). Notably, there were 5 intraprocedural cardiac arrests that occurred in the NYHA II and III group, one of which proceeded to extracorporeal membrane oxygenation and the other of which ultimately underwent implantation of LVAD. There were no cardiac arrests in the NYHA IV group, either intraprocedurally or immediately postprocedurally.

### Outcomes After VT Ablation Based on NYHA Functional Class

Rates of in-hospital death and 1-year mortality and cardiac transplantation were significantly higher among patients with NYHA IV HF compared with those with NYHA II and III HF (Table 3); these differences were consistent when examining outcomes only among patients with NICM in each group, although there was a more dramatic difference.
Table 2. Procedural Characteristics by NYHA Classification

<table>
<thead>
<tr>
<th>Variable</th>
<th>NYHA II and III (n=1254)</th>
<th>NYHA IV (n=111)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of hemodynamic support device</td>
<td>67 (7)</td>
<td>17 (22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epicardial mapping</td>
<td>335 (29)</td>
<td>29 (27)</td>
<td>0.823</td>
</tr>
<tr>
<td>Surgical epicardial access</td>
<td>25 (2)</td>
<td>6 (6)</td>
<td>0.036</td>
</tr>
<tr>
<td>No. of VTs induced</td>
<td>2.2±2.0</td>
<td>2.6±2.3</td>
<td>0.057</td>
</tr>
<tr>
<td>No. with unmappable VT</td>
<td>497 (57)</td>
<td>56 (58)</td>
<td>0.764</td>
</tr>
<tr>
<td>Fastest VT cycle length, ms</td>
<td>351±87</td>
<td>376±90</td>
<td>0.016</td>
</tr>
<tr>
<td>Slowest VT cycle length, ms</td>
<td>420±110</td>
<td>458±110</td>
<td>0.005</td>
</tr>
<tr>
<td>Procedure time, min</td>
<td>285±116</td>
<td>280±120</td>
<td>0.691</td>
</tr>
<tr>
<td>Noninducible or inducible for nonclinical VT on final PES</td>
<td>1028 (82)</td>
<td>88 (79)</td>
<td>0.521</td>
</tr>
<tr>
<td>Final PES not performed</td>
<td>54 (5)</td>
<td>12 (11)</td>
<td>0.010</td>
</tr>
<tr>
<td>Complications</td>
<td>82 (7)</td>
<td>11 (10)</td>
<td>0.246</td>
</tr>
</tbody>
</table>

Continuous variables are reported as mean±SD, unless specified. Categorical variables are reported as n (%). NYHA indicates New York Heart Association; PES, programmed electric stimulation; and VT, ventricular tachycardia.

Discussion

Study Results

In this multicenter collaborative study of patients undergoing VT ablation at tertiary-care ablation centers, we found that VT ablation in patients with severe HF could be safely performed, with reasonable intermediate-term outcomes. Freedom from recurrent VT was achieved in 64% of patients with NYHA IV HF, in whom significant morbidity was present at baseline. Compared with those with mild and moderate HF (NYHA II and III), patients with severe HF seemed to have a greater burden of VT and VT storm, as well as significantly greater comorbidities, and the threshold for performing the procedure may thus have been higher for the NYHA IV patients. Despite this higher expected morbidity, patients with severe HF and no VT recurrence had improved mortality compared with others in the same class but with recurrent VT after ablation. In fact, the survival among NYHA IV patients without recurrent VT was similar to that among patients with less severe HF.

Association Between Early VT Recurrence and Mortality After Ablation

Mortality was significantly increased across all of the NYHA functional classes when VT recurred ≤30 days after ablation (P<0.001; Figure 2). Early VT recurrence was strongly associated with mortality in this group, with a >8-fold increased risk of mortality among NYHA IV patients (Table 5; P<0.001). Conversely, among NYHA IV patients without early VT recurrence, survival was similar to that of NYHA II and III patients with early VT recurrence (86% versus 87%; Figure 2).

Correlates of VT Recurrence and Mortality Among NYHA IV Patients

Characteristics associated with shorter time to VT Recurrence in NYHA IV patients (Table 4) in unadjusted analysis included presence of CRT-D, hyperlipidemia, and intraoperative use of hemodynamic cardiac support devices. In multivariable analysis, only presence of CRT-D (P=0.020) and use of hemodynamic cardiac support devices (P=0.039) were significantly associated with VT recurrence, although the small number of subjects limited statistical power in these analyses.

Chronic kidney disease, use of intraprocedural hemodynamic cardiac support devices, VT recurrence, and early (≤30 days) VT recurrence were associated with subsequent death among NYHA IV patients after VT ablation in unadjusted analyses (Table 5). There was no difference in VT recurrence or survival based on ischemic versus nonischemic cause for structural heart disease. In multivariable analysis, early VT recurrence or any VT recurrence remained significantly associated with 1-year mortality among the group of patients with the most severe HF.
in whom VT recurred after ablation. This improvement may seem marginal, but incremental improvement in survival is significant among this very sick subset of patients. Patients with advanced HF and VT have the highest rate of mortality with concomitant HF risk.13 Our data suggest that, at selected ablation referral centers, VT ablation can still performed

**Figure 1.** Kaplan–Meier analysis illustrating survival of New York Heart Association class IV heart failure (NYHA IV HF) patients (blue) vs NYHA II and III HF patients (green) from time of recurrence among those with recurrent ventricular tachycardia (VT; 27% vs 71%).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable Analyses</th>
<th>Multivariable Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td><em>P</em> Value</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Age*</td>
<td>0.98 (0.94–1.01)</td>
<td>0.230</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>0.70 (0.37–1.33)</td>
<td>0.273</td>
</tr>
<tr>
<td>LVEF*</td>
<td>0.93 (0.87–1.00)</td>
<td>0.050</td>
</tr>
<tr>
<td>Presence of CRT-D*</td>
<td>0.52 (0.27–0.98)</td>
<td>0.045</td>
</tr>
<tr>
<td>VT storm/incessant VT</td>
<td>1.03 (0.51–2.10)</td>
<td>0.935</td>
</tr>
<tr>
<td>Hyperlipidemia*</td>
<td>3.46 (1.28–9.35)</td>
<td>0.014</td>
</tr>
<tr>
<td>Atrial fibrillation*</td>
<td>0.50 (0.24–1.02)</td>
<td>0.056</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.63 (0.83–3.21)</td>
<td>0.160</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>0.63 (0.33–1.22)</td>
<td>0.172</td>
</tr>
<tr>
<td>Antiarrhythmic drug use</td>
<td>0.71 (0.25–2.05)</td>
<td>0.530</td>
</tr>
<tr>
<td>Use of hemodynamic support device*</td>
<td>2.98 (1.19–7.44)</td>
<td>0.020</td>
</tr>
<tr>
<td>Partial success on final PES*</td>
<td>0.52 (0.26–1.06)</td>
<td>0.070</td>
</tr>
<tr>
<td>Inducible at final PES</td>
<td>1.23 (0.93–1.63)</td>
<td>0.145</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; CRT-D, cardiac resynchronization therapy–defibrillator; HR, hazard ratio; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PES, programmed electric stimulation; and VT, ventricular tachycardia.

*Variables with *P*-0.1 on univariable analysis, except for age, were included in multivariable model.
safely and lead to potential survival benefit among those with potentially reversible substrate among patients with advanced myocardial remodeling and failure. The outlook from this study is in contrast to ICD trials, which have suggested that many patients with the highest disease severity may be too sick to benefit.14,15 In other words, results from this study suggest that not all patients with NYHA IV HF and VT should be considered equal, and that there is potential benefit that may be achieved in ablation of such patients. More specifically, the presence of advanced HF and VT should not preclude consideration for ablation.

Another important finding not previously reported is that early VT recurrence was a significant marker of mortality after ablation, among all patients, although especially among patients with NYHA IV. NYHA IV patients with VT recurrence ≤30 days had a >8-fold increased risk of death in a year compared with similar patients who did not have early recurrence. Notably, however, NYHA IV patients without early VT recurrence had similar survival compared with NYHA II and III patients with early VT recurrence. In sum, these results suggest that NYHA IV patients with VT likely include a mixture of those with irreversibly advanced or extensive midmyocardial substrate and less advanced and treatable VT substrates; those with NICM as the cause for structural heart disease and VT likely comprise a significant proportion of the former, as demonstrated by a more marked rate of in-hospital mortality and early VT recurrence in this study. Among the latter, with potentially less advanced or irreversible VT substrate, elimination of VT could affect the risk of death, and ablation should not be discounted for VT management solely because of the presence of advanced HF. Conversely, recurrence of VT within 30 days of ablation of a patient with NYHA IV HF should accelerate consideration for heart transplantation or other advanced therapies.

### Previous Investigations Into VT Ablation in Patients With Severe HF

There is little information on this group of patients because they generally have been excluded from VT ablation trials and observational studies in the past. The only exception to this practice may have been in the Prophylactic Catheter Ablation for the Prevention of Defibrillator Therapy Study, in which NYHA IV was not an exclusion criterion, but the number included (reported together with NYHA III patients, totaling 25 of 128 patients) was small.16 This is the first study to exclusively evaluate the role of VT ablation in this group of patients seldom brought to the electrophysiology laboratory.

### Catheter Ablation as a Treatment of Last Resort for HF Patients

The threshold to offer ablation as a therapeutic option for the management of ventricular arrhythmias is much higher for those patients with severe HF compared with others. Even in the IVTCC, which comprised highly experienced centers for VT ablation, patients with severe HF only represented 5% of the population of subjects studied. This reluctance is likely
because of the concerns related to potential safety of the procedure, which can be prolonged, may involve periods of time in VT/VF, may require multiple shocks for VT/VF termination, and may lead to progressive low-output deterioration. Many times, by the time a patient with severe HF is offered ablation, it is after all other therapies have been exhausted, and the quality of life and prognosis for these patients has been greatly diminished with VT storm or multiple shocks.

In keeping with these ideas, the patients with severe HF in this population were more likely to have a greater number of comorbidities and severity of VT/VF. More NYHA IV patients presented with VT storm or incessant VT, ICD shocks, and syncope, and significantly more had failed antiarrhythmic drug treatment, especially amiodarone. More had CRT-D in place and were on β-blocker therapy. Although the time course of arrhythmia development and treatments was unable to be examined in this database, the increased prevalence of comorbid disease and greater VT burden suggest that ablation in these patients may have been deferred until all other options had been exhausted. Certainly among this group were markers of more diseased and complex myocardial and arrhythmogenic substrate.

**Differences in Procedural Strategy to Safely Perform Catheter Ablation in Patients With Severe HF**

Despite significant differences in baseline and procedural characteristics, the acute complication rate between groups did not differ significantly. Further, the 10% complication rate observed among the NYHA IV patients was comparable to the 6% to 15% complication rate that has been reported in other single- and multi-center studies evaluating VT ablation in patients with structural heart disease and without the same degree of HF. Not surprisingly, operators chose to use hemodynamic support more often in these patients. This procedural characteristic may have allowed for greater safety in performing the ablation and minimizing hemodynamic compromise because of sedation or anesthesia effects, VT induction, and, in some cases, mapping during VT. Notably, effective substrate-based ablation approaches that minimized the need for repetitive inductions of VT, or mapping during VT, were used in the majority of patients because of the presence of unmappable VT, which likely also played a great role in minimizing intraprocedural hemodynamic instability.

**Association of Reduced Mortality With Successful VT Ablation in Patients With Severe HF**

One of the main findings of this analysis was the apparent association between lack of recurrent VT after ablation and reduced mortality in patients with severe HF. Successful ablation in this group may indicate the presence of myocardial substrate that is either less advanced or still amenable to modification with ablation, as opposed to unsuccessful ablation in which the substrate may be too extensive, localized to the midmyocardium, or functionally unable to be modified. Nevertheless, this association of improved survival with lack of recurrent VT after ablation has been described in patients with less severe HF; the magnitude of difference seems to be most pronounced in NYHA IV patients. In addition, the timing of recurrence was demonstrated to be important, with
greater mortality difference observed in those with VT recurrence within 30 days of ablation. The mean time to death after early recurrence was 31 days, suggesting that the recurrence itself may be closely linked to the mode of death. However, although an association has been demonstrated, causation is unable to be proven by our analyses.

CRT trials may provide the largest body of information on prognosis and natural history of patients with severe HF, with mortality rates approaching 15% to 20% at 1 year among patients treated with optimal medical therapy. However, most of these patients did not have a history of VT/VF, and the overwhelming majority had NYHA III HF at baseline; thus, direct comparisons with the NYHA IV patients in this study are limited. In a subgroup analysis of the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure trial, 1-year mortality rates of NYHA IV patients ranged from 30% (CRT-D patients) to 44% (optimal medical therapy only patients). Although direct comparison is similarly limited in that these also were primary prevention patients, who had not previously demonstrated VT, the high mortality rate underscores the baseline poor prognosis and is comparable to the death rate observed among the NYHA IV patients in this study. Further, the improved survival after successful VT ablation among NYHA IV patients in this study offers hope that some degree of disease reversibility could exist even among NYHA IV patients with refractory ventricular arrhythmias.

Our data suggest that earlier consideration of advanced HF treatment options, such as LVAD and transplant, should be given in those patients who have early recurrence after VT ablation because of the very strong association with subsequent mortality within the next year. Although our data are consistent with the possibility of recurrent VT/VF as causing earlier demise, the recurrence may also be a marker for more complex HF morbidity. We think that there may be biological plausibility for a potential survival benefit with successful VT ablation because of the subsequent reduction in ICD therapies and antiarrhythmic use, possibly leading to improvement in cardiac function, in a group of patients with tenuous myocardial substrate, although these beliefs at this point are speculative. While our study is not designed to address this specific question, clinicians caring for these patients should note the association between early recurrence of VT/VF and subsequent mortality regardless of its cause.

Selection biases may also have been present. For example, if ablation was only performed among NYHA IV subjects perceived to be lower risk or that were otherwise anticipated to have greater success than other NYHA IV subjects with VT/VF, results would be biased in favor of ablation. Similarly, if there were NYHA IV patients thought to be too high risk for ablation, for whom ablation was not considered and who instead underwent immediate LVAD implantation or heart transplantation, the applicability of our results to all patients with NYHA class IV status is limited. We feel that these potential biases do not significantly diminish our findings because the NYHA IV subjects who did undergo ablation were fairly representative of others with NYHA IV in terms of comorbidities, but with even higher acuity of presentation.

In this database, outcomes on patients with early VT recurrence were not followed to assess the important question of whether intermediate-term mortality could be improved with additional ablation. Additional prospective studies should be performed to further clarify this issue.

We were unable to differentiate between cardiac and non-cardiac causes of death, although, assuming that some of the mechanisms of death were either noncardiac or unrelated to ablation, assessing all-cause mortality as the end point would only have biased the differences observed toward the null. Unlike other analyses of VT ablation, we did not include cardiac transplantation as an end point with mortality. We think that success in this very sick group of patients with VT should include the potential prolongation of life by limiting VT/VF recurrence and subsequent progression to advanced HF therapies because pump failure and refractory HF would not be cured with VT ablation in most of these cases. Although a greater proportion of NYHA IV patients ultimately underwent cardiac transplantation, there was no significant difference in the 30-day mortality rates after transplant between the NYHA IV and NYHA II and III groups; the effect of not censoring these patients from analysis at the time of transplant should thus not have significantly affected results.

Additional limitations include the fact that data specifically on change in HF status immediately after procedures were not collected, including follow-up creatinine levels, fluid balance, increased diuretic use, or titration of HF medications. As reported in the current analysis, there were 2 NYHA II and III patients who experienced intraprocedural cardiac arrest and required either extracorporeal membrane oxygenation or LVAD implantation, but detailed analysis of postprocedure effects on HF was not within the scope of the current database. Also a potential limitation of the database is that past medical history elements were collected from chart review of documented physician assessments in medical records, which were assumed to be correct and were not routinely double checked for accuracy. For instance, if chronic kidney disease was documented within the past medical history, it would have been included as a comorbidity for the subject. Finally, the mode of death could not be demonstrated based on the data collected, including whether ICD shocks resulting from recurrent VT correlated with mortality.

Despite its limitations, this is the largest study to date investigating VT ablation in patients with severe HF and provides insight into the feasibility, safety, and outcomes of VT.

Limitations

The limitations and inherent potential biases involved in observational research must be considered when interpreting our results. For example, referral bias likely limits how much our study results can be generalized to the practice of VT ablation as a whole. Members of the IVTCC are all higher volume, tertiary referral VT ablation centers and thus may have different patient populations and results compared with less specialized, lower volume sites. Ablation of such patients in this study was performed not only at tertiary referral centers with advanced ablation experience but also with on-site capability for interdisciplinary collaboration; these factors should all be considered and included in the management of NYHA IV patients with VT.

Our data suggest that earlier consideration of advanced HF treatment options, such as LVAD and transplant, should be given in those patients who have early recurrence after VT ablation because of the very strong association with subsequent mortality within the next year. Although our data are consistent with the possibility of recurrent VT/VF as causing earlier demise, the recurrence may also be a marker for more complex HF morbidity. We think that there may be biological plausibility for a potential survival benefit with successful VT ablation because of the subsequent reduction in ICD therapies and antiarrhythmic use, possibly leading to improvement in cardiac function, in a group of patients with tenuous myocardial substrate, although these beliefs at this point are speculative. While our study is not designed to address this specific question, clinicians caring for these patients should note the association between early recurrence of VT/VF and subsequent mortality regardless of its cause.
ablation, as well as offers potential direction in management should ablation fail to control VT/VF in such patients.

Conclusions

Despite significantly greater baseline comorbidities, VT RFA can be performed among NYHA class IV patients with a similar safety profile using strategies to minimize hemodynamic instability compared with those with mild and moderate HF. Recognizing that patients with severe HF have more complex and difficult-to-treat arrhythmia substrate, VT ablation in this group has acceptable outcomes, and there is the potential for significant intermediate-term benefit in comparison to other HF patients. Early VT recurrence after ablation in patients with severe HF is strongly associated with subsequent mortality and should prompt consideration for advanced HF therapies in this select population of patients. The elimination of recurrent VT in patients with NYHA IV may reduce mortality in those with potentially less advanced myocardial substrate and failure to a level comparable to NYHA II and III HF with arrhythmia recurrence.

Appendix

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References


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