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Ventricular Tachycardia Ablation versus Escalation of Antiarrhythmic Drugs

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ABSTRACT

BACKGROUND

Recurrent ventricular tachycardia among survivors of myocardial infarction with an implantable cardioverter–defibrillator (ICD) is frequent despite antiarrhythmic drug therapy. The most effective approach to management of this problem is uncertain.

METHODS

We conducted a multicenter, randomized, controlled trial involving patients with ischemic cardiomyopathy and an ICD who had ventricular tachycardia despite the use of antiarrhythmic drugs. Patients were randomly assigned to receive either catheter ablation (ablation group) with continuation of baseline antiarrhythmic medications or escalated antiarrhythmic drug therapy (escalated-therapy group). In the escalated-therapy group, amiodarone was initiated if another agent had been used previously. The dose of amiodarone was increased if it had been less than 300 mg per day or mexiletine was added if the dose was already at least 300 mg per day. The primary outcome was a composite of death, three or more documented episodes of ventricular tachycardia within 24 hours (ventricular tachycardia storm), or appropriate ICD shock.

RESULTS

Of the 259 patients who were enrolled, 132 were assigned to the ablation group and 127 to the escalated-therapy group. During a mean (±SD) of 27.9±17.1 months of follow-up, the primary outcome occurred in 59.1% of patients in the ablation group and 68.5% of those in the escalated-therapy group (hazard ratio in the ablation group, 0.72; 95% confidence interval, 0.53 to 0.98; P=0.04). There was no significant between-group difference in mortality. There were two cardiac perforations and three cases of major bleeding in the ablation group and two deaths from pulmonary toxic effects and one from hepatic dysfunction in the escalated-therapy group.

CONCLUSIONS

In patients with ischemic cardiomyopathy and an ICD who had ventricular tachycardia despite antiarrhythmic drug therapy, there was a significantly lower rate of the composite primary outcome of death, ventricular tachycardia storm, or appropriate ICD shock among patients undergoing catheter ablation than among those receiving an escalation in antiarrhythmic drug therapy. (Funded by the Canadian Institutes of Health Research and others; VANISH ClinicalTrials.gov number, NCT00905853.)

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Ventricular tachycardia caused by the scarring that occurs after myocardial infarction carries a substantial risk of death, a risk that is significantly reduced by the placement of an implantable cardioverter–defibrillator (ICD).[1] ICDs are implanted in more than 100,000 patients annually in the United States. Of these patients, 15% are initially treated with concomitant antiarrhythmic drug (AAD) therapy,[2] and up to 38% receive an appropriate shock for ventricular arrhythmia within 5 years.[3] ICDs effectively terminate ventricular tachycardia, but recurrent arrhythmias and ICD shocks may cause impairment in the quality of life,[4] are associated with an increased risk of death, heart failure, and hospitalization, and often require suppressive therapy, most commonly with AADs. If ventricular tachycardia recurs despite AAD therapy, clinicians and patients must choose either catheter ablation or an escalation in drug therapy.[5]

Randomized trials have shown that AAD therapy can reduce recurrent episodes of ventricular tachycardia in patients with ICDs. The rate of recurrent ventricular tachycardia was 15 to 44% lower among patients receiving sotalol than among those receiving either placebo or beta-blockers alone.[6,7] Amiodarone therapy reduced recurrent arrhythmias in the first year of treatment by 71%[7] and reduced the rate of death from arrhythmia[8] but has been associated with a substantial risk of side effects during long-term therapy.[9] Catheter ablation for ventricular tachycardia has also been shown to reduce the rate of recurrence in randomized trials,[10,11] and the absence of ventricular tachycardia after catheter ablation has been associated with increased survival in multicenter observational studies.[12] In the Ventricular Tachycardia Ablation versus Escalated Antiarrhythmic Drug Therapy in Ischemic Heart Disease (VANISH) trial, we compared catheter ablation with escalated AAD therapy in patients with ischemic cardiomyopathy and an ICD who had ventricular tachycardia despite first-line AAD therapy.

Methods

Trial Design

The VANISH trial was a multicenter, randomized, controlled trial that was conducted at 22 tertiary referral centers where catheter ablation of ventricular tachycardia was routinely performed; the centers were in Canada, Europe, the United States, and Australia. The study was approved by the research ethics committee at each participating site.

The executive committee designed and conducted the trial and analyzed the data. (Details regarding the trial committees are provided in the Supplementary Appendix, available with the full text of this article at NEJM.org.) Funding was provided by the Canadian Institutes of Health Research, with additional financial support from St. Jude Medical and Biosense Webster. The first author wrote the first draft of the manuscript, and all the authors made the decision to submit the manuscript for publication. The funders had no role in the design or conduct of the trial, in the analysis of the data, or in the authorship or submission of the manuscript. The authors vouch for the accuracy and completeness of the data and all analyses and for the fidelity of this report to the trial protocol, which is available at NEJM.org.

Patients

Patients were eligible for inclusion if they had had a myocardial infarction, had undergone placement of an ICD, and had had an episode of ventricular tachycardia during treatment with amiodarone or another class I or class III AAD within the previous 6 months. Episodes of ventricular tachycardia were defined as any one of the following: three or more episodes of ventricular tachycardia treated with antitachycardia pacing, of which at least one episode was symptomatic; one or more appropriate ICD shocks; three or more episodes of ventricular tachycardia within 24 hours; or sustained ventricular tachycardia at a rate below the programmed detection rate of the ICD. Qualifying episodes of ventricular tachycardia were required to be monomorphic and to have rates of less than 250 beats per minute. Details regarding the inclusion and exclusion criteria are provided in the Supplementary Appendix. All patients provided written informed consent.

Randomization and Interventions

Eligible patients were randomly assigned in a 1:1 ratio to catheter ablation (ablation group) or escalated AAD therapy (escalated-therapy group). Randomization was stratified according to center and whether the qualifying arrhythmia had occurred while the patient was being treated with amiodarone or an AAD other than amiodarone. A block-randomization design was used with randomly

permuted block sizes of 2 and 4 on the basis of a computerized random-number generator with sequentially numbered opaque, sealed envelopes for each stratum. Because of the nature of the interventions, patients and treating physicians were aware of study-group assignments.

Patients in the escalated-therapy group were treated with amiodarone or amiodarone plus mexiletine according to the drug and dose taken at the time of the index arrhythmia. Patients in whom qualifying arrhythmias had occurred during the administration of any AAD other than amiodarone were treated with amiodarone at a dose of 400 mg twice daily for 2 weeks, followed by a dose of 400 mg per day for 4 weeks and 200 mg per day thereafter. Patients in whom qualifying arrhythmias had occurred while they were receiving amiodarone at a daily dose of less than 300 mg were treated with a loading dose of 400 mg twice daily for 2 weeks, which was followed by 400 mg per day for 1 week and 300 mg per day thereafter.[13] Patients in whom qualifying arrhythmias had occurred despite taking at least 300 mg of amiodarone per day were treated with continued amiodarone with the addition of mexiletine (at a dose of 200 mg three times daily).

Patients in the ablation group underwent the procedure within 14 days after randomization. Procedures followed a standardized approach that specifically targeted all inducible ventricular tachycardias.[14] Details regarding the ablation procedure are provided in the Methods section in the Supplementary Appendix.

ICD PROGRAMMING

To minimize bias, ICDs were programmed according to a standardized protocol after randomization on the basis of the best evidence available at the time of study initiation.[15,16] Details regarding ICD programming are provided in the Methods section in the Supplementary Appendix.

OUTCOME MEASURES

The primary outcome was a composite of death occurring at any time after randomization or ventricular tachycardia storm (three or more documented episodes of ventricular tachycardia within 24 hours) or appropriate ICD shock after a 30-day treatment period. The 30-day treatment period was imposed to exclude nonfatal outcomes that might occur before adequate drug loading or actual performance of catheter ablation. Prespecified secondary outcomes included each of the components of the primary outcome and adverse effects. Details regarding the trial outcomes are provided in the Methods section in the Supplementary Appendix.

Clinical events and episodes of arrhythmia that were detected by ICDs were adjudicated in a blinded fashion by members of an independent committee, with review by two members for primary outcomes and a full committee review in case of disagreement. We prespecified that the primary outcome would include only episodes for which device electrograms were available for review (classified as category 1 events). In a secondary analysis, events were included for which the electrogram information had been overwritten but the tachycardia rate matched rates of adjudicated episodes of ventricular tachycardia for the same patient (i.e., a cycle length that differed from a previously adjudicated ventricular arrhythmia by less than 40 msec), classified as category 2 events.

Serious adverse events were defined as those that caused or prolonged hospitalization for cardiovascular causes or were life-threatening or fatal. Adverse events were attributed to ablation, AAD, or neither by a member of the events committee who was unaware of study-group assignments.

STATISTICAL ANALYSIS

We assumed that the primary outcome would occur in 35% of the patients in the escalated-therapy group after 2 years of follow-up. Accordingly, we calculated that enrolling 260 patients would provide a power of 80% to determine that the absolute risk of the primary outcome would be 12.25 percentage points lower in the ablation group than in the escalated-therapy group (reduction in relative risk, 35%),[1,17-19] allowing for a 2% loss to follow-up and a 2% rate of crossover at a significance level of 0.05 (two-sided). After 63 months, the overall rate of the primary outcome was higher than anticipated, and a sample-size reassessment suggested that the statistical power would be maintained with minimum follow-up truncated at 1 year. Interim safety analyses were performed during enrollment by an independent data and safety monitoring committee at 6-month intervals.

All analyses were conducted according to the intention-to-treat principle. Survival-analysis techniques were used to compare the incidence of the primary and secondary outcomes between the groups. The survival rates in each group were sum-

marized with the use of Kaplan–Meier product-limit estimates and compared with the use of nonparametric log-rank tests. Hazard ratios and confidence intervals were calculated with the use of Cox proportional-hazards models, which were also used to test for interactions in the planned subgroups. The underlying assumption of proportional hazards was tested and its validity confirmed. Descriptive variables are summarized by means of frequency distributions, means and standard deviations, or medians and interquartile ranges and tested with the use of Fisher's exact test, the t-test, or the Wilcoxon–Mann–Whitney test, as appropriate. Statistical testing was performed with the use of SAS software, version 9.4.

RESULTS

PATIENTS

From July 2009 through November 2014, we enrolled 259 patients at 22 centers (250 patients in Canada, 4 in Europe, 3 in the United States, and 2 in Australia). Of these patients, 132 were assigned to undergo catheter ablation and 127 to receive escalated AAD therapy (Fig. S1 in the Supplementary Appendix). The clinical characteristics of the patients at baseline were similar in the two groups (Table 1).

All the patients in the escalated-therapy group received the assigned treatment. Among the 132 patients in the ablation group, 129 underwent the procedure; 1 died of cardiac arrest, 1 died of sepsis, and 1 withdrew from the trial 3 days after randomization. Procedural characteristics of the ablations performed in either study group are described in Table S1 in the Supplementary Appendix.

Follow-up was completed in November 2015. Patients were followed for a mean (±SD) of 27.9±17.1 months from randomization to either death or the end of the trial (median follow-up, 23.4 months [interquartile range, 14.7 to 40.4]).

Among the 127 patients in the escalated-therapy group, 4 withdrew before the primary outcome was reached, along with 1 patient who underwent heart transplantation; 11 underwent catheter ablation. Among the 132 patients in the ablation group, 3 did not undergo the procedure, 4 patients withdrew before the primary outcome was reached, 3 patients underwent cardiac transplantation, and 4 received escalated AAD therapy. Further details are provided in Figure S1 in the Supplementary Appendix.

CLINICAL OUTCOMES

The primary outcome occurred in 78 of 132 patients (59.1%) in the ablation group and in 87 of 127 patients (68.5%) in the escalated-therapy group. The rate of the primary outcome was significantly lower in the ablation group than in the escalated-therapy group (hazard ratio in the ablation group, 0.72; 95% confidence interval [CI], 0.53 to 0.98; P=0.04) (Table 2 and Fig. 1). This difference was driven by trends toward reductions in rates of appropriate shocks and episodes of ventricular tachycardia storm, and it persisted when category 2 events were included in the analysis (hazard ratio, 0.72; 95% CI, 0.53 to 0.98; P=0.04). In a post hoc sensitivity analysis that included events occurring during the 30-day treatment period, the difference between groups was not significant (see the Results section in the Supplementary Appendix).

Throughout the trial, 36 patients (27.3%) in the ablation group and 35 (27.6%) in the escalated-therapy group died (hazard ratio, 0.96; 95% CI, 0.60 to 1.53; P=0.86). Ventricular tachycardia storm occurred in 32 patients (24.2%) in the ablation group and 42 patients (33.1%) in the escalated-therapy group (hazard ratio, 0.66; 95% CI, 0.42 to 1.05; P=0.08). Appropriate ICD shocks occurred in 50 patients (37.9%) and 54 patients (42.5%), respectively (hazard ratio, 0.77; 95% CI, 0.53 to 1.14; P=0.19) (Table 2 and Fig. 1).

With respect to secondary outcomes, there was a higher incidence of sustained ventricular tachycardia at a rate below the detection limit of the ICD at any time during the trial in the escalated-therapy group than in the ablation group; there was also a greater total number of episodes of such events (P=0.02 for both comparisons) (Table 2). There were no significant between-group differences in any other secondary outcome.

SUBGROUP ANALYSES

The rate of the primary outcome did not differ significantly between the two groups among the subgroup of patients who were not being treated with amiodarone at baseline (P=0.64) (Fig. 2). In contrast, the rate of the primary outcome was significantly lower in the ablation group than in the escalated-therapy group among patients in whom the index arrhythmia occurred despite the receipt of amiodarone (P=0.001; P=0.03 for interaction). Catheter ablation did not significantly alter the risk of death either in the subgroup that received amiodarone at baseline (hazard ratio,

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Escalated Therapy (N=127)	Catheter Ablation (N=132)
Age — yr	70.3±7.3	67.0±8.6
Male sex — no. (%)	118 (92.9)	123 (93.2)
Time since last myocardial infarction — yr	15.7±9.8	15.7±9.4
Previous PCI — no. (%)	62 (48.8)	50 (37.9)
Previous CABG — no. (%)	55 (43.3)	63 (47.7)
Diabetes — no. (%)	40 (31.5)	37 (28.0)
Hypertension — no. (%)	88 (69.3)	92 (69.7)
Renal insufficiency — no. (%)	26 (20.5)	23 (17.4)
Atrial fibrillation or flutter — no. (%)	47 (37.0)	52 (39.4)
NYHA functional class — no. (%)		
I	28 (22.0)	33 (25.0)
II	68 (53.5)	69 (52.3)
III	31 (24.4)	30 (22.7)
Ejection fraction — %	31.2±10.7	31.1±10.4
Implantable cardioverter–defibrillator — no. (%)		
Single-chamber	44 (34.6)	43 (32.6)
Dual-chamber	61 (48.0)	60 (45.5)
CRT defibrillator — no. (%)	22 (17.3)	29 (22.0)
Antiarrhythmic drug received at time of qualification — no. (%)		
Amiodarone	84 (66.1)	85 (64.4)
Dose <300 mg/day	73 (57.5)	77 (58.3)
Dose ≥300 mg/day	11 (8.7)	8 (6.1)
Other medication	43 (33.9)	47 (35.6)
Sotalol	43 (33.9)	46 (34.8)
Procainamide	0	1 (0.8)
Other medications — no./total no. (%)		
Beta-blocker	122/127 (96.1)	124/132 (93.9)
Angiotensin-converting–enzyme inhibitor	83/127 (65.4)	85/132 (64.4)
Angiotensin-receptor blocker	28/127 (22.0)	31/132 (23.5)
Diuretic	89/127 (70.1)	90/132 (68.2)
Digoxin	25/127 (19.7)	27/132 (20.5)
Aspirin	85/112 (75.9)	99/118 (83.9)
Calcium-channel blocker	19/127 (15.0)	14/132 (10.6)
Warfarin	42/112 (37.5)	47/119 (39.5)
Non-warfarin anticoagulant	12/127 (9.4)	11/132 (8.3)
Estimated GFR†	70.2±26.4	75.8±29.0
Sodium — mmol/liter	138.4±3.4	138.5±3.0
Potassium — mmol/liter	4.3±0.4	4.3±0.4
NT-proBNP — pg/ml	937.3±895.5	1010.3±1252.7

* Plus–minus values are means ±SD. There were no significant differences between the groups except for age (P=0.001). To convert the values for potassium to milligrams per deciliter, divide by 0.2558. CABG denotes coronary-artery bypass grafting, CRT cardiac resynchronization therapy, NT-proBNP N-terminal pro–brain natriuretic peptide, NYHA New York Heart Association, and PCI percutaneous coronary intervention.

† The estimated glomerular filtration rate (GFR) was calculated with the use of the Cockcroft–Gault formula.

Table 2. Trial Outcomes.*

Outcome	Escalated Therapy (N=127)	Catheter Ablation (N=132)	Hazard Ratio (95% CI)	P Value
	no. (%)			
Primary outcome†	87 (68.5)	78 (59.1)	0.72 (0.53–0.98)	0.04
Death	35 (27.6)	36 (27.3)	0.96 (0.60–1.53)	0.86
From cardiovascular causes‡	26	24		
From noncardiovascular causes	8	12		
From unknown cause	1	0		
Appropriate ICD shock after 30 days	54 (42.5)	50 (37.9)	0.77 (0.53–1.14)	0.19
Ventricular tachycardia storm after 30 days	42 (33.1)	32 (24.2)	0.66 (0.42–1.05)	0.08
Other outcomes				
Appropriate ICD shock at any time	54 (42.5)	56 (42.4)	0.97 (0.66–1.40)	0.85
Ventricular tachycardia storm at any time	46 (36.2)	38 (28.8)	0.74 (0.48–1.14)	0.17
Sustained ventricular tachycardia below ICD detection limit				
At any time	13 (10.2)	4 (3.0)	0.27 (0.09–0.84)	0.02
After 30 days	8 (6.3)	3 (2.3)	0.33 (0.09–1.25)	0.09
Cardioversion for ventricular tachycardia§	14 (11.0)	8 (6.1)	0.52 (0.22–1.23)	0.13
Appropriate ATP				
At any time	79 (62.2)	84 (63.6)	0.97 (0.71–1.32)	0.83
After 30 days	78 (61.4)	77 (58.3)	0.87 (0.63–1.19)	0.37
Inappropriate ICD shock				
At any time	11 (8.7)	13 (9.8)	1.08 (0.48–2.41)	0.86
After 30 days	11 (8.7)	13 (9.8)	1.08 (0.48–2.42)	0.85
Hospital admission for cardiac causes	39 (30.7)	33 (25.0)	0.76 (0.48–1.21)	0.25
	no. (mean no./person-yr)			
Total shocks or arrhythmia events¶				
ICD shock				
Appropriate	266 (2.09)	169 (1.28)	NA	0.28
Inappropriate	85 (0.67)	66 (0.50)	NA	0.46
Appropriate ATP	2453 (19.2)	1711 (13.0)	NA	0.27
Sustained ventricular tachycardia below ICD detection	18 (0.14)	4 (0.03)	NA	0.02

* ATP denotes antitachycardia pacing, ICD implantable cardioverter–defibrillator, and NA not applicable.
† The primary outcome was death at any time or ventricular tachycardia storm or appropriate shock from an ICD after the 30-day treatment period.
‡ Included in this category are deaths attributed to congestive heart failure: 18 in the escalated-therapy group and 17 in the ablation group.
§ This category (not a prespecified outcome) includes external, manual internal, and pharmacologic cardioversion.
¶ Included in this category are the total numbers of events (first event and all subsequent events).

0.80; 95% CI, 0.47 to 1.36; P=0.41) or in the subgroup that did not receive amiodarone (hazard ratio, 1.49; 95% CI, 0.57 to 3.94; P=0.42) (P=0.28 for interaction). No other significant interactions were observed in subgroups (Fig. 3), including a post hoc subgroup defined according to the enrollment volume at the study center (see the Results section in the Supplementary Appendix).

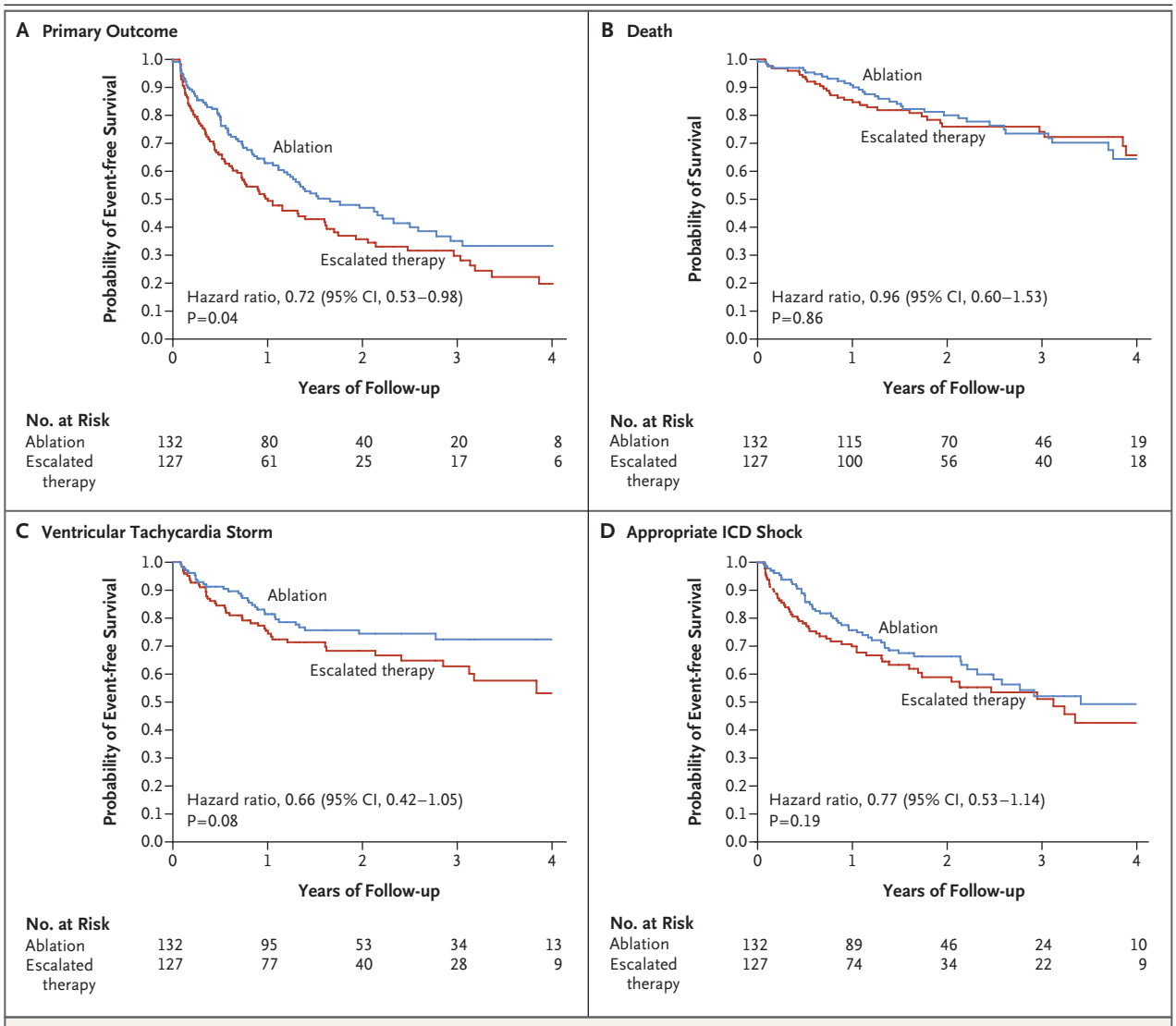

Figure 1. Primary Outcome and Its Components.

Panel A shows survival free from the primary outcome — death at any time or ventricular tachycardia storm or appropriate shock from an implantable cardioverter–defibrillator (ICD) after the 30-day treatment period — among patients treated with catheter ablation or escalated antiarrhythmic drug (AAD) therapy. Rates of death were similar in the two groups (Panel B). The significantly lower rate of the primary outcome in the ablation group was driven by lower rates of ventricular tachycardia storm (Panel C) and appropriate ICD shock (Panel D).

ADVERSE EVENTS

Among the patients in the escalated-therapy group, 3 deaths were attributed to AAD therapy (2 from pulmonary toxicity and 1 from hepatic dysfunction). Nonfatal hepatic dysfunction was more frequent in the escalated-therapy group than in the ablation group (6 patients vs. 0 patients, P=0.001), as was tremor or ataxia (6 patients vs. 0 patients, P=0.01) and drug side effects leading to therapy changes (6 patients vs. 0 patients, P=0.01). There were more frequent procedural complications among the patients in the ablation group than among those in the escalated-therapy group, including major bleeding (3 patients vs. 1 patient, P=0.62), vascular injury (3 patients vs. 0 patients, P=0.25), cardiac perforation (2 patients vs. 1 patient, P=1.00), and heart block (1 patient vs. 0 patients, P=0.49). In the escalated-therapy group, treatment-related adverse events were more frequent (51 vs. 22, P=0.002) and

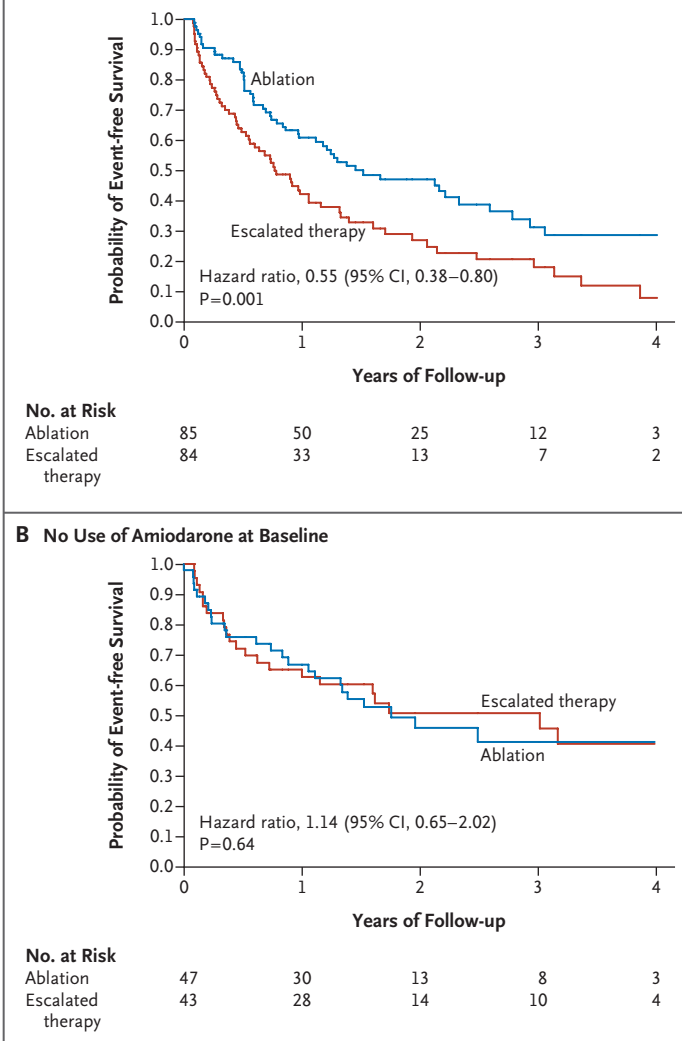

Figure 2. Primary Outcome, According to Receipt of Amiodarone during the Index Arrhythmia.

Panel A shows freedom from the primary outcome for patients in whom the qualifying arrhythmia occurred despite therapy with amiodarone (low or high dose) at baseline. Catheter ablation substantially reduced the incidence of the outcome in this subgroup. Panel B shows survival free from the primary outcome for patients in whom the qualifying arrhythmia occurred despite therapy with an AAD other than amiodarone (most commonly sotalol). There was no significant between-group difference in outcome in this subgroup.

occurred in more patients (39 vs. 20, P=0.003). (Details regarding adverse events are provided in Tables S2 and S3 in the Supplementary Appendix.)

DISCUSSION

Recurrent ventricular tachycardia is a common problem among patients who have ischemic cardiomyopathy with placement of an ICD and is usually managed with antiarrhythmic drugs, most commonly amiodarone. In our trial, catheter ablation in such patients was more effective than escalated AAD therapy in reducing the rate of the combined outcome of death at any time or ventricular tachycardia storm or ICD shocks after 30 days. In our trial, patients with recurrent ventricular tachycardia constituted a high-risk group, with more than half the patients continuing to have ventricular tachycardia and more than a quarter dying during the course of the trial despite being well treated for ischemic heart disease and ventricular dysfunction. Most of the deaths were attributed to congestive heart failure or noncardiac causes, with few deaths from arrhythmia. Neither of the two study treatments showed superiority with respect to mortality, perhaps because of the relatively high risk of death from nonarrhythmic causes. The benefit with respect to the primary outcome for ablation was driven by a reduction in the rates of ventricular tachycardia storm and ICD shocks. Sustained ventricular tachycardia at a rate below the detection limit of the ICD and adverse events that were attributed to treatment were more frequent among patients in the escalated-therapy group.

Consensus statements and guidelines recommend the use of catheter ablation when AAD therapy does not prevent recurrent ventricular tachycardia.[5,14,20] However, these recommendations have been based largely on expert opinion and nonrandomized case series. This trial provides evidence that catheter ablation should be preferred over escalation of AAD therapy for the reduction of recurrent ventricular tachycardia in this population.

Two randomized trials of catheter ablation have previously been completed in patients with ischemic cardiomyopathy and ventricular tachycardia. In the Ventricular Tachycardia Ablation in Coronary Heart Disease (VTACH) trial,[11] 110 patients with ischemic cardiomyopathy who were receiving an ICD for hemodynamically stable monomorphic ventricular tachycardia were randomly assigned to a group undergoing catheter ablation before ICD implantation or to a control group receiving no additional intervention; there was a significant benefit associated with ablation as compared with the control. In the Substrate Mapping and Ablation in Sinus Rhythm to Halt Ventricular Tachycardia (SMASH-VT) trial,[10] 128 patients with ischemic cardiomyopathy who had

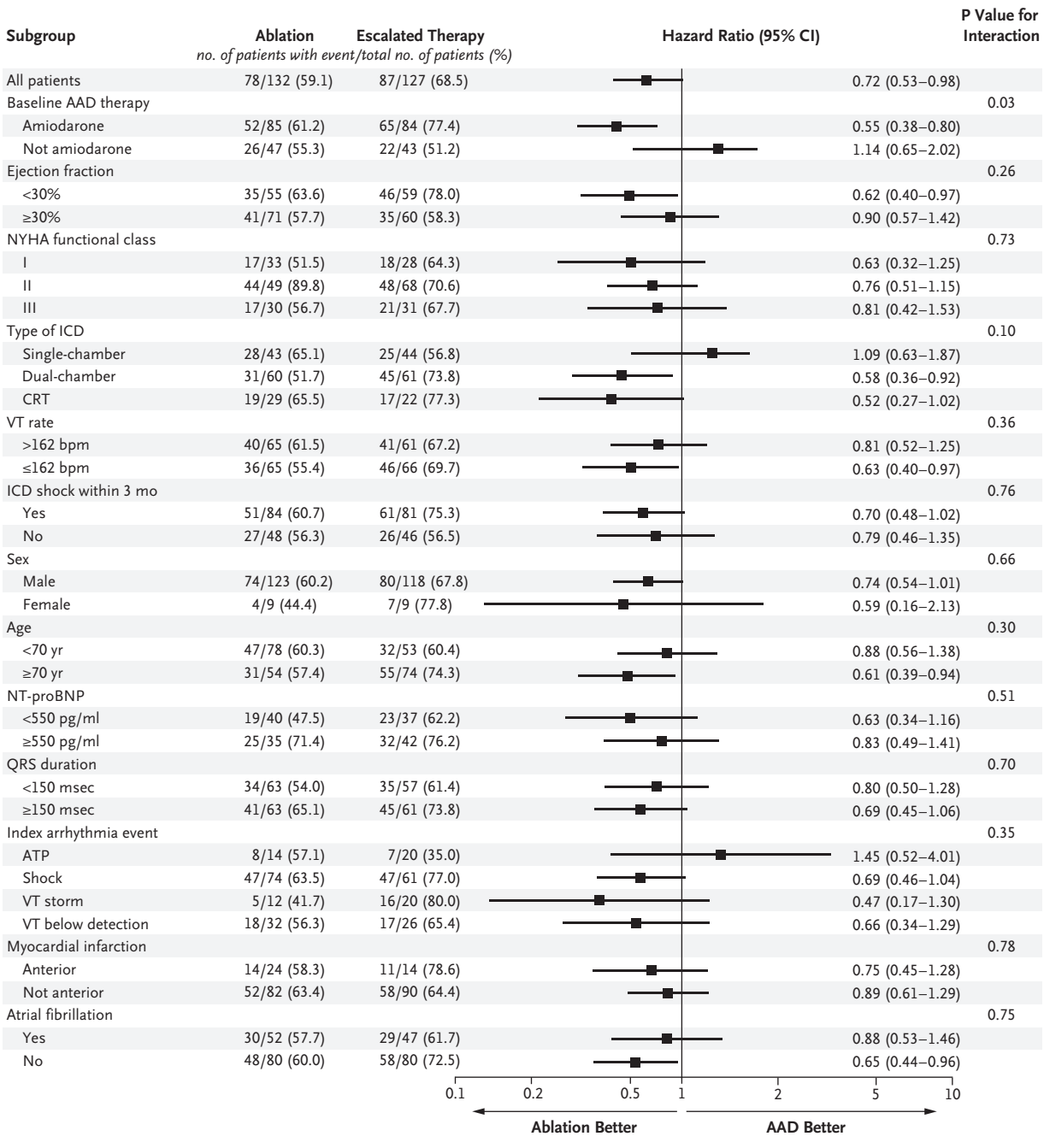

Figure 3. Subgroup Analyses of the Primary Outcome.

Hazard ratios and 95% confidence intervals are shown for the primary outcome in each prespecified subgroup. There were no significant interactions between subgroups and treatment assignment except for the baseline drug stratum (amiodarone vs. non-amiodarone, P=0.03 for interaction). ATP denotes antitachycardia pacing, CRT cardiac resynchronization therapy, NT-proBNP N-terminal pro–brain natriuretic peptide, NYHA New York Heart Association, and VT ventricular tachycardia.

hemodynamically unstable ventricular tachycardia and an ICD were randomly assigned to undergo substrate-guided ablation or no ablation. At 2 years, the rate of ventricular tachycardia was 12% among patients in the ablation group as compared with 33% in the control group. However, neither of these previous trials used systematic treatment with escalated AAD therapy in the control group.

A significant benefit of catheter ablation with respect to the primary outcome in our trial was observed only among patients in whom the index arrhythmia had occurred despite amiodarone therapy at baseline. These patients were treated with either ongoing amiodarone plus ablation or an escalation of their AAD therapy with a higher dose of amiodarone or the addition of mexiletine. No significant between-group difference in the primary outcome was observed among patients who were enrolled after a ventricular arrhythmia that occurred during receipt of a non-amiodarone AAD. These patients were treated with either a continuation of their baseline AAD therapy plus catheter ablation or the initiation of amiodarone.

Our trial has several important limitations. First, it was not powered to assess the effect of the two treatments on mortality. Second, although the practitioners who performed catheter ablation in our trial were experienced in the procedure, it is possible that specialized referral centers for ablation of ventricular tachycardia could have achieved better procedural outcomes. However, the inclusion of multiple centers increases the likelihood that the findings can be generalized. Third, we enrolled patients who had a high disease burden relatively late in the course of advanced cardiac disease and evaluated second-line therapy for ventricular tachycardia. Thus, further study is required to show whether catheter ablation or AAD therapy is the most effective first-line therapy for scar-related ventricular tachycardia.

In conclusion, among patients with ischemic cardiomyopathy who had recurrent ventricular tachycardia and an ICD despite first-line AAD therapy, the rate of the composite outcome of death at any time or ventricular tachycardia storm or appropriate ICD shock after 30 days was lower than that among patients who received escalated AAD therapy. In addition, treatment-attributed adverse events were more frequent in the escalated-therapy group than in the ablation group.

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