# Effect of Baseline Antiarrhythmic Drug on Outcomes With Ablation in Ischemic Ventricular Tachycardia

## A VANISH Substudy (Ventricular Tachycardia Ablation Versus Escalated Antiarrhythmic Drug Therapy in Ischemic Heart Disease)

**BACKGROUND:** The VANISH trial (Ventricular Tachycardia Ablation Versus Escalated Antiarrhythmic Drug Therapy in Ischemic Heart Disease) compared the effectiveness of escalated antiarrhythmic drug therapy to catheter ablation in patients with prior myocardial infarction, an implanted defibrillator, and ventricular tachycardia (VT). The effectiveness of these interventions in patients on sotalol versus amiodarone was compared.

**METHODS AND RESULTS:** Analysis was conducted based on whether patients had recurrent VT, despite amiodarone (amio-refractory) or nonamiodarone drugs (sotalol-refractory). Outcomes included death, VT storm, appropriate implantable cardioverter defibrillator shock, and any ventricular arrhythmia. At baseline, 169 (65.2%) were amio-refractory, and 90 (34.7%) were sotalol-refractory (1 patient on procainamide rather than sotalol). Amio-refractory patients had more renal insufficiency (23.7% versus 10%; *P*=0.0008), worse New York Heart Association class (82.3% II/III versus 65.5%; *P*=0.0003), and lower ejection fraction (29±9.7% versus 35.2±11%; *P*<0.0001). Within the amio-refractory group, ablation resulted in reduction of any ventricular arrhythmia compared with escalated drug therapy (hazard ratio, 0.53; 95% confidence interval, 0.31–0.9), *P*=0.020). Sotalol-refractory patients had trends toward higher mortality and VT storm with ablation, with no effect on implantable cardioverter defibrillator shocks. Within the escalated drug therapy arm, amio-refractory patients had a higher rate of the composite outcome (hazard ratio, 1.94; 95% confidence interval, 1.14–3.29; *P*=0.0144) and a trend to higher mortality (hazard ratio, 2.40; 95% confidence interval, 0.93–6.22; *P*=0.07), whereas mortality was not different between amio- and sotalol-refractory patients within the ablation treatment group.

**CONCLUSIONS:** Patients with amio-refractory VT have a higher rate of ventricular arrhythmia and mortality than those with sotalol-refractory VT and derive greater benefit of catheter ablation than for patients with sotalol-refractory VT who are switched to amiodarone.

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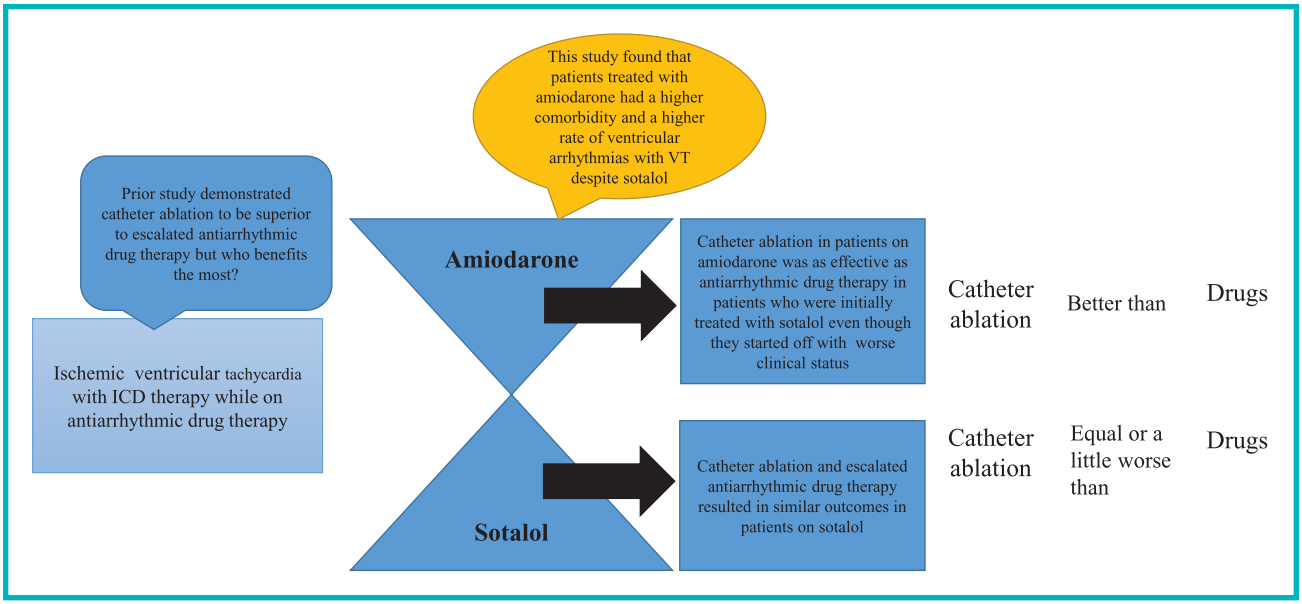


## WHAT IS KNOWN?

- Catheter ablation has been proven to be superior to antiarrhythmic drugs to prevent recurrent ventricular arrhythmia and death in patients with ischemic heart disease. Treatment-attributed adverse events were also lower with catheter ablation than with escalated drug therapy in these patients.

## WHAT THE STUDY ADDS?

- Patients were more ill on amiodarone.
- Mortality was higher in patients on amiodarone but was no longer significant after adjusting for baseline differences.
- In patients on sotalol, amiodarone as the next step in therapy resulted in the same outcomes as ablation, whereas in patients on amiodarone, catheter ablation led to improved outcomes.
- Patients who have failed amiodarone therapy likely have an arrhythmic substrate that will be less responsive to additional medical therapy, and catheter ablation provides the greatest benefit.

Ventricular tachycardia (VT) in the setting of ischemic heart disease is known to portend a poor prognosis.[1,2] Implantable cardioverter defibrillators (ICDs) have demonstrated a reduction in mortality in the setting of ischemic heart disease both in patients who presented with prior ventricular arrhythmia and those with reduced ejection fraction, found to be at risk.[1–4] Subsequent analyses have demonstrated that ICD shocks are associated with an increase in mortality[5–7] and reduced quality of life.[8–10] Catheter ablation for patients with ischemic cardiomyopathy and VT despite first-line antiarrhythmic drug therapy was superior to escalation of antiarrhythmic pharmacotherapy in the VANISH study (Ventricular Tachycardia Ablation Versus Escalated Antiarrhythmic Drug Therapy in Ischemic Heart Disease), with a 28% relative risk reduction in a composite end point of mortality, VT storm, or ICD shock.[11] Patients in this study were enrolled with VT occurring during administration of amiodarone (n=169) or nonamiodarone antiarrhythmic drugs (sotalol, n=89; procainamide, n=1); randomization was stratified by whether patients had VT, despite amiodarone (amio-refractory) or nonamiodarone (sotalol-refractory). Sotalol-refractory patients were randomly treated with either amiodarone or catheter ablation, whereas amio-refractory patients were randomly treated with escalated drug dosing (amiodarone reloading and higher dose or addition of mexiletine) or catheter ablation. The amio-refractory group had a greater relative reduction in the primary outcome with catheter ablation compared with the sotalol-refractory group. The influence of baseline antiarrhythmic drug therapy on secondary outcomes has not been described. It remains unclear whether differences in outcome were because of differences in patient characteristics, or because of differences in the treatment regimen, and these issues are addressed by this prespecified analysis.

## METHODS

The detailed protocol of the VANISH study has been published previously.[11] The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results. Briefly, the VANISH study was a randomized clinical trial, with blinded end-point evaluation of 259 patients with prior myocardial infarction, an ICD, and VT, comparing escalated antiarrhythmic drug therapy (amiodarone 2–300 mg/d±mexiletine 200 mg TID) to catheter ablation with

ongoing antiarrhythmic drug therapy (amiodarone or sotalol). The primary outcome was a composite of time to death, VT storm, or ICD shock for ventricular arrhythmia, after a 30-day treatment period. VT storm was defined as ≥3 documented episodes of VT within 24 hours. ICD programming was standardized in all patients. The study took place from July 2009 until November 2014 in 22 centers from Canada, Europe, United States, and Australia. The VANISH study was approved by all participating institutional review committees, and the subjects gave informed consent for their participation.

This study examined all patients enrolled into the study, comparing those who were on amiodarone at baseline (amio-refractory) to the nonamiodarone group (sotalol-refractory). The outcomes are each of the individual components of the primary outcome: death, appropriate ICD shock, and VT storm. The secondary outcomes are also analyzed and include appropriate ICD antitachycardia pacing, inappropriate ICD shocks, and documented sustained VT below detection rate of the ICD. A composite outcome of all ventricular arrhythmia events was also analyzed, which consisted of appropriate ICD shock, appropriate ICD antitachycardia pacing, VT storm, and documented sustained VT below detection rate of the ICD.

## Analysis

Baseline demographic information was summarized using descriptive statistics. Categorical data were presented as frequencies and percentages. Continuous data were presented as median with interquartile range or as mean±SD depending on the distribution of data. Time-to-event analyses for the secondary end points were performed by censoring at the time of death or study exit.

Survival rates were summarized for escalated antiarrhythmic drug therapy and catheter ablation groups, according to baseline antiarrhythmic drug therapy, using Kaplan–Meier product-limit estimates. Adjusted analyses using the Cox proportional hazards model were performed for the following variables: left ventricular ejection fraction, renal disease, age, sex, β-blocker use, and New York Heart Association class. All analyses were performed in SAS, version 9.4 (SAS Institute, Cary, NC).

# RESULTS

There were 169 (65.3%) patients whose qualifying arrhythmia occurred despite administration of amiodarone at the time of entry into the study (the amiodarone-refractory group); 89 (34.3%) patients were on sotalol, and 1 (0.4%) patient was on procainamide, comprising the sotalol-refractory group. The baseline characteristics of the 2 groups are presented in Table 1. The mean age in the amio-refractory and sotalol-refractory groups was 68.4±8.4 years versus 69.1±7.7 years (*P*=0.49), respectively. The main differences between the 2 groups were a higher rate of renal insufficiency (23.7% versus 10%; *P*=0.008), higher New York Heart Association class (82.3% II/III versus 65.5%; *P*=0.0003), lower ejection fraction (29±9.7 versus 35.2±11; *P*<0.0001), and higher rate of cardiac resynchronization therapy (25.4% versus 8.9%; *P*=0.005) in the amio-refractory group. Patients in the amio-refractory group at baseline had a lower use of β-blockers (92.3% versus 100%; *P*=0.005), higher use of diuretic (75.1% versus 57.8%; *P*=0.005), and higher use of digoxin (24.3% versus 12.2%; *P*=0.02). In the escalated drug-treated group, there were 11 (6.5%) patients of those on amiodarone who received mexiletine.

## Outcomes Within Amio-Refractory and Sotalol-Refractory Groups

Within the amio-refractory patients, there was no significant difference between ablation and escalated drug-treated groups in the time to death (Figure 1A and 1B) or first appropriate ICD shock (Table 2). The ablation-treated patients did have a significant reduction in VT storm (hazard ratio [HR], 0.46; 95% confidence interval [CI], 0.26–0.82; *P*=0.008), need for antitachycardia pacing for VT (HR, 0.61; 95% CI, 0.41–0.9; *P*=0.12), and any ventricular arrhythmia (HR, 0.53; 95% CI, 0.31–0.90; *P*=0.020; Figure 2A and 2B). In the sotalol-refractory patients, there were no differences in death, appropriate ICD shock, or any VT, when comparing the catheter ablation to escalated antiarrhythmic drug therapy groups.

## Outcomes Between Amio-Refractory and Sotalol-Refractory Groups

In patients treated with ablation, there was no significant difference in mortality comparing the amio-refractory and sotalol-refractory groups (HR, 1.54; 95% CI, 0.74–3.19; *P*=0.25; Table 3). In patients treated with escalated antiarrhythmic drug therapy, a higher mortality rate was seen among amio-refractory patients compared with those in the sotalol-refractory group (HR, 2.73; 95% CI, 1.19–6.26; *P*=0.018); this did not reach statistical significance in the adjusted multivariate model (HR, 2.4; 95% CI, 0.93–6.22; *P*=0.07; Table 4). There was no difference in recurrent ventricular arrhythmias except for a higher rate of antitachycardia pacing for VT in the amio-refractory group (HR, 1.93; 95% CI, 1.11–3.36; *P*=0.020), when treated with escalated antiarrhythmic drugs. When comparing all patients in the amio-refractory group to all patients in the sotalol-refractory group, there was a higher rate of mortality (HR, 2.03; 95% CI, 1.18–3.51; *P*=0.011) and appropriate ICD shock (HR, 1.57; 95% CI, 1.03–2.41; *P*=0.037) in the amio-refractory group (Table 5). When adjusted for baseline characteristics, these differences in mortality were no longer significant (HR, 1.44; 95% CI, 0.79–2.63; *P*=0.24).

**Table 1. Characteristics of the 2 Groups by Baseline Antiarrhythmic Drug Use**

| Characteristics* | Amiodarone (N=169) | Sotalol (N=90) | *P* Value |
|---|---|---|---|
| Age, y† | 68.4±8.4 | 69.1±7.7 | 0.49 |
| Male sex, n (%) | 157 (92.9%) | 84 (93.3%) | 1 |
| Time since last MI, y | 15.3±9.5 | 16.4±9.7 | 0.39 |
| Prior PCI, n (%) | 72 (42.6%) | 40 (44.4%) | 0.79 |
| Prior coronary artery bypass surgery, n (%) | 79 (46.7%) | 39 (43.3%) | 0.69 |
| Diabetes mellitus, n (%) | 52 (30.8%) | 25 (27.8%) | 0.67 |
| Hypertension, n (%) | 116 (68.6%) | 64 (71.1%) | 0.78 |
| Renal insufficiency, n (%) | 40 (23.7%) | 9 (10%) | 0.008 |
| Atrial fibrillation or atrial flutter, n (%) | 72 (42.6%) | 27 (30%) | 0.06 |
| NYHA FC, n (%) | | | |
| I | 30 (17.8%) | 31 (34.4%) | 0.0003 |
| II | 88 (52.1%) | 49 (54.4%) | |
| III | 51 (30.2%) | 10 (11.1%) | |
| Ejection fraction, % | 29±9.7 | 35.2±11 | <0.0001 |
| Single-chamber ICD, n (%) | 55 (32.5%) | 32 (35.6%) | 0.005 |
| Dual-chamber ICD, n (%) | 71 (42%) | 50 (55.6%) | |
| CRT defibrillator, n (%) | 43 (25.4%) | 8 (8.9%) | |
| Medication use | | | |
| Antiarrhythmic drug at time of qualification | | | |
| Nonamiodarone, n (%) | | | |
| Sotalol, n (%) | NA | 89 (98.9%) | NA |
| Procainamide, n (%) | NA | 1 (1.1%) | |
| Amiodarone, n (%) | 169 (100%) | 0 (0%) | NA |
| Dose <300 mg/d | 150 (88.8%) | NA | |
| Dose ≥300 mg/d, n (%) | 19 (11.2%) | NA | |
| Other medications | | | |
| β-Blocker, n (%)* | 156 (92.3%) | 90 (100%) | 0.005 |
| ACE inhibitor, n (%) | 109 (64.5%) | 59 (65.6%) | 0.89 |
| ARB, n (%) | 37 (21.9%) | 22 (24.4%) | 0.64 |
| Diuretic, n (%) | 127 (75.1%) | 52 (57.8%) | 0.005 |
| Digoxin, n (%) | 41 (24.3%) | 11 (12.2%) | 0.02 |
| Aspirin, n (%) | 126 (81.3%) | 58 (77.3%) | 0.49 |
| Calcium channel blocker, n (%) | 22 (13%) | 11 (12.2%) | 1 |
| Warfarin, n (%) | 64 (40.8%) | 25 (33.8%) | 0.38 |
| Nonwarfarin anticoagulant, n (%) | 15 (8.9%) | 8 (8.9%) | 1 |
| Estimated GFR (Cockroft–Gault) | 68.5±27.9 | 87±25.5 | <0.0001 |
| Sodium, mmol/L | 138.5±3.3 | 138.3±2.9 | 0.61 |
| Potassium, mmol/L | 4.3±0.4 | 4.3±0.45 | 0.99 |
| NT-proBNP, pg/mL | 1181.8±1226.9 | 586.0±573.2 | <0.0001 |

ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CRT, cardiac resynchronization therapy; GFR, glomerular filtration rate; ICD, implantable cardioverter defibrillator; MI, myocardial infarction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA FC, New York Heart Association functional class; and PCI, percutaneous coronary intervention.

*Plus–minus values are means±SD; median and interquartile ranges are shown when indicated; categorical values are n (%).

†The qualifying event occurred during procainamide administration for 1 patient.

## DISCUSSION

Patients enrolled in the VANISH study were stratified by whether the qualifying arrhythmia occurred despite amiodarone versus nonamiodarone drug and the analysis of the difference in the primary outcome between strata was prespecified. In this substudy, we found that patients with amio-refractory VT at baseline who were treated with escalated drug therapy had substantially higher rates of death and ventricular arrhythmia than the sotalol-refractory group. Among patients treated with catheter ablation, these differences were no longer evident. The differing effects on mortality, with a trend toward harm with catheter ablation in the sotalol-refractory group, as compared with a trend toward benefit with ablation in the amio-refractory group are intriguing although not statistically significant. Patients with amio-refractory VT have a higher level of comorbidity, including worse New York Heart Association class, more renal insufficiency, and lower ejection fraction. This higher level of comorbidity in the amio-refractory group was associated with higher rates of mortality and recurrence of ventricular arrhythmia. Pre-enrollment drug status was no longer independently predictive of outcome once adjustment for these comorbidities was performed. These subgroups are too small to draw firm conclusions about effects on mortality.

Amiodarone is a powerful antiarrhythmic drug and has been shown to reduce VT in prior studies of ventricular arrhythmia, in the presence of an ICD (HR, 0.27; *P*<0.001).[1] It is substantially better than any other drug for the reduction of VT[12] but is plagued by the risk of complications during longer term administration. When used as preventive therapy for patients with heart failure, it has resulted in reductions in sudden arrhythmic death but no effect on overall mortality.[4,5,12,13] In the SCD-HeFT trial (Sudden Cardiac Death in Heart Failure Trial), patients with reduced ejection fraction and heart failure were randomly allocated to placebo, amiodarone, or ICD implant, stratified by functional class. In the functional class III stratum, amiodarone was associated with increased mortality[14] suggesting that some of

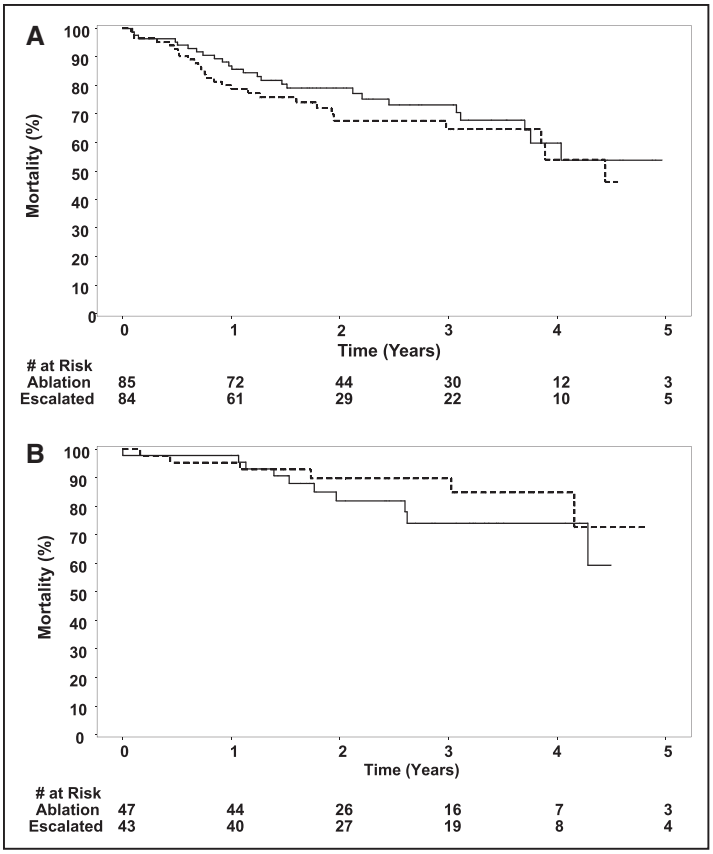


**Figure 1. Mortality rate in the ablation (solid line) vs the escalated antiarrhythmic drug (dotted line) group.**
**A**, Amio-refractory group (hazard ratio, 0.8; 95% confidence interval [CI], 0.47–1.36; *P*=0.41). **B**, Sotalol-refractory group (hazard ratio, 1.49; 95% CI, 0.57–3.94; *P*=0.42).

amiodarone's benefit is offset by harm. Potential amiodarone side effects are numerous and often relate to longer term exposure. In a summary of trials studying amiodarone for the primary prevention of sudden death with varying follow-up, pulmonary toxicity was seen in 2.9%, thyroid toxicity in 3.6%, hepatic toxicity in 1.8%, and bradycardia in 2.8% during 12 to 46 months of follow-up.[15] It is possible that the differential impact of higher dose amiodarone in comparison with catheter ablation is because of the drug itself in patients with more advanced heart failure as observed in the SCD-HeFT trial and that catheter ablation is thus more effective, but it

**Table 2. Outcomes by Randomized Groups According to Baseline Antiarrhythmic Drug Strata**

| | Amio-Refractory (N=169) | | | | Sotalol-Refractory (N=90) | | | |
|---|---|---|---|---|---|---|---|---|
| Outcome | Ablation (n=85) | Escalated Drug Therapy (n=84) | HR (95% CI) | *P* Value | Ablation (n=47) | Escalated Drug Therapy (n=43) | HR (95% CI) | *P* Value |
| Death | 26 (30.6%) | 28 (33.3%) | 0.8 (0.47–1.36) | 0.41 | 10 (21.3%) | 7 (16.3%) | 1.49 (0.57–3.94) | 0.42 |
| Death (person-years, 95% CI) | 13.8 (8.5–19.0) | 16.5 (11.0–23.8) | … | … | 8.6 (4.1–15.9) | 6.0 (2.4–12.3) | … | … |
| Appropriate ICD shock | 35 (41.2%) | 39 (46.4%) | 0.7 (0.44–1.11) | 0.13 | 15 (31.9%) | 15 (34.9%) | 0.87 (0.43–1.79) | 0.71 |
| VT storm | 19 (22.4%) | 31 (36.9%) | 0.46 (0.26–0.82) | 0.008 | 13 (27.7%) | 11 (25.6%) | 1.26 (0.56–2.81) | 0.58 |
| Appropriate ICD ATP | 49 (57.7%) | 57 (67.9%) | 0.61 (0.41–0.9) | 0.012 | 28 (59.6%) | 21 (48.8%) | 1.55 (0.87–2.76) | 0.14 |
| Inappropriate ICD shocks | 4 (4.7%) | 7 (8.3%) | 0.48 (0.14–1.64) | 0.24 | 9 (19.2%) | 4 (9.3%) | 1.85 (0.56–6.15) | 0.31 |
| Documented sustained VT below detect | 3 (3.5%) | 5 (6%) | 0.51 (0.12–2.15) | 0.36 | 0 (0%) | 3 (7%) | NA | NA |
| Composite ventricular arrhythmia* | 23 (27.1%) | 35 (41.7%) | 0.53 (0.31–0.9) | 0.020 | 20 (42.6%) | 16 (37.2%) | 1.32 (0.69–2.56) | 0.40 |

ATP indicates antitachycardia pacing; CI, confidence interval; HR, hazard ratio; ICD, implantable cardioverter defibrillator; and VT, ventricular tachycardia.
*Consists of appropriate ICD shock, appropriate ICD antitachycardia pacing, VT storm, and documented sustained VT below detection rate of the ICD.

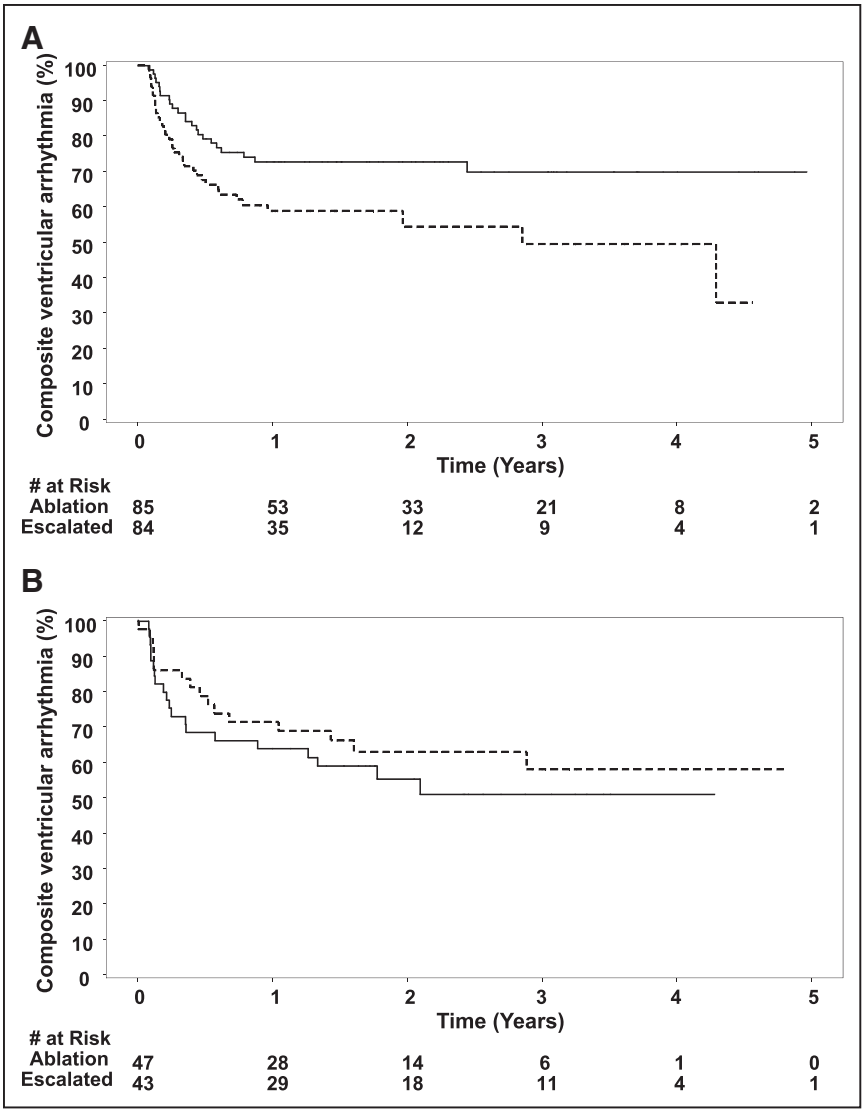


**Figure 2. Rate of composite ventricular arrhythmia in the ablation (solid line) vs the escalated antiarrhythmic drug (dotted line) group.** **A**, Amio-refractory group (hazard ratio, 0.53; 95% confidence interval [CI], 0.31–0.9; *P*=0.020). **B**, Sotalol-refractory group (hazard ratio, 1.32; 95% CI, 0.69–2.56; *P*=0.40).

is also possible that it is the comorbidities of patients who receive amiodarone therapy that drive their outcomes or that amiodarone administration affects catheter ablation outcomes. In the VANISH study, there were significantly more treatment-attributed adverse events in the escalated drug therapy group including nonfatal hepatic dysfunction, tremor, and drug intolerance (51 events versus 22 events in the ablation group; *P*=0.002).

**Table 3. Outcomes by Baseline Antiarrhythmic Drug Within Ablation Arm**

| Outcome | Amio-Refractory (n=85) N (%) | Sotalol-Refractory (n=47) N (%) | Adjusted HR* (95% CI) | *P* Value |
|---|---|---|---|---|
| Death | 26 (30.6%) | 10 (21.3%) | 1.08 (0.48–2.4) | 0.86 |
| Appropriate ICD shock | 35 (41.2%) | 15 (31.9%) | 1.2 (0.61–2.36) | 0.61 |
| VT storm | 19 (22.4%) | 13 (27.7%) | 0.8 (0.37–1.75) | 0.58 |
| Appropriate ICD ATP | 49 (57.7%) | 28 (59.6%) | 0.88 (0.52–1.49) | 0.64 |
| Inappropriate ICD shocks | 4 (4.7%) | 9 (19.2%) | 0.41 (0.1–1.74) | 0.23 |
| Documented sustained VT below detect | 3 (3.5%) | 0 (0%) | NA | NA |
| Composite ventricular arrhythmia† | 23 (27.1%) | 20 (42.6%) | 0.65 (0.33–1.29) | 0.22 |

ATP indicates antitachycardia pacing; CI, confidence interval; HR, hazard ratio; ICD, implantable cardioverter defibrillator; NYHA, New York Heart Association; and VT, ventricular tachycardia.

*Adjusted for baseline variables, including left ventricular ejection fraction, NYHA, renal insufficiency, and β-blockers.

†Consists of appropriate ICD shock, appropriate ICD antitachycardia pacing, VT storm, and documented sustained VT below detection rate of the ICD.

**Table 4. Outcomes by Baseline Antiarrhythmic Drug Within Escalated Drug Therapy Arm**

| Outcome | Amio-Refractory (n=84) N (%) | Sotalol-Refractory (n=43) N (%) | Adjusted HR* (95% CI) | Log-Rank *P* Value |
|---|---|---|---|---|
| Death | 28 (33.3) | 7 (16.3) | 2.4 (0.93–6.22) | 0.07 |
| Appropriate ICD shock | 39 (46.4) | 15 (34.9) | 1.59 (0.82–3.07) | 0.17 |
| VT storm | 31 (36.9) | 11 (25.6) | 1.69 (0.77–3.69) | 0.19 |
| Appropriate ICD ATP | 57 (67.9) | 21 (48.8) | 1.93 (1.11–3.36) | 0.020 |
| Inappropriate ICD shocks | 7 (8.3) | 4 (9.3) | 0.69 (0.15–3.2) | 0.63 |
| Documented sustained VT below detect | 5 (6) | 3 (7) | 0.72 (0.11–4.53) | 0.72 |
| Composite ventricular arrhythmia† | 35 (41.7) | 16 (37.2) | 1.11 (0.58–2.15) | 0.75 |

ATP indicates antitachycardia pacing; CI, confidence interval; HR, hazard ratio; ICD, implantable cardioverter defibrillator; NYHA, New York Heart Association; and VT, ventricular tachycardia.

*Adjusted for baseline variables, including left ventricular ejection fraction, NYHA, renal insufficiency, and β-blockers.

†Consists of appropriate ICD shock, appropriate ICD antitachycardia pacing, VT storm, and documented sustained VT below detection rate of the ICD.

Whether these adverse events have a long-term effect on mortality is unclear.[11]

In contrast, sotalol does not result in the same degree of benefit in reduction of ventricular arrhythmia. The OPTIC trial (Optimal Pharmacological Therapy in Cardioverter Defibrillator Patients) randomized patients with ventricular arrhythmia to β-blocker, sotalol, or amiodarone. Patients on sotalol had a nonsignificant reduction in ICD shocks (HR, 0.61; $P$=0.055).[12] A single study by Pacifico et al[16] demonstrated a significant reduction in recurrent VT with sotalol (49% relative risk reduction; $P$<0.001). Other smaller, (n≤100) single-center trials previously estimated the relative reduction in VT with sotalol at 39% in comparison with placebo[17] or found either a neutral or increased risk in comparison with β-blockers.[18,19] Sotalol has been similar to other antiarrhythmic drugs, conferring a risk of ventricular proarrhythmia concomitantly with its benefit[13] but is considered to have a relatively good safety profile and is thus a frequent choice for first-line therapy for patients without high risk of sotalol-induced proarrhythmia.[20] In this study, the continuation of sotalol in the catheter ablation group may have contributed to a trend toward an increase in mortality, as compared with continuing and not escalating amiodarone (200 mg/d). Alternatively, it is possible that the difference in trends was either because of chance or because of a risk associated with catheter ablation.

This study provides important insight into which patients might benefit the most from catheter ablation. We have demonstrated that patients who have failed amiodarone therapy likely have an arrhythmic substrate that will be less responsive to escalating medical therapy, and catheter ablation provides greater benefit. Interestingly, catheter ablation seems to have similar efficacy to initiation of amiodarone for patients who are having recurrent VT, despite therapy with sotalol, but this observation is limited to the follow-up available in the present study. Longer follow-up may detect the risk associated with long-term use of high-dose amioda-

**Table 5. Overall Outcomes According to Baseline Antiarrhythmic Drug**

| Outcome | Amio-Refractory (n=169) N (%) | Sotalol-Refractory (n=90) N (%) | Unadjusted HR (95% CI) | Unadjusted *P* Value | Adjusted HR* (95% CI) | *P* Value |
|---|---|---|---|---|---|---|
| Composite of death, appropriate ICD shock and VT storm | 117 (69.2%) | 48 (53.3%) | 1.54 (1.1–2.16) | 0.012 | 1.36 (0.94–1.96) | 0.10 |
| Death | 54 (32%) | 17 (18.9%) | 2.03 (1.18–3.51) | 0.011 | 1.44 (0.79–2.63) | 0.24 |
| Appropriate ICD shock | 74 (43.8%) | 30 (33.3%) | 1.57 (1.03–2.41) | 0.037 | 1.39 (0.87–2.22) | 0.16 |
| VT storm | 50 (29.6%) | 24 (26.7%) | 1.24 (0.76–2.01) | 0.39 | 1.11 (0.65–1.92) | 0.70 |
| Appropriate ATP | 49 (57.7%) | 28 (59.6%) | 1.34 (0.95–1.89) | 0.094 | 1.27 (0.87–1.84) | 0.22 |
| Inappropriate ICD shocks | 4 (4.7%) | 9 (19.2%) | 0.49 (0.22–1.08) | 0.078 | 0.48 (0.17–1.33) | 0.16 |
| Documented sustained VT below detect | 3 (3.5%) | 0 (0%) | 1.57 (0.42–5.93) | 0.50 | 1.13 (0.21–6.16) | 0.89 |
| Composite ventricular arrhythmia† | 23 (27.1%) | 20 (42.6%) | 0.86 (0.57–1.31) | 0.49 | 0.84 (0.52–1.34) | 0.46 |

ATP indicates antitachycardia pacing; CI, confidence interval; HR, hazard ratio; ICD, implantable cardioverter defibrillator; NYHA, New York Heart Association; and VT, ventricular tachycardia.

*Adjusted for baseline variables, including left ventricular ejection fraction, NYHA, renal insufficiency, and β-blockers.

†Consists of appropriate ICD shock, appropriate ICD antitachycardia pacing, VT storm, and documented sustained VT below detection rate of the ICD.

rone. Clinical decisions in this setting may need to consider the initial procedural risk of catheter ablation in comparison with the longer term risks associated with amiodarone therapy. Patient preferences, comorbidities, individualized procedural risk assessment, and estimated prognosis may all need to be taken into account to identify the optimal therapy for a patient with recurrent ventricular arrhythmias, despite nonamiodarone antiarrhythmic drug therapy.

There are limitations to the interpretation of these findings, including the relatively small number of patients and events in each group. Using adjusted analysis, we attempted to account for baseline differences in amio-refractory versus sotalol-refractory patients; nonetheless, this adjustment may be incomplete. The findings remain exploratory but provide useful insight into the relative effects of catheter ablation to antiarrhythmic drug therapy in the ischemic population.

## CONCLUSION

Catheter ablation provides greater relative benefit than escalation of antiarrhythmic drug therapy for patients who experience recurrent VT, despite chronic oral amiodarone therapy, with the greatest effect on reduction of VT storm. In contrast, outcomes of ablation are similar to those of initiating chronic amiodarone therapy for patients who are failing sotalol.

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## FOOTNOTES

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# Effect of Baseline Antiarrhythmic Drug on Outcomes With Ablation in Ischemic Ventricular Tachycardia: A VANISH Substudy (Ventricular Tachycardia Ablation Versus Escalated Antiarrhythmic Drug Therapy in Ischemic Heart Disease)

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