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Catheter Ablation or Antiarrhythmic Drugs for Ventricular Tachycardia

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ABSTRACT

BACKGROUND

Patients with ventricular tachycardia and ischemic cardiomyopathy are at high risk for adverse outcomes. Catheter ablation is commonly used when antiarrhythmic drugs do not suppress ventricular tachycardia. Whether catheter ablation is more effective than antiarrhythmic drugs as a first-line therapy in patients with ventricular tachycardia is uncertain.

METHODS

In an international trial, we randomly assigned in a 1:1 ratio patients with previous myocardial infarction and clinically significant ventricular tachycardia (defined as ventricular tachycardia storm, receipt of appropriate implantable cardioverter-defibrillator [ICD] shock or antitachycardia pacing, or sustained ventricular tachycardia terminated by emergency treatment) to receive antiarrhythmic drug therapy or to undergo catheter ablation. All the patients had an ICD. Catheter ablation was performed within 14 days after randomization; sotalol or amiodarone was administered as antiarrhythmic drug therapy according to prespecified criteria. The primary end point was a composite of death from any cause during follow-up or, more than 14 days after randomization, ventricular tachycardia storm, appropriate ICD shock, or sustained ventricular tachycardia treated by medical intervention.

RESULTS

A total of 416 patients were followed for a median of 4.3 years. A primary end-point event occurred in 103 of 203 patients (50.7%) assigned to catheter ablation and in 129 of 213 (60.6%) assigned to drug therapy (hazard ratio, 0.75; 95% confidence interval, 0.58 to 0.97; $P=0.03$). Among patients in the catheter ablation group, adverse events within 30 days after the procedure included death in 2 patients (1.0%) and nonfatal adverse events in 23 patients (11.3%). Among the patients assigned to drug therapy, adverse events that were attributed to antiarrhythmic drug treatment included death from pulmonary toxic effects in 1 patient (0.5%) and nonfatal adverse events in 46 patients (21.6%).

CONCLUSIONS

Among patients with ischemic cardiomyopathy and ventricular tachycardia, an initial strategy of catheter ablation led to a lower risk of a composite primary end-point event than antiarrhythmic drug therapy. (Funded by the Canadian Institutes of Health Research and others; VANISH2 ClinicalTrials.gov number, NCT02830360.)

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*A list of the investigators in the VANISH2 trial is provided in the Supplementary Appendix, available at NEJM.org.

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CME



IMPLANTABLE CARDIOVERTER-DEFIBRILLATORS (ICDs) improve survival in patients with myocardial scar after a myocardial infarction and ventricular tachycardia by delivering antitachycardia pacing or an electrical shock.^{1,2} Unfortunately, ICDs do not prevent ventricular tachycardia. Approximately one third of persons with an ICD will have episodes of ventricular tachycardia and receive an ICD shock within 3 years after implantation.³ Among patients with an ICD, those with recurrent ventricular tachycardia have impaired quality of life,^{4,5} more hospitalizations for heart failure, and worse survival than those without episodes of ventricular tachycardia. Patients with clusters of ventricular tachycardia episodes (often referred to as electrical storms) are at particularly increased risk for death from any cause.^{6,7} The use of antiarrhythmic drugs or catheter ablation to suppress recurrent ventricular tachycardia is often warranted. These therapies have different risks and efficacies, and comparative studies to guide clinical decisions are limited, as reported in society guidelines.⁸⁻¹⁰

The two drugs most commonly used to reduce the risk of ventricular tachycardia are sotalol^{11,12} and amiodarone.¹² Sotalol is less effective than amiodarone but has a lower risk of adverse effects during long-term therapy and is often preferred for patients who do not have severe ventricular dysfunction, renal impairment, or electrical storm. Amiodarone has greater risk of noncardiac toxic effects than sotalol but greater efficacy and is preferred for patients with more severe ventricular dysfunction or electrical storm.⁸ Catheter ablation has also been shown to reduce the risk of recurrent ventricular tachycardia, but it is associated with a risk of procedural complications and is usually considered only after drug therapy fails.¹³⁻¹⁶

The Ventricular Tachycardia Antiarrhythmics or Ablation in Ischemic Heart Disease (VANISH) trial showed that ablation and continuation of baseline antiarrhythmic medications in patients with ventricular tachycardia and ischemic cardiomyopathy led to a lower risk of a composite of death, appropriate ICD shock, or ventricular tachycardia storm than escalation of antiarrhythmic drug therapy.¹⁷ We conducted the VANISH2 trial to compare catheter ablation with systematic antiarrhythmic drug therapy as a first-line treatment strategy in patients with an ICD,

ischemic cardiomyopathy, and ventricular tachycardia who had no history of nonresponse to antiarrhythmic drug therapy.

METHODS

TRIAL DESIGN AND OVERSIGHT

We conducted this investigator-initiated, multicenter, open-label, randomized trial with blinded adjudication of end-point events at 22 centers in Canada, the United States, and France. Details regarding the trial design are provided in the Supplementary Appendix, available with the full text of this article at NEJM.org. The trial protocol (available at NEJM.org) has been described previously¹⁸ and was approved by the institutional research ethics committee at each participating center. Details regarding the response to the coronavirus disease 2019 (Covid-19) pandemic are provided in the Supplementary Appendix.

Data monitoring and collection were performed by staff at the Nova Scotia Health Cardiovascular Research Unit. Data were analyzed by staff at the University of Ottawa Cardiovascular Research Methods Centre and the steering committee. The first author wrote the first draft of the manuscript and designed the trial in collaboration with the executive committee. All the authors gathered the data, made the decision to submit the manuscript for publication, and vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol. The funders had no role in the trial design; selection of the participating centers; enrollment of the patients; collection, storage, analysis, and interpretation of the data; preparation of the manuscript; or decision to submit the manuscript for publication.

PATIENTS

Patients were eligible for inclusion if they had a history of myocardial infarction and had had at least one of the following ventricular tachycardia events within the preceding 6 months while not being treated with antiarrhythmic drugs: sustained monomorphic ventricular tachycardia terminated by pharmacologic therapy or electrical cardioversion; three or more episodes, including one symptomatic episode, of ventricular tachycardia treated with antitachycardia pacing by an ICD; five or more episodes of monomorphic ventricular tachycardia regardless of symptoms; one

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or more appropriate ICD shocks; or three episodes of sustained ventricular tachycardia within 24 hours. Detailed inclusion and exclusion criteria are provided in the Supplementary Appendix. All the patients provided written informed consent.

RANDOMIZATION AND INTERVENTIONS

Eligible patients were randomly assigned in a 1:1 ratio to undergo catheter ablation (catheter ablation group) or receive antiarrhythmic drug therapy (drug therapy group). Randomization was performed with concealed assignment according to a Web-based program (IWRS; Dacima Software) and the use of block randomization with masked randomly permuted block sizes stratified according to eligibility for sotalol or amiodarone treatment and enrolling center. Patients were considered to be eligible to receive sotalol if they had an estimated glomerular filtration rate of at least 30 ml per minute per 1.73 m² of body-surface area, a New York Heart Association functional class of I or II, a left ventricular ejection fraction of at least 20%, no history of torsades de pointes, no history of an unacceptable side-effect profile with beta-blocker or sotalol treatment, no abnormal QT prolongation, and a qualifying arrhythmia that was not classified as a ventricular tachycardia storm.

Patients who were eligible to receive sotalol were randomly assigned to receive the drug at a dose of 120 mg orally twice daily or to undergo catheter ablation; those who were not eligible for sotalol treatment were randomly assigned to receive amiodarone or undergo catheter ablation. Amiodarone therapy was initiated at a dose of 400 mg orally twice daily for 2 weeks, continued at a dose of 400 mg daily for 4 weeks, and then maintained at a dose of 200 mg daily.¹²

Patients assigned to catheter ablation underwent the procedure within 14 days after randomization. Catheter ablation procedures were conducted according to a standardized approach, which included the induction of ventricular tachycardia and electroanatomic mapping of the ventricular substrate potentially responsible for ventricular tachycardia, with delivery of radiofrequency energy at the potentially arrhythmic substrate to render ventricular tachycardia noninducible. Additional details about the catheter ablation procedure are provided in the Supplementary Appendix.

ICD PROGRAMMING AND FOLLOW-UP

ICDs were programmed according to a standardized protocol that was based on published guidelines (details are provided in the Supplementary Appendix).¹⁸⁻²⁰ Patients were treated with guideline-directed medications and followed at 3 and 6 months after randomization and every 6 months thereafter until the end of the trial, which occurred 2 years after the last patient had undergone randomization.

TRIAL END POINTS

The primary end point was a composite of death from any cause during follow-up or, more than 14 days after randomization, appropriate ICD shock, ventricular tachycardia storm (at least three ventricular tachycardia events within 24 hours), or treated sustained ventricular tachycardia below the detection limit of the ICD. The 14-day treatment period was imposed to exclude nonfatal outcomes that might occur before the administration of an adequate dose of antiarrhythmic drug or the performance of catheter ablation.

Prespecified secondary end points included the components of the primary end point, as well as other arrhythmia episodes or adverse clinical events.¹⁸ Clinical events and arrhythmia episodes detected by ICDs were adjudicated by committee members who were unaware of treatment assignments. Primary end-point events were reviewed by two committee members and by the full committee in case of disagreement.

SAFETY OUTCOMES

Serious adverse events were defined as those leading to death, hospitalization for cardiovascular causes for at least 24 hours, or prolongation of hospitalization. Other safety events were defined as adverse outcomes that did not meet these criteria or involved thyroid dysfunction or liver dysfunction. Treatment-related adverse events were defined as those that occurred within 30 days after catheter ablation or, in the case of events related to antiarrhythmic drug therapy, as those that led to drug discontinuation or dose reduction and were considered by the event-adjudication committee to be definitely or likely due to antiarrhythmic drug therapy.

STATISTICAL ANALYSIS

We estimated that a sample size of 416 patients would provide the trial with 85% power to detect

a reduction of 35% in the relative risk of a primary end-point event, using a two-sided log-rank test with a 0.05 level of significance. We based this estimation on the assumption that a primary end-point event would occur in 17.5% of patients in the drug therapy group at 1 year, a uniform accrual over 5 years of recruitment with minimum of 2 years of follow-up for all the patients, a loss to follow-up of 2%, and a crossover of 3% from the drug therapy group to the catheter ablation group and 1% from the catheter ablation group to the drug therapy group. Interim safety analyses were performed by an independent data and safety monitoring committee at 6-month intervals during the enrollment period.

Descriptive variables were summarized with the use of frequency distributions, means and standard deviations, or medians and interquartile ranges and were tested with the use of Fisher's exact test, t-tests, or the Wilcoxon–Mann–Whitney test, as appropriate. Analyses were performed according to the intention-to-treat principle. Survival analysis techniques were used to compare the incidence of the primary and secondary end-point events between the two trial groups. Survival was summarized with Kaplan–Meier product-limit estimates, which were compared with the use of nonparametric log-rank tests. For secondary nonfatal end-point events, a competing-risk analysis was performed, with death as the competing risk. The probability of the occurrence of a nonfatal secondary end-point event was estimated with the cumulative incidence function, and the cumulative incidence curves were compared with the use of the Fine–Gray subdistribution hazard model.

Hazard ratios and confidence intervals were calculated with Cox proportional-hazard models, which were also used to test for interactions among the prespecified subgroups. The assumption of proportional hazards was tested, and its validity was confirmed. All tests were conducted at an alpha level of 0.05. The widths of the confidence intervals have not been adjusted for multiplicity, so the intervals should not be used to infer definitive treatment effects for the secondary end points or in subgroups. Statistical testing was performed with SAS software, version 9.4 (SAS Institute).

RESULTS

PATIENTS

From November 10, 2016, to June 6, 2022, a total of 424 patients who met the eligibility criteria were enrolled and underwent randomization at 22 centers. Of these patients, 8 were enrolled during the onset of the Covid-19 pandemic and were excluded from the analysis and followed in a registry (details are provided in the Supplementary Appendix).¹⁸ The representativeness of the trial population is shown in Table S1 in the Supplementary Appendix. Of the remaining 416 patients, 203 were assigned to catheter ablation and 213 to drug therapy. The flow of patients in the trial is shown in Figure S1.

The baseline clinical characteristics of the patients appeared to be similar in the two trial groups, although a higher percentage of patients in the catheter ablation group had undergone percutaneous coronary intervention and a higher percentage of patients in the drug therapy group were taking antiplatelet therapy (Table 1 and Table S2). All the patients in the drug therapy group received antiarrhythmic drugs. In the catheter ablation group, 200 of 203 patients underwent catheter ablation (1 patient withdrew consent, 1 had an intracardiac thrombus, and 1 had a heparin allergy). The characteristics of the catheter ablation procedures are provided in Table S3.

Follow-up was completed on June 6, 2024. All the patients were followed until death or completion of the trial; the median follow-up was 4.3 years (interquartile range, 2.5 to 5.7). In the drug therapy group, 5 patients were lost to follow-up after a median of 15 months, and 3 underwent catheter ablation. In the catheter ablation group, 5 patients underwent heart transplantation, 9 were lost to follow-up after a median of 49 months, and 17 received antiarrhythmic drug therapy (6 patients received treatment for atrial fibrillation, 2 for frequent premature ventricular complexes, 5 for ventricular tachycardia during the treatment period, 2 for late ventricular tachycardia at 48 and 78 months, 1 because ablation had not been performed owing to left ventricular thrombus, and 1 after a single episode of ventricular tachycardia that had been treated by antitachycardia pacing 2.5 weeks after randomization).

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Catheter Ablation (N=203)	Drug Therapy (N=213)
Age — yr	67.7±8.6	68.4±8.0
Male sex — no. (%)	193 (95.1)	197 (92.5)
Race or ethnic group — no. (%)†		
Asian	4 (2.0)	5 (2.3)
Black	1 (0.5)	4 (1.9)
Indigenous	2 (1.0)	5 (2.3)
Other	2 (1.0)	2 (0.9)
White	122 (60.1)	134 (62.9)
Unknown	73 (36.0)	66 (31.0)
Existing ICD — no. (%)	179 (88.2)	188 (88.3)
Time since last myocardial infarction — yr	13.3±9.9	14.8±10.4
Previous percutaneous coronary intervention — no. (%)	128 (63.1)	121 (56.8)
Previous coronary-artery bypass grafting — no. (%)	82 (40.4)	88 (41.3)
Diabetes — no. (%)	79 (38.9)	83 (39.0)
Hypertension — no. (%)	160 (78.8)	169 (79.3)
Renal insufficiency — no. (%)	31 (15.3)	23 (10.8)
Atrial fibrillation or flutter — no. (%)	70 (34.5)	72 (33.8)
New York Heart Association functional class — no. (%)		
I	87 (42.9)	89 (41.8)
II	99 (48.8)	107 (50.2)
III	17 (8.4)	17 (8.0)
Ejection fraction — %	34.0±11.0	34.3±10.3
Type of ICD — no. (%)		
Single-chamber	66 (32.5)	77 (36.2)
Dual-chamber	94 (46.3)	100 (46.9)
Cardiac-resynchronization therapy	43 (21.2)	36 (16.9)
Eligible for amiodarone therapy — no. (%)	108 (53.2)	109 (51.2)
Eligible for sotalol therapy — no. (%)	95 (46.8)	104 (48.8)
Type of qualifying arrhythmia within 6 mo before enrollment — no. (%)		
VT storm: ≥3 VT events within 24 hr	48 (23.6)	58 (27.2)
≥1 Appropriate ICD shock	106 (52.2)	109 (51.2)
≥3 Episodes of VT treated with ATP, at least one of which was symptomatic	30 (14.8)	32 (15.0)
≥5 Episodes of VT treated with ATP regardless of symptoms	37 (18.2)	37 (17.4)
Sustained monomorphic VT terminated by therapy or cardioversion‡	65 (32.0)	65 (30.5)

* Plus–minus values are means ±SD. Percentages may not sum to 100 because of rounding. ATP denotes antitachycardia pacing, ICD implantable cardioverter–defibrillator, and VT ventricular tachycardia.

† Race or ethnic group was reported by the patient. More than one group could be reported.

‡ Sustained monomorphic VT was documented on a 12-lead electrocardiogram or rhythm strip and terminated by pharmacologic therapy or electrical cardioversion.

Table 2. Primary and Secondary End Points.

End Point	Catheter Ablation (N=203)	Drug Therapy (N=213)	Hazard Ratio (95% CI)*
Primary end point†	103 (50.7)	129 (60.6)	0.75 (0.58–0.97)
Secondary end points			
Death from any cause during follow-up	45 (22.2)	54 (25.4)	0.84 (0.56–1.24)
Appropriate ICD shock after 14 days	60 (29.6)	81 (38.0)	0.75 (0.53–1.04)
VT storm after 14 days	44 (21.7)	50 (23.5)	0.95 (0.63–1.42)
Treated sustained VT below the detection limit of the ICD after 14 days	9 (4.4)	35 (16.4)	0.26 (0.13–0.55)

* The widths of the confidence intervals for the secondary end points have not been adjusted for multiplicity and should not be used to infer definitive treatment effects.

† The primary end point was a composite of death from any cause during follow-up or, more than 14 days after randomization, appropriate ICD shock, VT storm (at least three VT events within 24 hours), or treated sustained VT below the detection limit of the ICD. $P=0.03$ for the comparison of the catheter ablation group with the drug therapy group.

CLINICAL OUTCOMES

A primary end-point event occurred in 103 patients (50.7%) in the catheter ablation group and in 129 patients (60.6%) in the drug therapy group (hazard ratio, 0.75; 95% confidence interval [CI], 0.58 to 0.97; $P=0.03$) (Table 2 and Fig. 1). Death was reported in 45 patients (22.2%) in the catheter ablation group and in 54 patients (25.4%) in the drug therapy group (hazard ratio, 0.84; 95% CI, 0.56 to 1.24). Appropriate ICD shock after 14 days occurred in 60 patients (29.6%) in the catheter ablation group and 81 (38.0%) in the drug therapy group (hazard ratio, 0.75; 95% CI, 0.53 to 1.04); ventricular tachycardia storm (after 14 days) occurred in 44 (21.7%) and 50 (23.5%), respectively (hazard ratio, 0.95; 95% CI, 0.63 to 1.42); and treatment of sustained ventricular tachycardia below the detection limit of the ICD (after 14 days) occurred in 9 (4.4%) and 35 (16.4%), respectively (hazard ratio, 0.26; 95% CI, 0.13 to 0.55) (Table 2 and Fig. 2). Results of primary end-point analyses according to subgroup are shown in Figure 3, and those according to sotalol and amiodarone eligibility are shown in Figure S2.

The number of episodes of appropriate antitachycardia pacing, appropriate ICD shocks, treatment of ventricular tachycardia below the detection limit of the ICD, and ventricular tachycardia storm events are shown in Table S4 and Table S5. A total of 1383 episodes of appropriate ICD shock or antitachycardia pacing (1.91 events

per person-year) occurred in the catheter ablation group, and 2195 episodes (6.14 events per person-year) occurred in the drug therapy group (mean difference, -4.22 events per person-year; 95% CI, -9.01 to 0.56) (Table S5).

SAFETY

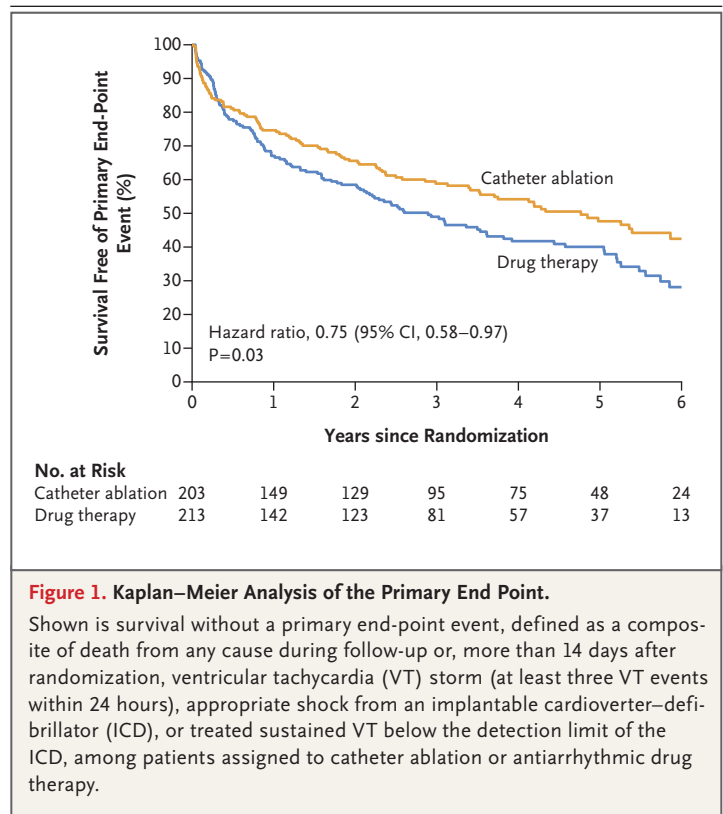
Adverse events according to treatment assignment are shown in Tables S6 through S9. Serious nonfatal adverse events occurred in 57 patients (28.1%) assigned to catheter ablation and in 65 (30.5%) assigned to drug therapy. During the trial, 319 catheter ablations occurred, including 240 procedures among 200 of the 203 patients in the catheter ablation group and 79 procedures among 63 of the 213 patients in the drug therapy group. Among patients in the catheter ablation group, adverse events within 30 days after the procedure included death in 2 patients (1.0%) and nonfatal adverse events in 23 patients (11.3%), with nonfatal stroke and cardiac perforation occurring in 2 patients (1.0%) and 1 patient (0.5%), respectively. Among the patients in the drug therapy group, 1 patient (0.5%) died of pulmonary toxic effects attributed to antiarrhythmic drug treatment, and 7 patients (3.3%) had pulmonary infiltrates or fibrosis attributed to antiarrhythmic drug treatment. Overall, 46 patients (21.6%) assigned to drug therapy and 7 patients (3.4%) assigned to catheter ablation had a nonfatal adverse event attributed to antiarrhythmic drug treatment that led to drug discontinuation or dose reduction.

DISCUSSION

In this trial, catheter ablation led to a lower risk of a composite of death from any cause during follow-up or, more than 14 days after randomization, appropriate ICD shock, ventricular tachycardia storm, or treated sustained ventricular tachycardia below the detection limit of the ICD than antiarrhythmic drug therapy among patients with ventricular tachycardia and ischemic cardiomyopathy. Catheter ablation and antiarrhythmic drug therapy can reduce the risk of recurrent ventricular tachycardia and ICD shock,^{11-14,21} but both approaches are associated with adverse events and have imperfect efficacy. Determining when to use these therapies is an important clinical decision.^{22,23} The use of drugs as initial therapy followed by ablation if drug therapy fails is common practice and concordant with current guidelines,^{8,16} given that ablation is superior to the escalation of drug therapy in reducing the risk of a composite of death, appropriate ICD shock, or VT storm.¹⁷

Among patients with at least one appropriate ICD shock, ventricular tachycardia storm, sustained ventricular tachycardia terminated by emergency treatment, or multiple recurrences of ventricular tachycardia treated by antitachycardia pacing, catheter ablation was more effective than drug therapy in reducing the risk of a composite of death from any cause during follow-up, appropriate ICD shock, ventricular tachycardia storm, or treated sustained ventricular tachycardia below the detection limit of the ICD. This difference appeared to be due to a lower number of appropriate ICD shock events and episodes of treated sustained ventricular tachycardia below the detection limit of the ICD (both after 14 days) in the catheter ablation group. Overall, the number of ventricular tachycardia events was lower in the catheter ablation group than in the drug therapy group. Our findings are consistent with those of previous smaller randomized trials that suggested the effectiveness of catheter ablation.^{13-15,22,24}

The risks of death from any cause and ventricular arrhythmia were high during our trial, despite treatment. During the follow-up period, nearly 24% of the patients died, 26% had ventricular tachycardia storm, 37% received an appropriate



ICD shock, and 11% had treated sustained ventricular tachycardia below the detection limit of the ICD. These findings are consistent with previous observations that recurrent ventricular tachycardia is associated with worse outcomes despite the presence of an ICD, which shows the importance of determining appropriate treatment strategies in this group.⁶

Catheter ablation is associated with a risk of procedural complications. These complications were more common among patients assigned to receive catheter ablation as an initial treatment strategy, with death occurring in 2 patients, non-fatal stroke occurring in 2 patients, cardiac perforation occurring in 1 patient, and vascular injury occurring in 5 patients (of whom 2 patients had major bleeding). Antiarrhythmic drug therapy also has risks that contribute to worse outcomes.²³ In the drug therapy group, death due to pulmonary toxicity occurred in 1 patient, pulmonary infiltrates or fibrosis occurred in 7 patients, and gastrointestinal, neurologic, thyroid-related, or liver-related adverse effects that led to drug dose

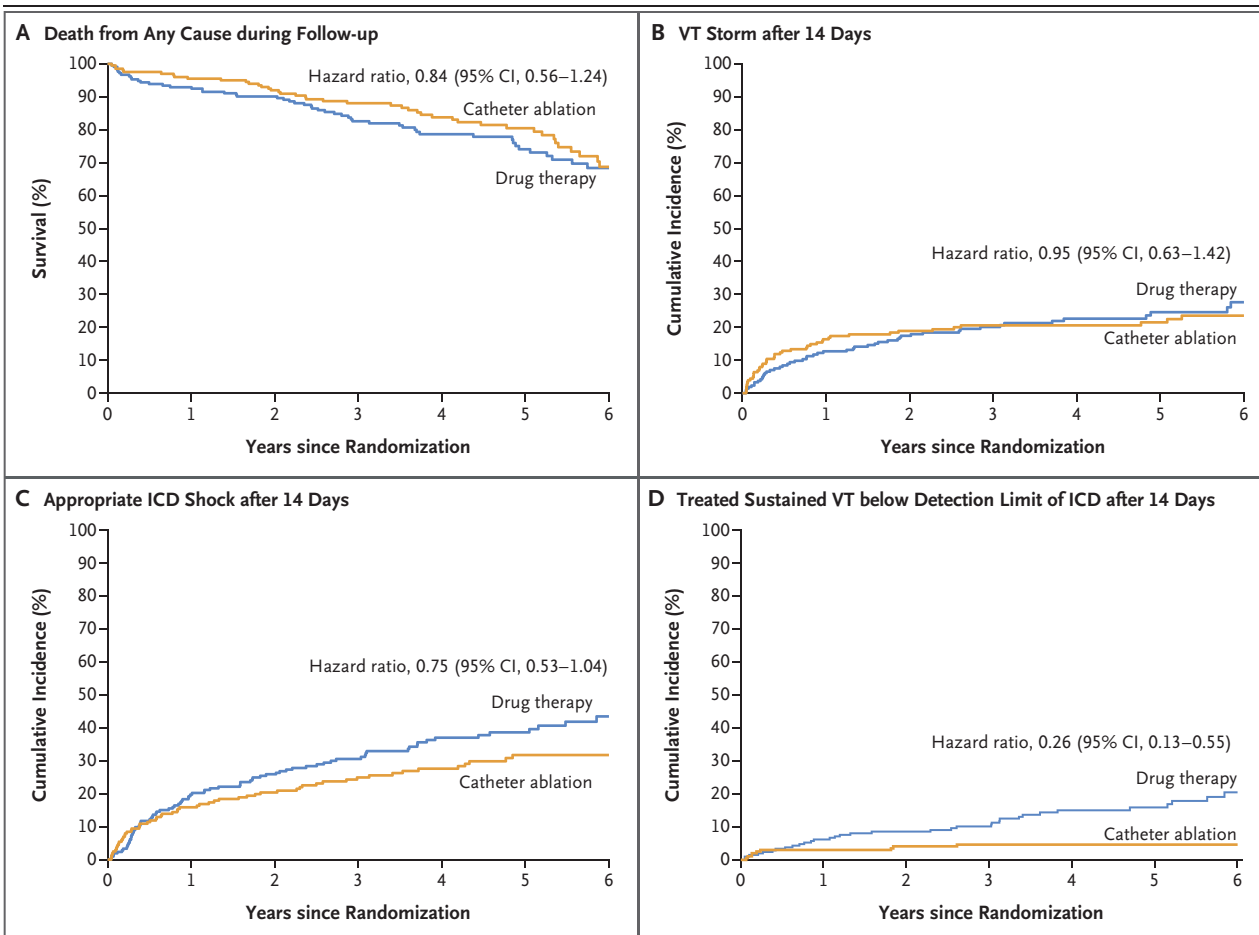


Figure 2. Kaplan–Meier Analysis of Components of the Primary End Point.

Panel A shows the percentage of patients who survived, in the analysis of death from any cause during follow-up. Panel B shows the cumulative incidence of VT storm more than 14 days after randomization. Panel C shows the cumulative incidence of appropriate ICD shock more than 14 days after randomization. Panel D shows the cumulative incidence of treated sustained VT below the detection limit of the ICD more than 14 days after randomization. Hazard ratios in Panels B through D were calculated with adjustment for the competing risk of death. The widths of the confidence intervals have not been adjusted for multiplicity and should not be used to infer definitive treatment effects.

adjustment or discontinuation occurred in 25 patients.

Our trial has several limitations. The trial was not designed to detect the effect of treatment on mortality or other individual components of the primary end point. The effectiveness of catheter ablation and the risk of procedural complications may be influenced by the skill and experience of the team performing the procedure; however, the differences among the clinical centers that enrolled the trial participants supports the generalizability of our findings. Future changes in ablation

technology or the development of new antiarrhythmic drugs may influence the interpretation of our findings. In this trial, ICDs were uniformly programmed according to recommendations in evidence-based guidelines. Future studies may identify other ICD programming settings to reduce the incidence of ventricular tachycardia below the detection limit of the ICD without increasing the risk of delivery of inappropriate therapies. Although the follow-up period in our trial was relatively long, the adverse effects of amiodarone treatment increase with time, and longer follow-up may be needed to

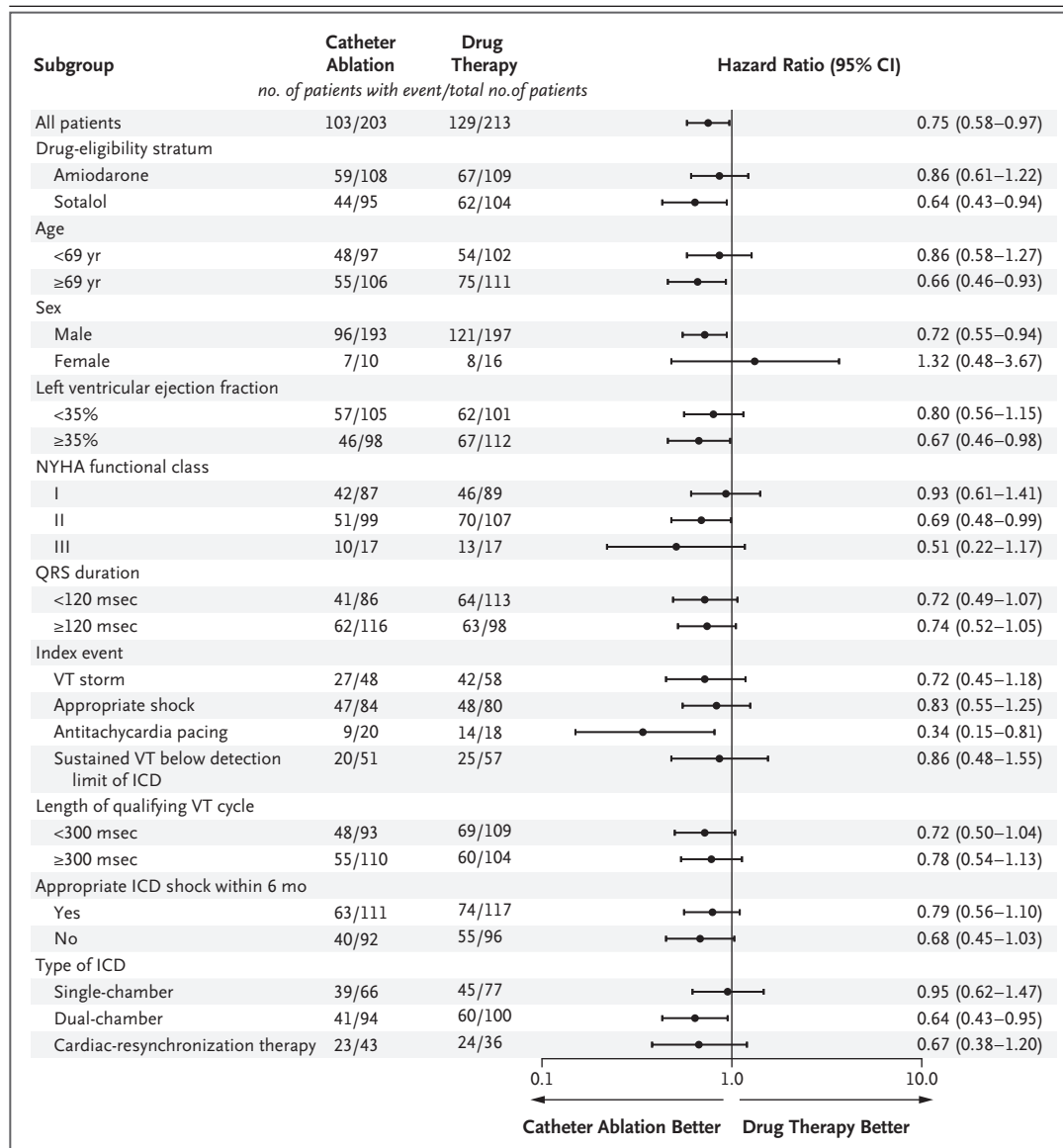


Figure 3. Subgroup Analyses of the Primary End Point.

Shown are hazard ratios and 95% confidence intervals for the primary end point in prespecified subgroups according to baseline characteristics. Data on the QRS duration were missing for two patients in the drug therapy group and one patient in the catheter ablation group. The widths of the confidence intervals in the subgroup analyses have not been adjusted for multiplicity and should not be used to infer definitive treatment effects. NYHA denotes New York Heart Association.

fully understand differences in outcomes related to amiodarone use.

This multicenter, randomized trial involving patients with ischemic cardiomyopathy who had ventricular tachycardia and an ICD showed that an initial strategy of catheter ablation led to a

lower risk of a composite of death from any cause during follow-up or, more than 14 days after randomization, appropriate ICD shock, ventricular tachycardia storm, or treated sustained ventricular tachycardia below the detection limit of the ICD than antiarrhythmic drug therapy.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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REFERENCES

1. Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. *N Engl J Med* 1997; 337:1576-83.
2. Connolly SJ, Hallstrom AP, Cappato R, et al. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials: AVID, CASH and CIDS studies: Antiarrhythmics vs Implantable Defibrillator study, Cardiac Arrest Study Hamburg, Canadian Implantable Defibrillator Study. *Eur Heart J* 2000;21: 2071-8.
3. Bennett MT, Brown ML, Koehler J, Lexcen DR, Cheng A, Cheung JW. Trends in implantable cardioverter-defibrillator programming practices and its impact on therapies: insights from a North American remote monitoring registry 2007-2018. *Heart Rhythm* 2022;19:219-25.
4. Sears SF, Rosman L, Sasaki S, et al. Defibrillator shocks and their effect on objective and subjective patient outcomes: results of the PainFree SST clinical trial. *Heart Rhythm* 2018;15:734-40.
5. Perini AP, Kutiyfa V, Veazie P, et al. Effects of implantable cardioverter/defibrillator shock and antitachycardia pacing on anxiety and quality of life: a MADIT-RIT substudy. *Am Heart J* 2017; 189:75-84.
6. Elskkari I, Parkash R, Tang A, et al. Mortality risk increases with clustered ventricular arrhythmias in patients with implantable cardioverter-defibrillators. *JACC Clin Electrophysiol* 2020;6:327-37.
7. Samuel M, Elskkari I, Sapp JL. Ventricular tachycardia burden and mortality: association or causality? *Can J Cardiol* 2022;38:454-64.
8. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation* 2018; 138(13):e272-e391.
9. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J* 2022;43:3997-4126.
10. Deyell MW, AbdelWahab A, Angaran P, et al. 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society position statement on the management of ventricular tachycardia and fibrillation in patients with structural heart disease. *Can J Cardiol* 2020;36:822-36.
11. Pacifico A, Hohnloser SH, Williams JH, et al. Prevention of implantable-defibrillator shocks by treatment with sotalol. *N Engl J Med* 1999;340:1855-62.
12. Connolly SJ, Dorian P, Roberts RS, et al. Comparison of beta-blockers, amiodarone plus beta-blockers, or sotalol for prevention of shocks from implantable cardioverter defibrillators: the OPTIC Study: a randomized trial. *JAMA* 2006;295:165-71.
13. Reddy VY, Reynolds MR, Neuzil P, et al. Prophylactic catheter ablation for the prevention of defibrillator therapy. *N Engl J Med* 2007;357:2657-65.
14. Kuck K-H, Schaumann A, Eckardt L, et al. Catheter ablation of stable ventricular tachycardia before defibrillator implantation in patients with coronary heart disease (VTACH): a multicentre randomised controlled trial. *Lancet* 2010; 375:31-40.
15. Tung R, Xue Y, Chen M, et al. First-line catheter ablation of monomorphic ventricular tachycardia in cardiomyopathy concurrent with defibrillator implantation: the PAUSE-SCD randomized trial. *Circulation* 2022;145:1839-49.
16. Cronin EM, Bogun FM, Maury P, et al. 2019 HRS/EHRA/APHRS/LAHS expert consensus statement on catheter ablation of ventricular arrhythmias. *Heart Rhythm* 2020;17(1):e2-e154.
17. Sapp JL, Wells GA, Parkash R, et al. Ventricular tachycardia ablation versus escalation of antiarrhythmic drugs. *N Engl J Med* 2016;375:111-21.
18. Sapp JL, Tang ASL, Parkash R, Stevenson WG, Healey JS, Wells G. A randomized clinical trial of catheter ablation and antiarrhythmic drug therapy for suppression of ventricular tachycardia in ischemic cardiomyopathy: the VANISH2 trial. *Am Heart J* 2024;274:1-10.
19. Wilkoff BL, Fauchier L, Stiles MK, et al. 2015 HRS/EHRA/APHRS/SOLAECE expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. *Heart Rhythm* 2016;13(2):e50-e86.
20. Stiles MK, Fauchier L, Morillo CA, Wilkoff BL. 2019 HRS/EHRA/APHRS/LAHS focused update to 2015 expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. *Heart Rhythm* 2020; 17(1):e220-e228.

21. Kuck K-H, Tilz RR, Deneke T, et al. Impact of substrate modification by catheter ablation on implantable cardioverter-defibrillator interventions in patients with unstable ventricular arrhythmias and coronary artery disease: results from the multicenter randomized controlled SMS (Substrate Modification Study). *Circ Arrhythm Electrophysiol* 2017;10(3): e004422.
22. Della Bella P, Baratto F, Vergara P, et al. Does timing of ventricular tachycardia ablation affect prognosis in patients with an implantable cardioverter defibrillator? results from the multicenter randomized PARTITA trial. *Circulation* 2022;145: 1829-38.
23. Willems S, Tilz RR, Steven D, et al. Preventive or deferred ablation of ventricular tachycardia in patients with ischemic cardiomyopathy and implantable defibrillator (BERLIN VT): a multicenter randomized trial. *Circulation* 2020;141: 1057-67.
24. Arenal Á, Ávila P, Jiménez-Candil J, et al. Substrate ablation vs antiarrhythmic drug therapy for symptomatic ventricular tachycardia. *J Am Coll Cardiol* 2022;79: 1441-53.

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