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## FREEDOM FROM RECURRENT VENTRICULAR TACHYCARDIA AFTER CATHETER ABLATION IS ASSOCIATED WITH IMPROVED SURVIVAL IN PATIENTS WITH STRUCTURAL HEART DISEASE:

AN INTERNATIONAL VT ABLATION CENTER COLLABORATIVE GROUP STUDY

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#### **CONFLICTS OF INTEREST:**

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#### Abstract

**Background**—The impact of catheter ablation of ventricular tachycardia (VT) on all-cause mortality remains unknown.

**Objective**—To examine the association between VT recurrence after ablation and survival in patients with scar-related VT.

**Methods**—Analysis of 2,061 patients with structural heart disease referred for catheter ablation of scar-related VT from 12 international centers was performed. Data on clinical and procedural variables, VT recurrence, and mortality were analyzed. Kaplan-Meier analysis was used to estimate freedom from recurrent VT, transplant, and death. Cox proportional hazards frailty models were used to analyze the effect of risk factors on VT recurrence and mortality.

**Results**—One-year freedom from VT recurrence was 70% (72% in ischemic and 68% in nonischemic cardiomyopathy). 57 (3%) patients underwent cardiac transplantation and 216 (10%) died during follow-up. At one year, the estimated rate of transplant and/or mortality was 15% (same for ischemic and non-ischemic cardiomyopathy). Transplant-free survival was significantly higher in patients without VT recurrence compared to those with recurrence (90% vs. 71%, p<0.001). In multivariable analysis, recurrence of VT after ablation showed the highest risk for

transplant and/or mortality (HR 6.9 (5.3-9.0); p<0.001). In patients with EF<30% and across all NYHA classes, improved transplant-free survival was seen in those without VT recurrence.

**Conclusions**—Catheter ablation of VT in patients with structural heart disease results in 70% freedom from VT recurrence, with an overall transplant and/or mortality rate of 15% at 1 year. Freedom from VT recurrence is associated with improved transplant-free survival, independent of heart failure severity.

#### Keywords

ablation; ventricular tachycardia

## INTRODUCTION

Catheter ablation has been shown to reduce recurrent ventricular tachycardia (VT) and appropriate implantable cardioverter-defibrillator (ICD) therapies in patients with structural heart disease.<sup>1</sup> It has been historically regarded as a palliative option to minimize the morbidity and adverse effects of ICD shocks on quality of life. By reducing ICD shocks and VT recurrence, it is plausible for catheter ablation to have a beneficial impact on mortality. Yet, data on patient outcomes after ablation has been limited to single-center observational cohorts, prospective multi-center registries, and small randomized trials primarily evaluating VT recurrence.<sup>2-11</sup> Therefore, the rate of survival in patients undergoing catheter ablation and the impact of VT recurrence on all-cause mortality in patients with structural heart disease is unknown. The aim of this study was to assess the outcomes of patients after catheter ablation and the impact of successful VT ablation on survival in patients with structural heart disease from the largest analysis of multi-center data to date.

## METHODS

International VT Ablation Center Collaborative Group (IVTCC)

The IVTCC includes 12 international sites that specialize in VT management (Supplemental Table 1) and have developed a shared database. Retrospective analysis of consecutive VT ablation procedures between 2002-2013 was performed at a coordinating center (UCLA) in patients that met the following inclusion criteria:

1) Structural heart disease with ischemic (ICM) and/or nonischemic (NICM) cardiomyopathy with left ventricular ejection fraction (EF) <55%. Left ventricular EF>55% was included in cases of RV and hypertrophic cardiomyopathy.

2) Catheter ablation for monomorphic VT

- 3) Myocardial scar identified with electroanatomic mapping
- 4) Clinical follow-up for VT recurrence, transplant, and mortality.

The diagnosis of ICM was established by history of myocardial infarction with focal wall motion abnormality or fixed perfusion defect correlated with coronary stenosis or prior coronary intervention. Etiologies for NICM included arrhythmogenic right ventricular cardiomyopathy (ARVC), hypertrophic, valvular, sarcoidosis, toxin-induced, congenital,

Chagasic, and idiopathic dilated cardiomyopathy. Collection of data was approved by Institutional Review Boards of the participating centers.

#### Ablation Procedure

The approach to ablation of VT across centers was substrate-based modification of scar guided by electroanatomic mapping. All procedures were performed under conscious sedation or general anesthesia with systemic intravenous anticoagulation administered when mapping the LV endocardium. Epicardial ablation was performed at the discretion of the operator and utilized the percutaneous technique described by Sosa et al.<sup>12</sup> In cases of prior cardiac surgery or adhesions that impaired the ability to map the epicardium, surgical access was used to perform epicardial mapping and ablation.<sup>13</sup> Hemodynamic support devices (extracorporeal membrane oxygenation, Impella (Abiomed, Danvers, MA), or intra-aortic balloon counterpulsation) were used at the discretion of the operator.

Programmed stimulation using up to two sites, with two drive drains and triple extrastimuli down to a minimum of 200ms or ventricular refractory period was performed for induction of VT. Electroanatomic maps were created during sinus rhythm using CARTO (Biosense Webster, Diamond Bar, CA) or NAVX (St. Jude Medical, Minneapolis, MN) with standard low voltage settings (<1.5mV).<sup>2</sup> Entrainment mapping was performed when VT was hemodynamically tolerated. An isthmus was defined by classical entrainment criteria as a site that demonstrated concealed fusion with a postpacing interval within 30 ms of the VT cycle length, where the stimulus to QRS interval was equal to EGM-QRS.<sup>14</sup> Pace-mapping was utilized to help localize ablation in regions where matches with the targeted VT were seen and sites with longer stimulus-QRS latency were ablated.<sup>15</sup> Regions of late activation or local conduction delay as evidence by split, fractionated or isolated late potentials were tagged and targeted for ablation.<sup>6,16</sup> The elimination of sustained monomorphic VT inducibility served as the common desired procedural endpoint and programmed stimulation was performed after ablation unless hemodynamic instability or procedural duration was prohibitive.<sup>1</sup>

RF ablation was performed using a standard non-irrigated catheter (Navi-Star, Biosense-Webster, Diamond Bar, CA), open-irrigated catheter (ThermoCool, ThermoCool SF, or Navistar RMT 3.5 mm, Biosense-Webster, Diamond Bar, CA) or closed-loop irrigated catheter (Chili, Boston Scientific, Natick MA) at 30-50W, temperature limit 42-45°C.

#### Follow-up and Endpoints

Data and follow-up from the most recent ablation was reported in patients who underwent multiple procedures. Patients were seen in follow-up with office visits and device interrogations to monitor for VT recurrence. Recurrent VT/VF was defined as documented sustained VT/VF or any appropriate ICD therapy, including anti-tachycardia pacing. The date of VT recurrence, cardiac transplant, or death was noted in addition to the last follow-up date. Antiarrhythmic therapy after ablation was at the discretion of the treating physician. Transplant-free survival in patients with follow-up to 12 months was assessed in those with and without recurrence of VT.

#### **Statistical Analysis**

Categorical variables are summarized as frequencies and percentages, and compared using chi-square or Fisher's exact tests. Continuous data are reported as mean±standard deviation or medians with 25%-75% percentiles. A two-sample Student's t-test or Wilcoxon rank-sum test was used to determine differences between groups.

Kaplan-Meier survival curves were used to estimate freedom from recurrent VT, transplant, and death. Separate Kaplan-Meier curves are displayed for patients with and without VT recurrence at one year to visualize differences in survival times. Log-rank tests were not performed because VT recurrence is time-dependent, which is explicitly modeled in the multivariable analyses. Subgroup analysis was performed in patients with ICM and NICM, EF < 30%, and NYHA class I-IV. Univariate analysis was used to evaluate the association of clinical and procedural variables on VT recurrence and mortality.

Multivariable Cox proportional hazards frailty model with VT recurrence as a timedependent covariate was used to analyze the association between VT recurrence and mortality adjusted for age, sex, EF, NYHA class, diabetes mellitus, chronic kidney disease, ischemic cardiomyopathy, atrial fibrillation, cardiac resynchronization (CRT), ICD shocks, VT storm (>3 episodes/24 hours), antiarrhythmics, prior ablation, beta-blockers, history of ICD, number of VTs induced, epicardial ablation, procedural time, procedural complications, hemodynamic support device, post-ablation noninducibility with centers as random effects. Additionally, interactions between EF and ICM with VT recurrence and NYHA class with VT recurrence were evaluated.

Incomplete variables were handled using a multiple imputation approach with 10 imputations for multivariable analysis; imputations were based on an iterative Markov chain Monte Carlo method and initial values were generated by an expectation–maximization algorithm (missing at random assumption). The number of observations was indicated in the univariate analysis. In addition to performing multiple imputation analysis for missing data, a Cox hazard regression analysis with frailty model of the subgroup of patients who had complete data was performed (n=751). The patient characteristics of patients with complete cases compared to those with missing variables (incomplete cases) are shown in (Supplemental Table 2). A p value of <0.05 was considered statistically significant. All analyses were performed using SAS 9.3 (SAS institute, Cary, NC).

## RESULTS

#### **Patient and Procedural Characteristics**

Between 2002 and 2013, 2,061 patients (87% male, median age 65 years (55-72 years)) underwent catheter ablation for scar-mediated VT at 12 centers with median follow-up of 527 days (208-1048 days). Complete follow-up through one year was available for 79% of the cohort with censoring of 444 patients before 1 year. The median EF was 31% (24-42%) and 29% of patients had NYHA class I, 37% NYHA class II, 28% NYHA class III, and 6% NYHA class IV functional status. Etiologies of NICM included 72% idiopathic, 9.2% ARVC, 5.0% valvular, 4.3% myocarditis, 3.6% hypertrophic, 1.8% congenital, 0.8% toxin-induced, and 0.1% Chagasic cardiomyopathy.

An ICD was present in 87% of the population, and 26% had CRT. The presenting indication for ablation was ICD shocks in 65% and electrical storm (>3 VT episodes in 24 hours) in 35%. Medical therapy included beta blockers in 79% and amiodarone in 55%. Overall, 18% of the population was refractory to 2 antiarrhythmic drugs and 39% had a history of prior ablation (1, n=536 and 2, n=276). The baseline patient characteristics are summarized in TABLE 1.

Procedural characteristics are shown in TABLE 2. A median of 2 VTs was induced per patient, with 12% having no inducible VT throughout the procedure. In 56% of patients, induced VT was unmappable due to hemodynamic instability. Epicardial ablation was performed in 25% of cases. After ablation, 67% of patients were non-inducible for sustained monomorphic VT, although 5% were not tested.

#### Safety and Efficacy

Procedure-related complications occurred in 127 (6%) patients. Of these, 2 patients (0.1%) died during the procedure and 6 (0.3%) required cardiopulmonary resuscitation. 35 (1.7%) cases were complicated by hemopericardium (16 related to epicardial approach), with 8 patients (0.4%) requiring surgical intervention. Complications related to vascular access occurred in 32 (1.6%) patients. Stroke or transient ischemic attack was observed in 10 patients (0.5%), heart block in 19 (0.9%), venous thrombo-embolism in 7 (0.3%), and coronary artery injury in 4 (0.2%).

Freedom from VT recurrence in the overall cohort was 70% (72% in patients with ICM and 68% in NICM), with 28% patients taking amiodarone and 10% on other anti-arrhythmic drugs. (FIGURE 1) During follow-up, 57 (3%) patients underwent cardiac transplantation (12% for refractory VT, 68% for advanced heart failure, and 20% for both) and 216 (10%) died. The estimated rate of transplant and/or death was 15% (ICM: 15%, NICM: 15%) at one year. Kaplan-Meier estimate for the combined freedom from VT recurrence, transplant, and mortality was 70% (72% in patients with ICM and 67% in NICM) at one year. (FIGURE 2) Amongst patients without prior ablation, outcomes were similar to the overall cohort, with 73% freedom from VT recurrence, transplant, and mortality.

Amongst patients who died, a higher rate of VT recurrence was observed compared to those who survived (55% vs. 22%, p<0.001). The one-year overall probability of transplant-free survival was higher in patients without VT recurrence compared to those who recurred (90% vs. 71%). (FIGURE 3). The observed difference was independent of cardiomyopathy type (ICM: 89% vs. 72%, p<0.001; NICM: 92% vs. 72%, p<0.001).

#### **Predictors Of VT Recurrence**

Patients with recurrent VT were more likely to have NICM, advanced NYHA status, ICD, CRT, lower EF, electrical storm, shocks, 2 antiarrhythmic drugs. (TABLE 1) During the procedure, epicardial ablation, a greater number of induced VTs, longer procedure time, and sustained monomorphic VT post-ablation was observed more frequently in patients with VT recurrence. (TABLE 2) Univariate Cox analysis is shown in Supplemental Table 3.

In the Cox multiple regression frailty analysis, the highest probability of VT recurrence was associated with increasing NYHA class, female gender, 2 antiarrhythmic drugs, electrical storm, deferred post-ablation testing, and any sustained monomorphic VT inducible after ablation. Ischemic cardiomyopathy and higher EF were associated with lower probability of VT recurrence. (FIGURE 4)

#### **Predictors Of Transplant and Mortality**

Patients who died or underwent transplant were older and had higher rates of hyperlipidemia, diabetes mellitus, atrial fibrillation, chronic kidney disease, advanced heart failure, ICD, CRT, lower EF, electrical storm, shocks, amiodarone, and 2 antiarrhythmic drugs. (TABLE 1) During the procedure, patients who died were more likely to have hemodynamic support devices used, a greater number of VTs induced, procedural complications, and longer procedural times. A higher rate of mappable VTs and noninducibility post-ablation was observed in patients who survived. (TABLE 2) Univariate Cox analysis is shown in Supplemental Table 4.

In the Cox multiple regression frailty analysis, transplant or death was associated with older age, NYHA class III and IV, chronic kidney disease, electrical storm, and use of hemodynamic support devices. While deferred post-ablation testing (HR 1.972 (1.248-3.116); p=0.004) and inducibility of any sustained monomorphic VT post-ablation (HR 1.994 (1.480-2.687); p<0.001) were associated with a higher probability of transplant or death, recurrence of VT after ablation was associated with the highest risk (HR 6.901 (5.282-9.017); p<0.001). Higher EF was associated with a lower probability for transplant or death. (FIGURE 4) Complete-case analysis showed a higher hazard ratio (HR 9.796 (6.137-15.636); p<0.001) for mortality with VT recurrence as compared to multiple imputation analysis. (Supplemental FIGURE 1)

#### Interaction of recurrence, HF status, and EF with mortality

On both univariate and multivariable analysis, higher rates of both VT recurrence and mortality were observed in patients with lower EF and higher NYHA status. Subgroup analysis of patients with EF <30% demonstrated that for both ICM and NICM, patients without VT recurrence had improved transplant-free survival compared to those with VT recurrence (83% vs. 59%, adjusted HR 8.345 (5.607-12.422); p<0.001 for VT recurrence) and (81% vs. 53%, adjusted HR of 6.746 (4.211-10.807); p<0.001 for VT recurrence), respectively. The same trend was seen in patients with EF 30 in ICM patients (93% vs. 89%, adjusted HR 3.190 (1.517-6.707); p=0.002 for VT recurrence) and NICM patients (96% vs. 84%, adjusted HR 9.293 (4.867-17.743); p<0.001 for VT recurrence). (FIGURE 5)

Analysis of mortality by heart failure status demonstrated a consistent improvement in transplant-free survival in patients without VT recurrence compared to those with recurrence across NYHA I (97% vs. 85%, adjusted HR 8.338 (3.616-19.229); p<0.001 for VT recurrence), NYHA II (92% vs. 79%, adjusted HR 6.842 (4.196-11.157); p<0.001 for VT recurrence), NYHA III (85% vs. 59%, adjusted HR 6.681 (4.466-9.994); p<0.001 for VT recurrence) and NYHA IV (65% vs. 31%, adjusted HR 6.911 (3.959-12.064); p<0.001 for

VT recurrence) functional classes with a larger differential risk for mortality seen with increasing heart failure severity. (FIGURE 6)

Kaplan-Meier estimates suggest that NYHA IV patients without recurrence had comparable transplant-free survival compared to NYHA III patients with recurrent VT (65% vs. 59%) and NYHA III patients without recurrence had comparable transplant-free survival compared to NYHA II patients with VT recurrence (85% vs. 79%). NYHA II patients without recurrence seemed to have improved statistically significant transplant-free survival compared to NYHA I patients with recurrent VT (92% vs. 85%)

## DISCUSSION

The present study draws upon some of the most experienced centers around the world and demonstrates that catheter ablation of scar-related VT results in a 70% freedom from VT recurrence, transplant, and mortality at one year. Patients referred for VT ablation have a transplant/mortality rate of 15% at one year. Freedom from recurrent VT after catheter ablation is strongly associated with a significant reduction in all-cause mortality, independent of EF and heart failure status.

Catheter ablation has been shown to decrease VT recurrence in patients presenting with ICD shocks and electrical storm across observational cohort studies and randomized trials.<sup>2,4,8-11,17,18</sup> However, freedom from VT recurrence has been associated with improved survival only in a few single-center studies specializing in VT ablation <sup>19-21</sup>, limiting the generalizability of these results. This present data represents the largest study to date to assess the outcomes, and in particular, survival of patients with catheter ablation of VT using data from multiple centers.

Large sample sizes are required to assess for incremental mortality benefit of catheter ablation beyond ICD implantation. Recently, ICD shocks and therapy have been shown to be predictive of increased mortality<sup>22,23</sup>, highlighting the biologic plausibility for improvement in survival with successful catheter ablation. Shocks have the potential to be deleterious possibly by worsening heart failure, where ICDs appeared to shift the mode of death towards an increase in non-arrhythmic mortality, offsetting arrhythmic mortality benefit in the immediate post-infarct period.<sup>24,25</sup> Alternatively, ventricular arrhythmias that prompt ICD therapy may reflect more advanced disease. Goldenberg et al. highlighted a Ushaped relationship between the severity of heart failure and mortality benefit from ICD therapy.<sup>26</sup> Regardless of the mechanisms underlying worsened outcomes with ICD therapies, the present analysis demonstrates that the association of improved mortality in patients without recurrence after ablation was seen across all NYHA classes, with a greater hazard ratio in patients with lower EF and more advanced heart failure. Patients without VT recurrence after ablation with NYHA IV and NYHA III status had similar transplant-free survival compared to patients with recurrent VT in NYHA III and NYHA II, respectively, suggesting that catheter ablation therapy may not have a U-shaped therapeutic curve, but rather an increasing benefit with advancing heart failure severity.

This multi-center experience demonstrates an overall improvement in the success rate of scar-related VT ablation (70%) compared with a ~50% freedom from VT previously reported<sup>8-10</sup>, which may contribute to the lower one-year mortality rate observed (10% vs. 18% in the Multicenter ThermoCool Ventricular Tachycardia Ablation Trial). As the field of catheter ablation has advanced over the past decade, the implementation of electroanatomic mapping, irrigated ablation technology<sup>9</sup>, epicardial mapping and ablation<sup>27,28</sup>, imaging<sup>29</sup>, improved identification of critical sites during sinus rhythm<sup>30</sup>, and more extensive ablation aimed to homogenize scar<sup>5,6,31</sup> have likely improved efficacy.

Consistent with previous studies, lower EF, advanced NYHA, and multiple VT morphologies are associated with higher recurrence rates.<sup>9,19,32</sup> The observed increase in mortality associated with use of hemodynamic support devices may reflect their discretionary implementation as a marker of disease severity. Patients with NICM have been shown to have inferior outcomes relative to ICM due to the heterogeneous nature of disease and differences in scar biology which may reduce ablation targets and increase VT recurrence.<sup>33</sup> As NICM is a heterogeneous and frequently idiopathic condition, we chose to include multiple etiologies with the requirement that VT was related to scar identified on electroanatomic mapping.

Acute procedural success has been shown to have prognostic implications for mortality in single-center studies and a recent meta-analysis.<sup>4,19,21,34</sup> In the present analysis, success after catheter ablation was defined as freedom from VT recurrence. Assessing acute procedural success with programmed stimulation has three major limitations: extrastimulus testing has been shown to have variable reproducibility <sup>8,35</sup>, some patients are noninducible prior to ablation, and VT induction is frequently less aggressive or deferred post-ablation due to concerns of prolonged procedure time and hemodynamic instability. The results of the present study underscore these limitations as 12% were noninducible pre-ablation, 5% were not tested post-ablation, and 58% of patients rendered noninducible for any monomorphic VT post-ablation had recurrence at follow-up. Despite these limitations, noninducibility still serves as the most commonly employed procedural endpoint and was predictive of both VT recurrence and mortality in this study.

### LIMITATIONS

The present analysis is retrospective and represents outcomes at specialized tertiary referral centers. Given the expertise of the centers in catheter ablation of VT, the results may not be completely applicable to centers that do not perform these procedures as frequently. Further, many ablation procedures performed at referral centers are after initial attempts fail. Although the approach to catheter ablation of VT is similar, there is inevitably individual practice variability across centers, which prompted frailty analysis. Due to the retrospective multi-center nature of this study, some clinical and procedural characteristics were not available for analysis. Therefore, multivariable analysis was performed by two methods, using multiple imputation techniques and complete-case analysis. The cohort with incomplete variables was sicker than those with complete data, which lead to a conservative estimate of the association between VT recurrence and mortality using imputation. The hazard ratio for VT recurrence when using the complete cases was even higher than that

derived by the multiple imputation analysis, suggesting that the multiple imputation hazard ratio is a more conservative estimate of the actual risk. Nonetheless, this data comprises the largest collection of outcomes after VT ablation in patients with structural heart disease.

A causal relationship between VT recurrence and mortality cannot be concluded based on this analysis as clinical variables not accounted for may influence both the propensity for VT recurrence and mortality. There is a possibility that patients who were referred for ablation were inherently different from patients who were not. Additionally, ICD programming was not uniform across patients. This study highlights the need for prospective randomized clinical trials to examine the impact of ablation on survival as VT ablation is still perceived as a palliative therapy of last resort.

## CONCLUSIONS

Catheter ablation of VT in patients with structural heart disease results in a 70% freedom from recurrence, with an overall combined transplant and mortality rate of 15% at one year. Freedom from VT recurrence after catheter ablation is strongly associated with improved transplant-free survival, independent of heart failure severity. Successful VT ablation may have benefit beyond arrhythmia control, supporting a shift from its current role as a therapy of last resort.

## **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations

VT	ventricular tachycardia
ICD	implantable cardioverter defibrillator
EF	ejection fraction
NYHA	New York Heart Association

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#### **CLINICAL PERSPECTIVE**

Catheter ablation has been shown to decrease recurrence of VT and ICD shocks. In clinical practice, it has historically been implemented as a last resort strategy. Given that ICD shocks have been strongly correlated with increased risk for mortality in patients with heart failure, it is plausible that successful catheter ablation may improve survival. As the majority of VT ablation studies are limited by sample size and power due to the specialized nature of the procedure, the present multi-center retrospective study is the largest to date to examine the relationship between VT recurrence and mortality. The major findings of this present analysis are that freedom from VT recurrence after catheter ablation is strongly associated with improved transplant-free survival, independent of ejection fraction and heart failure severity. This signal supports the transition of catheter ablation to a more preemptive strategy in the management of patients with structural heart disease and VT. Prospective clinical trials are necessary and ongoing to examine the potential mortality impact of catheter ablation.



**FIGURE 1.** Kaplan-Meier estimate of freedom from VT in the overall cohort.



**FIGURE 2.** Kaplan-Meier estimate of VT and transplant-free survival in the overall cohort.



## FIGURE 3.

Kaplan-Meier display of transplant-free survival between patients with and without VT recurrence.

Effect	Transplant/Mortality	Hazard Ratio (95% CI)	P	VT Recurrence	Hazard Ratio (95% CI)	P
Patient Characteristics	1	10		1	and the second	
ICD-	H++++	0.685 (0.376 - 1.245)	0.214	H + I	1.328 (0.910 - 1.940)	0.141
EF Pre-Ablation (+5%)-	•	0.858 (0.796 - 0.925)	<0.001	*	0.936 (0.895 - 0.980)	0.004
Beta-Blocker-	H-	0.878 (0.620 - 1.244)	0.464	H-4	0.958 (0.758 - 1.213)	0.724
Ischemic Cardiomyopathy-	H+H	0.999 (0.753 - 1.325)	0.994	H++ 1	0.613 (0.502 - 0.749)	<0.001
Atrial Fibrillation-	H	1.028 (0.782 - 1.352)	0.843	<b>⊢</b> ♠–1	1.000 (0.805 - 1.243)	0.999
Amiodarone -	H	1.057 (0.767 - 1.456)	0.737	⊢ <del>•</del> ∺	0.914 (0.745 - 1.123)	0.392
≥2.AAD-	H	1.062 (0.774 - 1.458)	0.708	3	1.295 (1.031 - 1.626)	0.026
Age (+5y)-	•	1.066 (1.001 - 1.136)	0.048		1.031 (0.991 - 1.074)	0.130
ICD Shocks-	H H	1.104 (0.782 - 1.559)	0.573	<b>⊢</b> ●	1.266 (0.986 - 1.625)	0.064
Prior VT Ablations (+1)-	(e)	1.112 (0.971 - 1.273)	0.126	IHI	1.030 (0.933 - 1.136)	0.563
Female-	1-0-1	1.187 (0.806 - 1.747)	0.386	·	1.395 (1.087 - 1.791)	0.009
CRT-	H+H	1.204 (0.913 - 1.587)	0.188	1++-1	1.141 (0.924 - 1.410)	0.220
Diabetes Mellitus-	H+H	1.369 (1.036 - 1.809)	0.027	H-	1.132 (0.913 - 1.402)	0.259
Chronic Kidney Disease	1+++	1.438 (1.094 - 1.891)	0.009	H-	1.083 (0.880 - 1.332)	0.453
Electrical Storm-	iii 🕂	1.499 (1.135 - 1.980)	0.004	1- <b>-</b> -1	1.285 (1.060 - 1.557)	0.011
NYHA: II v. I-		1.506 (0.914 - 2.479)	0.108	1	1.409 (1.078 - 1.842)	0.012
NYHA: III v. I-	1 H-	2.308 (1.403 - 3.798)	0.001	1	1.447 (1.068 - 1.961)	0.017
NYHA: IV v. I-	1 H-	3.681 (2.004 - 6.760)	<0.001	1	1.734 (1.115 - 2.697)	0.015
Procedural Characteristics				1		
Ablation: Epi v. Endo-	H-+	0.767 (0.379 - 1.552)	0.461		0.812 (0.538 - 1.225)	0.320
Ablation: Endo + Epi v. Endo-	H	0.959 (0.665 - 1.385)	0.825	<b>→</b>	1.026 (0.798 - 1.319)	0.841
Procedure Time (+15m)-	•	0.996 (0.975 - 1.017)	0.697	•	1.014 (0.999 - 1.030)	0.067
VTs Induced: 1 v. 0-	H-	1.285 (0.703 - 2.350)	0.416		0.955 (0.678 - 1.345)	0.792
VTs induced: 2 v. 0-	1	1.625 (0.900 - 2.935)	0.107	1	1,304 (0.915 - 1,858)	0.142
VTs Induced: ≥ 3 v. 0-	1	1.522 (0.851 - 2.721)	0.157	<u>k</u>	1,350 (0.951 - 1.918)	0.093
Procedural Complications-	H-	1.298 (0.836 - 2.015)	0.246		0.803 (0.539 - 1.197)	0.281
Hemodynamic Support Device-	1	2.128 (1.415 - 3.199)	<0.001		1.023 (0.684 - 1.532)	0.910
Outcomes						
Acute: Not Tested v. NI-	11	1.972 (1.248 - 3.116)	0.004		1.581 (1.080 - 2.315)	0.019
Acuto: Partial/Failure v. NI-	1.00	1.994 (1.480 - 2.687)	<0.001	· • • •	1,375 (1,112 - 1,699)	0.003
WT December 1		6 901 (5 282 - 9 017)	<0.001	1		

#### FIGURE 4.

Hazard ratio plot of multivariable Cox proportional hazard regression for transplant/ mortality and VT recurrence.



#### FIGURE 5.

Kaplan-Meier display of transplant-free survival by VT recurrence in patients with EF greater and less than 30%.



#### FIGURE 6.

Kaplan-Meier display of transplant-free survival by VT recurrence in in patients by NYHA class.

Patient characteristics by VT recurrence and mortality

	VT Recurre	ence within 12 Mon	ths	Transplant/I	eath within 12 Mc	onths
N (%) or median (Q1-Q3)	Yes (N=536)	No (N=1525)	p value	Yes (N=273)	No (N=1788)	p value
Age (y)	65.0 (55.0-72.0)	64.0 (54.0-72.0)	0.341	66.0 (59.0-74.0)	64.0 (54.0-72.0)	<0.001
Female	81 (15.1)	185 (12.1)	0.083	35 (12.8)	230 (12.9)	1
ICM	257 (47.9)	838 (55.0)	0.006	147 (53.8)	948 (53.0)	0.850
EF Pre-Ablation	28.0 (20.0-40.0)	35.0 (25.0-45.0)	<0.001	24.0 (20.0-30.0)	35.0 (25.0-45.0)	<0.001
NYHA			<0.001			<0.001
Ι	92 (18.8)	466 (32.5)		23 (8.9)	535 (32.1)	
П	193 (39.5)	525 (36.6)		71 (27.6)	647 (38.8)	
Ш	164 (33.5)	372 (25.9)		113 (44.0)	423 (25.4)	
IV	40 (8.2)	71 (5.0)		50 (19.5)	61 (3.7)	
ICD	487 (92.8)	1251 (84.2)	<0.001	250 (94.7)	1488 (85.2)	<0.001
CRT	165 (31.4)	348 (23.4)	<0.001	107 (40.5)	406 (23.3)	<0.001
Electrical Storm	220 (43.8)	464 (32.3)	<0.001	147 (57.4)	537 (31.9)	<0.001
ICD Shocks	344 (72.7)	869 (62.7)	<0.001	176 (76.2)	1037 (63.7)	<0.001
Hypertension	285 (58.8)	753 (56.4)	0.407	140 (58.6)	898 (56.8)	0.662
Atrial Fibrillation	163 (33.5)	394 (28.7)	0.052	97 (39.3)	460 (28.5)	0.004
Diabetes Mellitus	128 (24.4)	305 (20.6)	0.073	92 (35.4)	341 (19.5)	<0.001
Chronic Kidney Disease	169 (31.7)	436 (28.7)	0.213	126 (46.5)	479 (26.9)	<0.001
Baseline Creatinine	1.1 (0.9-1.5)	1.1 (0.9-1.4)	0.199	1.3 (1.0-1.7)	1.1 (0.9-1.3)	<0.001
Beta-Blocker	433 (81.5)	1173 (78.3)	0.123	226 (83.7)	1380 (78.4)	0.056
Amiodarone	283 (59.1)	737 (54.0)	0.061	172 (71.1)	848 (52.9)	<0.001
2 AAD	110 (23.0)	228 (16.7)	0.003	66 (27.3)	272 (17.0)	<0.001
Prior VT Ablations	0.0 (0.0-1.0)	$0.0\ (0.0-1.0)$	0.019	$0.0\ (0.0-1.0)$	$0.00\ (0.0-1.0)$	0.001
Min-Max	0.0-7.0	0.0-10.0		0.0-6.0	0.0-10.0	

Procedural characteristics by VT recurrence and mortality

	VT Recurrence v	vithin 12 Months		Transplant/Death	within 12 Months	
N (%) or median (Q1-Q3)	Yes (N=536)	No (N=1525)	p value	Yes (N=273)	No (N=1788)	p value
Hemodynamic Support Device	32 (7.9)	63 (5.3)	0.068	39 (19.9)	56 (4.0)	<0.001
Epicardial Access	178 (37.5)	404 (29.3)	0.001	83 (33.7)	499 (31.1)	0.440
Ablation			0.040			0.131
Endo	350 (72.2)	1049 (75.6)		186 (74.1)	1213 (74.8)	
Epi	24 (4.9)	94 (6.8)		9 (3.6)	109 (6.7)	
Endo+Epi	106 (21.9)	236 (17.0)		54 (21.5)	288 (17.8)	
Number of VTs Induced			<0.001			<0.001
0	40 (8.4)	176 (12.7)		15 (6.0)	201 (12.5)	
1	116 (24.4)	503 (36.2)		52 (20.8)	567 (35.2)	
2	131 (27.6)	318 (22.9)		72 (28.8)	377 (23.4)	
3	188 (39.6)	391 (28.2)		111 (44.4)	468 (29.0)	
VT Mappability			0.193			<0.001
All Unmappable	149 (40.4)	394 (38.8)		93 (46.3)	450 (38.0)	
All Mappable	150 (40.7)	462 (45.5)		63 (31.3)	549 (46.4)	
Both Unmappable and						
Mappable	70 (19.0)	160 (15.7)		45 (22.4)	185 (15.6)	
Fastest TCL	340 (290-394)	330 (280-392)	0.563	362 (310-428)	330 (280-390)	<0.001
Slowest TCL	410 (344-500)	390 (323-470)	0.012	450 (380-540)	384 (320-460)	<0.001
Acute Outcome			<0.001			<0.001
Noninducible	286 (57.5)	991 (70.5)		105 (42.5)	1172 (70.8)	
Partial/Failure	176 (35.4)	365 (26.0)		116 (47.0)	425 (25.7)	
Not Tested	35 (7.0)	50 (3.6)		26 (10.5)	59 (3.6)	
Total Lesion Time (m)	35.5 (20.2-54.0)	32.1 (17.0-53.8)	0.392	38.1 (24.1-60.5)	32.0 (17.0-53.2)	0.012
Procedure Time (m)	294.0 (222.0-390.0)	247.4 (187.1-339.9)	<0.001	300 (230-418)	251 (193-344)	<0.001
Procedural Complications	30 (6.3)	07 (7.0)	0.671	30 (12.3)	97 (6.0)	<0.001

## Univariate Cox analysis for VT recurrence

	HR (95% CI)	P value
Age (+5y)	1.033 (1.000, 1.068)	0.051
Female	1.306 (1.031, 1.654)	0.027
ICM	0.810 (0.684, 0.959)	0.015
EF Pre-Ablation (+5%)	0.871 (0.841, 0.902)	< 0.001
NYHA (Ref=I)		
II	1.721 (1.343, 2.206)	< 0.001
III	2.077 (1.609, 2.682)	< 0.001
IV	2.811 (1.939, 4.075)	< 0.001
ICD	2.361 (1.697, 3.285)	< 0.001
CRT	1.524 (1.268, 1.833)	< 0.001
Electrical Storm	1.583 (1.327, 1.888)	< 0.001
ICD Shocks	1.714 (1.400, 2.099)	< 0.001
Syncope	1.064 (0.779, 1.453)	0.697
Prior VT Ablation	1.159 (1.065, 1.261)	< 0.001
Prior Heart Surgery	1.023 (0.842, 1.243)	0.820
Hypertension	1.123 (0.937, 1.346)	0.208
Hyperlipidemia	1.224 (1.019, 1.470)	0.030
Atrial Fibrillation	1.209 (1.002, 1.460)	0.048
Diabetes Mellitus	1.343 (1.100, 1.640)	0.004
Chronic Kidney Disease	1.308 (1.089, 1.570)	0.004
Baseline Creatinine	1.165 (1.052, 1.290)	0.003
Amiodarone	1.237 (1.031, 1.484)	0.022
2 AAD	1.522 (1.230, 1.883)	< 0.001
Beta Blocker	1.251 (1.005, 1.558)	0.045
Hemodynamic Support Device	1.727 (1.203, 2.478)	0.003
Epi Access	1.316 (1.093, 1.585)	0.004
Ablation (Ref=Endo)		
None	2.272 (0.940, 5.490)	0.068
Epi	0.761 (0.503, 1.151)	0.196
Endo+Epi	1.237 (0.995, 1.537)	0.055
Number of VTs Induced		
1	1.031 (0.719, 1.476)	0.870
2	1.867 (1.310, 2.660)	< 0.001
3	2.226 (1.582, 3.133)	< 0.001
VT Mappability (Ref=All Unmappable)		
Both Unmappable and Mappable	1.291 (0.972, 1.716)	0.078
All Mappable	0.765 (0.610, 0.959)	0.021

	HR (95% CI)	P value
Total Lesion Time	1.000 (0.997, 1.004)	0.832
Procedure Time (+15m)	1.031 (1.020, 1.043)	< 0.001
Acute Outcome		
Not Tested	2.400 (1.689, 3.410)	< 0.001
Partial/Failure	1.845 (1.529, 2.227)	< 0.001
Procedural Complications	1.098 (0.759, 1.590)	0.619

#### Univariate Cox analysis for transplant/mortality

	HR (95% CI)	P value
Age (+5y)	1.153 (1.094, 1.216)	< 0.001
Female	0.997 (0.692, 1.437)	0.989
ICM	1.139 (0.891, 1.455)	0.298
EF Pre-Ablation (+5%)	0.696 (0.655, 0.739)	< 0.001
NYHA (Ref=I)		
П	2.361 (1.457, 3.824)	< 0.001
III	5.483 (3.466, 8.672)	< 0.001
IV	13.525 (8.149,	< 0.001
ICD	2.983 (1.741, 5.113)	< 0.001
CRT	2.192 (1.705, 2.818)	< 0.001
Electrical Storm	2.639 (2.047, 3.403)	< 0.001
ICD Shocks	2.008 (1.477, 2.731)	< 0.001
Syncope	1.244 (0.806, 1.921)	0.324
Prior VT Ablation	1.214 (1.087, 1.355)	< 0.001
Prior Heart Surgery	1.188 (0.906, 1.558)	0.212
Hypertension	1.093 (0.839, 1.425)	0.510
Hyperlipidemia	1.426 (1.080, 1.882)	0.012
Atrial Fibrillation	1.474 (1.131, 1.920)	0.004
Diabetes Mellitus	2.186 (1.682, 2.841)	< 0.001
Chronic Kidney Disease	2.589 (2.027, 3.308)	< 0.001
Baseline Creatinine	1.382 (1.271, 1.503)	< 0.001
Amiodarone	2.125 (1.599, 2.823)	< 0.001
2 AAD	1.822 (1.364, 2.434)	< 0.001
Beta Blocker	1.340 (0.969, 1.854)	0.077
Hemodynamic Support Device	4.847 (3.399, 6.913)	< 0.001
Epi Access	1.104 (0.843, 1.446)	0.474
Ablation (Ref=Endo)		
None	1.366 (0.339, 5.506)	0.661
Ері	0.569 (0.291, 1.111)	0.098
Endo+Epi	1.151 (0.843, 1.571)	0.376
Number of VTs Induced		
1	1.218 (0.685, 2.165)	0.503
2	2.535 (1.452, 4.429)	0.001
3	2.936 (1.706, 5.052)	< 0.001
VT Mappability (Ref=All Unmappable)		
Both Unmappable and Mappable	1.336 (0.933, 1.913)	0.114
All Mappable	0.542 (0.391, 0.751)	< 0.001

	HR (95% CI)	P value
Total Lesion Time	1.004 (1.000, 1.008)	0.077
Procedure Time (+15m)	1.033 (1.016, 1.049)	< 0.001
Acute Outcome		
Not Tested	4.272 (2.740, 6.660)	< 0.001
Partial/Failure	3.028 (2.318, 3.955)	< 0.001
Procedural Complications	2.300 (1.559, 3.393)	< 0.001