ORIGINAL ARTICLE

Surgical Ablation of Atrial Fibrillation during Mitral-Valve Surgery

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ABSTRACT

BACKGROUND

Among patients undergoing mitral-valve surgery, 30 to 50% present with atrial fibrillation, which is associated with reduced survival and increased risk of stroke. Surgical ablation of atrial fibrillation has been widely adopted, but evidence regarding its safety and effectiveness is limited.

METHODS

We randomly assigned 260 patients with persistent or long-standing persistent atrial fibrillation who required mitral-valve surgery to undergo either surgical ablation (ablation group) or no ablation (control group) during the mitral-valve operation. Patients in the ablation group underwent further randomization to pulmonary-vein isolation or a biatrial maze procedure. All patients underwent closure of the left atrial appendage. The primary end point was freedom from atrial fibrillation at both 6 months and 12 months (as assessed by means of 3-day Holter monitoring).

RESULTS

More patients in the ablation group than in the control group were free from atrial fibrillation at both 6 and 12 months (63.2% vs. 29.4%, P<0.001). There was no significant difference in the rate of freedom from atrial fibrillation between patients who underwent pulmonary-vein isolation and those who underwent the biatrial maze procedure (61.0% and 66.0%, respectively; P=0.60). One-year mortality was 6.8% in the ablation group and 8.7% in the control group (hazard ratio with ablation, 0.76; 95% confidence interval, 0.32 to 1.84; P=0.55). Ablation was associated with more implantations of a permanent pacemaker than was no ablation (21.5 vs. 8.1 per 100 patient-years, P=0.01). There were no significant between-group differences in major cardiac or cerebrovascular adverse events, overall serious adverse events, or hospital readmissions.

CONCLUSIONS

The addition of atrial fibrillation ablation to mitral-valve surgery significantly increased the rate of freedom from atrial fibrillation at 1 year among patients with persistent or long-standing persistent atrial fibrillation, but the risk of implantation of a permanent pacemaker was also increased. (Funded by the National Institutes of Health and the Canadian Institutes of Health Research; ClinicalTrials.gov number, NCT00903370.)

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Atrial fibrillation, which is associated with reduced survival and increased risk of stroke, is present in 30 to 50% of patients presenting for mitral-valve surgery.[1,2] The development of open surgical procedures for the ablation of atrial fibrillation has led to their widespread application during cardiac operations, but their effectiveness and safety have not been rigorously established. It is hypothesized that long-term outcomes can be improved by successful ablation in patients with preexisting persistent or long-standing persistent atrial fibrillation who are undergoing mitral-valve surgery.

The Cox maze III operation (sometimes called the "cut-and-sew" maze operation) is a complex surgical procedure for the control of atrial fibrillation. Developed in 1992, the procedure involves the creation of a "maze" of surgical incisions in both the right and left atria to interrupt macro-reentrant circuits that are thought to be responsible for the propagation of atrial fibrillation. Newer insights into the pathophysiological mechanisms of atrial fibrillation and the development of other tissue-ablation technologies (e.g., radiofrequency ablation and cryoablation) have encouraged frequent attempts at atrial fibrillation ablation during heart surgery. Almost all current approaches to ablation during surgery include pulmonary-vein isolation, which is the simplest, most rapidly completed set of ablation lesions; it involves the creation of circumferential ablation lesions around the pulmonary veins. In contrast, the biatrial maze lesion set, which is performed with contemporary ablation devices, requires right and left atriotomies, a longer duration of cardiopulmonary bypass, and the creation of endocardial ablation lesions extending to the mitral and tricuspid annuli.

Current American Heart Association (AHA)–American College of Cardiology (ACC)–Heart Rhythm Society (HRS) guidelines state that it is reasonable to perform atrial fibrillation ablation in selected patients undergoing other types of cardiac surgery but acknowledge that there are limited data on which to base this recommendation (level C evidence).[3] Moreover, although pulmonary-vein isolation is used more frequently than the biatrial maze procedure, data on the comparative effectiveness of the two procedures are also limited. Uncertainty regarding both the benefits of surgical ablation and the choice of lesion sets has led to wide variation in practice among surgeons.[4] In this randomized trial involving patients with persistent or long-standing persistent atrial fibrillation who were undergoing mitral-valve surgery, we sought to determine the effect of surgical ablation on the recurrence of atrial fibrillation in the first year after surgery and to explore the effects of two different ablation procedures (pulmonary-vein isolation or biatrial maze procedure) on freedom from atrial fibrillation during the same period.

Methods

Trial Design and Oversight

This trial was performed at 20 centers in the Cardiothoracic Surgical Trials Network (CTSN); the design of the trial has been published previously.[5] The trial was conducted under an investigational-device exemption, because only devices using cryoablation were approved for the treatment of atrial fibrillation when the study began; other energy sources (e.g., radiofrequency) were not approved at that time. The trial was designed to evaluate ablation as a therapeutic approach, not to support Food and Drug Administration approval for any individual device.

The CTSN investigators designed the trial protocol, which was approved by the institutional review board at each participating center. The investigators also collected and analyzed the data and wrote the manuscript. A coordinating center, an independent adjudication committee, and a data and safety monitoring board appointed by the National Institutes of Health oversaw trial progress. There was no support from a commercial entity in this trial. The investigators vouch for the accuracy and completeness of the data and for the fidelity of this report to the trial protocol, which is available with the full text of this article at NEJM.org.

Patients and Interventions

This trial enrolled adult patients with persistent or long-standing persistent atrial fibrillation who also had mitral-valve disease requiring surgical intervention. According to the 2012 HRS guidelines in place during the trial,[6] persistent atrial fibrillation was defined as non–self-terminating atrial fibrillation lasting more than 7 days, or less than 7 days if cardioversion was required. The definition was revised per AHA-ACC-HRS guidelines in 2014 and limited simply to continu-

ous atrial fibrillation for more than 7 days.[3] Long-standing persistent atrial fibrillation was defined as continuous atrial fibrillation for more than 12 months.[6] Detailed eligibility criteria have been reported[5] and are described in the Supplementary Appendix, available at NEJM.org. All participating patients provided written informed consent.

Eligible patients were randomly assigned, in a 1:1 ratio, to undergo either surgical ablation or no ablation (control group) during the mitral-valve operation after the induction of anesthesia. Patients in the ablation group underwent further randomization to one of two lesion sets: pulmonary-vein isolation or biatrial maze. Randomization was performed after intraoperative transesophageal echocardiography confirmed the absence of a left atrial thrombus. Randomization was stratified according to center. All patients also underwent closure of the left atrial appendage to reduce the risk of formation of a left atrial thrombus. The surgical-ablation procedures and postoperative management are described in the Supplementary Appendix, including Figure S1.

END POINTS

The primary end point was freedom from atrial fibrillation at both 6 months and 12 months after surgery, as assessed by means of 3-day continuous Holter monitoring. Patients who died before the 12-month assessment or who were too ill to undergo assessment of atrial fibrillation were considered not to have had a response to treatment, as were patients who underwent any ablation therapy for atrial fibrillation after the index procedure.

Secondary end points included a composite of major cardiac or cerebrovascular adverse events (death, stroke, hospitalization for heart failure, worsening heart failure [as defined by an increase of one or more classes in the New York Heart Association classification], or mitral-valve reintervention), mortality, the need for rhythm-related interventions, quality of life (as assessed by means of the Atrial Fibrillation Severity Scale [AFSS] and the physical and mental subscales of the Medical Outcomes Study 12-Item Short Form Health Survey [SF-12]), and rehospitalization.

The primary safety end point was a composite of death, stroke, heart failure, myocardial infarction, rehospitalization for cardiac causes, transient ischemic attack, pulmonary embolism, peripheral embolism, excessive bleeding, deep sternal-wound infection or mediastinitis, damage to the specialized conduction system necessitating implantation of a permanent pacemaker, or damage to peripheral structures such as the esophagus, within 30 days after the procedure or hospital discharge (whichever was later).

Follow-up assessments were conducted by telephone interview at 3, 6, and 9 months and in person at 12 months. Investigators were unaware of the trial outcomes, and the personnel at all core laboratories were unaware of the treatment-group assignments. Definitions of end points are provided in the Supplementary Appendix.

STATISTICAL ANALYSIS

The primary null hypothesis was that there would be no difference between randomization groups in the proportion of patients free from atrial fibrillation. We tested this hypothesis in an intention-to-treat analysis using a chi-square test, at a 0.05 alpha level. Patients with missing data (not owing to death) had their primary end point imputed (with the use of a multiple-imputation model with five iterations), on the assumption that data were missing at random. We calculated that enrollment of 260 patients would give the study 90% power to detect an absolute increase of 20 percentage points (from 25% to 45%) in the proportion of patients free from atrial fibrillation with ablation therapy.[5,7] We conducted a planned interim analysis using the Lan–DeMets approach with an O'Brien–Fleming–type spending function when approximately 50% of the patients had reached their 1-year follow-up; therefore, a P value of less than 0.049 was considered to indicate statistical significance in the final analysis of the primary end point. No inferential hypotheses were specified to compare the ablation subgroups (pulmonary-vein isolation vs. biatrial maze procedure).

The hazards of major cardiac or cerebrovascular adverse events and death from any cause were compared between groups with the use of Cox proportional-hazards models. Between-group differences in adverse-event and hospitalization rates were tested with the use of Poisson regression, differences in quality-of-life scores with the use of Student's t-tests, and differences in categorical outcomes with the use of chi-square tests.

RESULTS

PATIENTS

Between 2010 and 2013, a total of 3502 patients were screened, 1082 were found to be eligible, and 260 underwent randomization (133 to mitral-valve surgery with ablation and 127 to mitral-valve surgery alone) (Fig. S2 in the Supplementary Appendix). In the ablation group, 67 patients were randomly assigned to pulmonary-vein isolation and 66 to the biatrial maze procedure. The groups had similar baseline characteristics (Table 1, and Table S1 in the Supplementary Appendix for the ablation subgroups), and 11.2% were taking class III antiarrhythmic drugs. Preoperatively, 45.8% of all patients had persistent atrial fibrillation, and 54.2% had long-standing persistent atrial fibrillation (median duration, 66 months [interquartile range, 37 to 132]).

All but one patient (in the group assigned to mitral-valve surgery alone) underwent the planned primary mitral-valve surgical procedure (55.6% underwent mitral-valve repair, and 44.4% underwent mitral-valve replacement). In addition, non–ablation-related procedures were performed in 61.4% of the patients. The duration of cardiopulmonary bypass was approximately 15 minutes longer in the ablation group than in the control group (P=0.03). There was one crossover in each treatment group.

HEART RHYTHM

Significantly more patients in the ablation group than in the control group were free from atrial fibrillation at both 6 months and 12 months (primary end point) (63.2% vs. 29.4%, P<0.001) (Fig. 1A). A total of 20.0% of the patients did not have primary end-point data on Holter-monitor recordings, vital status, or subsequent ablations (see Fig. S2 in the Supplementary Appendix), and outcomes were imputed. The relative success ratio (ablation group:control group) was 2.15 (95% confidence interval [CI], 1.54 to 3.00) on the basis of observed data and 1.96 (95% CI, 1.45 to 2.63) on the basis of imputed data. The rate of freedom from atrial fibrillation was similar among patients assigned to pulmonary-vein isolation and those assigned to the biatrial maze procedure (61% and 66%, respectively; P=0.60) (Fig. 1B).

One ablation procedure was performed after the index surgery in the ablation group and three were performed in the control group; 6.0% of the patients in the ablation group and 9.5% of the patients in the control group underwent electrical cardioversion after the initial 3 months after the index surgery. At 1 year, 13.2% of the patients in the ablation group and 14.6% of the patients in the control group were taking class I or III antiarrhythmic drugs.

MORTALITY AND MAJOR CARDIAC OR CEREBROVASCULAR ADVERSE EVENTS

At 1 year, mortality did not differ significantly between the ablation group and the control group (6.8% and 8.7%, respectively; P=0.57) (Table 2) or between patients who underwent pulmonary-vein isolation and those who underwent the biatrial maze procedure (7% and 6%, respectively; P=1.00) (Table S2 in the Supplementary Appendix). At 30 days, mortality was also similar in the ablation and control groups (2.3% and 3.9%, respectively; P=0.49). Figure 2A shows the Kaplan–Meier plot of survival (hazard ratio for death with ablation, 0.76; 95% CI, 0.32 to 1.84; P=0.55). The most frequent causes of death were heart failure (20%), sepsis (20%), bleeding (10%), and respiratory failure (10%). The 1-year risk of any major cardiac or cerebrovascular adverse event was 23.3% in the ablation group and 20.5% in the control group (P=0.58); the Kaplan–Meier plot is shown in Figure 2B (hazard ratio with ablation, 1.12; 95% CI, 0.67 to 1.89; P=0.66). There was also no significant difference between the groups in any of the individual components of the composite end point at 12 months (Table 2, and Table S2 in the Supplementary Appendix for the ablation subgroups).

ADVERSE EVENTS AND HOSPITALIZATIONS

The primary safety end point at 30 days was similar in the ablation group and the control group (31.6% and 22.8%, respectively; P=0.11), as was the rate of serious adverse events at 1 year (143.8 and 120.1 events per 100 patient-years, respectively; P=0.12) (Table 2, and Table S2 in the Supplementary Appendix for the ablation subgroups). However, there was a significantly higher rate of permanent pacemaker implantation in the ablation group than in the control group (21.5 vs. 8.1 implantations per 100 patient-years; 1-year incidence rate ratio, 2.64; 95% CI, 1.20 to 6.41; P=0.01) (see Table S3 in the Supplementary Appendix for timing and indications). The mean

Table 1. Baseline and Operative Characteristics of the Patients.*

Characteristic	Mitral-Valve Surgery Alone (N=127)	Mitral-Valve Surgery plus Ablation (N=133)
Female sex — no. (%)	63 (49.6)	57 (42.9)
Age — yr	69.4±10.0	69.7±10.4
White race — no. (%)†	112 (88.2)	116 (87.2)
Hispanic ethnic group — no. (%)†	8 (6.3)	10 (7.5)
Diabetes — no. (%)	28 (22.0)	30 (22.6)
Renal insufficiency — no. (%)	5 (3.9)	8 (6.0)
Previous CABG — no. (%)	4 (3.1)	7 (5.3)
Previous PCI — no. (%)	11 (8.7)	20 (15.0)
Cerebrovascular disease — no. (%)	13 (10.2)	22 (16.5)
Use of anticoagulant — no. (%)	97 (76.4)	105 (78.9)
Use of class III antiarrhythmic drug — no. (%)	15 (11.8)	14 (10.5)
NYHA class III or IV — no./total no. (%)‡	62/126 (49.2)	56/133 (42.1)
Atrial fibrillation status — no. (%)§		
Long-standing persistent	71 (55.9)	70 (52.6)
Persistent	56 (44.1)	63 (47.4)
Occurrence of atrial fibrillation at least once daily — no./total no. (%)¶	89/111 (80.2)	85/117 (72.6)
SF-12 physical-function score‖	37.9±8.8	38.4±8.0
Cause of mitral-valve disease — no. (%)		
Organic disease	73 (57.5)	75 (56.4)
Functional nonischemic mitral regurgitation	48 (37.8)	43 (32.3)
Ischemic mitral regurgitation	6 (4.7)	15 (11.3)
Left ventricular ejection fraction — %	56.5±7.7	55.1±7.6
Left atrial volume during early diastole — ml	139.8±111.0	127.2±69.1
Mitral-valve surgery — no./total no. (%)**		
Valve replacement††	61/126 (48.4)	54/133 (40.6)
Valve repair	65/126 (51.6)	79/133 (59.4)
Concomitant procedure — no./total no. (%)**		
Surgical management of tricuspid regurgitation	48/126 (38.1)	50/133 (37.6)
Aortic-valve replacement	20/126 (15.9)	14/133 (10.5)
CABG	25/126 (19.8)	27/133 (20.3)
Other	11/126 (8.7)	16/133 (12.0)
Duration of cardiopulmonary bypass — min‡‡	132.5±51.0	147.8±63.3
Duration of aortic cross-clamping — min	95.9±36.3	102.9±41.5

* Plus–minus values are means ±SD. There were no significant differences in baseline and operative characteristics between the study groups unless otherwise noted. CABG denotes coronary-artery bypass grafting, and PCI percutaneous coronary intervention.

† Race and ethnic group were self-reported.

‡ New York Heart Association (NYHA) functional classes range from I to IV, with higher classes indicating worse condition.

§ Long-standing persistent atrial fibrillation was defined as continuous atrial fibrillation for more than 12 months. Persistent atrial fibrillation was defined as non–self-terminating atrial fibrillation lasting more than 7 days, or less than 7 days if pharmacologic or electrical cardioversion was required.

¶ The frequency of atrial fibrillation was determined by patients' responses to question 3 of the Atrial Fibrillation Severity Scale questionnaire.

‖ Scores on the Medical Outcomes Study 12-Item Short Form Health Survey (SF-12) range from 0 to 100, with higher scores indicating a better outcome.

** One patient assigned to mitral-valve surgery alone withdrew consent before the index surgery.

†† A total of 21 patients (34.4%) who underwent mitral-valve surgery alone and 17 patients (31.5%) who underwent mitral-valve surgery plus ablation received a mechanical valve. A total of 40 patients (65.6%) who underwent mitral-valve surgery alone and 37 patients (68.5%) who underwent mitral-valve surgery plus ablation received a bioprosthetic valve.

‡‡ P=0.03.

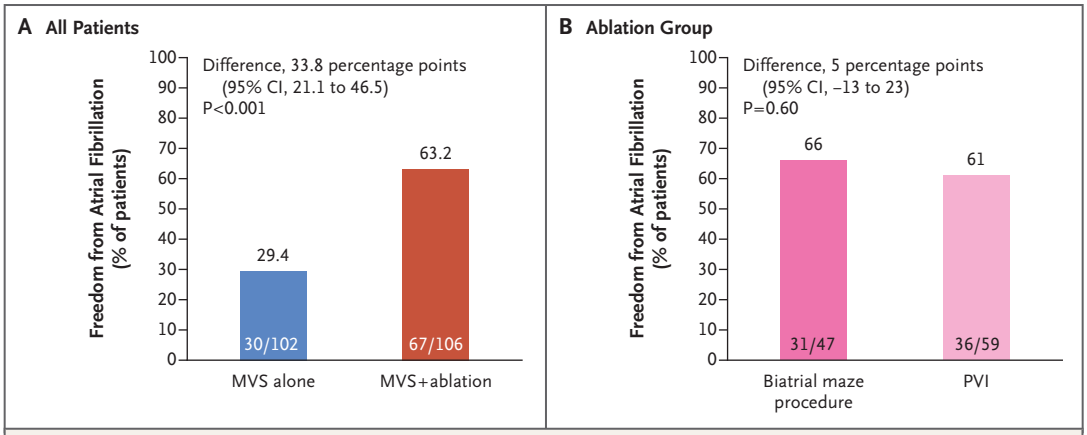

Figure 1. Freedom from Atrial Fibrillation.

Freedom from atrial fibrillation was defined as the absence of the condition at both 6 months and 12 months, as assessed by means of 3-day Holter monitoring. MVS denotes mitral-valve surgery, and PVI pulmonary-vein isolation.

total length of stay during the index hospitalization was similar in the ablation group and the control group (13.2±8.8 and 12.4±10.3 days, respectively; P=0.31), as were rehospitalization rates. The most frequent reasons for readmission were recurrent atrial fibrillation and heart failure.

QUALITY OF LIFE

At 12 months, more patients in the control group than in the ablation group had at least daily episodes of atrial fibrillation (as assessed by the AFSS) (45.2% vs. 19.8%, P<0.001). No other significant between-group differences were observed at 12 months with respect to quality-of-life or functional-status measures (Table 3, and Table S4 in the Supplementary Appendix for ablation subgroups).

DISCUSSION

In this trial, patients with persistent or long-standing persistent atrial fibrillation who were undergoing mitral-valve surgery were randomly assigned to ablation of atrial fibrillation or no ablation at the time of the surgery. We found that the rate of freedom from atrial fibrillation at both 6 months and 12 months after surgery (as assessed by means of 3-day Holter monitoring) was 63.2% with ablation and 29.4% without. The current trial enrolled a substantial number of patients with "difficult to manage" atrial fibrillation, including elderly patients and patients with atrial fibrillation of relatively long duration before surgery. These factors have been associated with a reduced likelihood of ablation success.[7-9]

Our results are consistent with those of observational studies and several smaller randomized trials, all of which have shown that surgical ablation is associated with an increased rate of freedom from atrial fibrillation.[10-24] Although selected single-center studies have shown rates of postablation freedom from atrial fibrillation of 80% or more, 1-year estimates of approximately 70% are more typical.[1,2] One previous trial evaluated 224 patients undergoing a wide range of cardiac surgeries.[23] The investigators used a single 24-hour electrocardiographic (ECG) recording at 12 months to screen for recurrence of atrial fibrillation and found that 60.2% of patients who had undergone ablation, as compared with 35.5% who had not undergone ablation, were free from atrial fibrillation. Observed freedom from atrial fibrillation varies with the rigor of rhythm assessment. As compared with long-term monitoring, spot ECG recordings tend to overestimate success by approximately 12 percentage points.[25] A study that used continuous monitoring with an implantable loop recorder after ablation in patients with long-standing persistent atrial fibrillation showed a success rate of 65% at 1 year,[26] a finding very similar to that of our trial.

Nested within the ablation group of this trial was a comparison of pulmonary-vein isolation with the biatrial maze procedure. Pulmonary-vein isolation is directed chiefly at the triggers of atrial fibrillation, whereas maze lesion sets can interrupt

Table 2. Clinical End Points, Serious Adverse Events, and Hospitalizations at 1 Year.

End Point or Event	Mitral-Valve Surgery Alone (N=127)	Mitral-Valve Surgery plus Ablation (N=133)	P Value
	no. of patients (%)		
Clinical end points			
Death	11 (8.7)	9 (6.8)	0.57
Stroke	2 (1.6)	4 (3.0)	0.68
Increase of one or more classes in NYHA classification*	4 (3.9)	7 (6.1)	0.46
Rehospitalization for heart failure	7 (5.5)	12 (9.0)	0.28
Mitral-valve reoperation	2 (1.6)	1 (0.8)	0.62
Composite end point†	26 (20.5)	31 (23.3)	0.58
	no. of events (no./100 patient-yr)		
Serious adverse events			
Heart failure	13 (11.7)	18 (14.9)	0.51
Stroke			
Ischemic	2 (1.8)	4 (3.3)	0.47
Hemorrhagic	0	1 (0.8)	0.32
Conduction abnormality necessitating a permanent pacemaker‡	9 (8.1)	26 (21.5)	0.01
Nonperioperative myocardial infarction	1 (0.9)	2 (1.7)	0.61
Renal failure	2 (1.8)	4 (3.3)	0.47
Bleeding	6 (5.4)	7 (5.8)	0.91
Ventricular arrhythmia	5 (4.5)	4 (3.3)	0.64
Pneumonia	10 (9.0)	3 (2.5)	0.04
Sepsis	3 (2.7)	6 (5.0)	0.38
Respiratory failure	16 (14.4)	6 (5.0)	0.02
All serious adverse events§	133 (120.1)	174 (143.8)	0.12
Hospitalization			
Any rehospitalization	54 (50.8)	77 (66.6)	0.12
Readmission for cardiovascular causes	28 (26.3)	41 (35.5)	0.22

* Data were missing for 25 patients who underwent mitral-valve surgery alone and 19 patients who underwent mitral-valve surgery plus ablation.

† The composite end point of major cardiac or cerebrovascular adverse events included death, stroke, hospitalization for heart failure, worsening heart failure (as defined by an increase of one or more classes in the NYHA classification), or mitral-valve reintervention.

‡ This category includes both serious and nonserious conduction abnormalities necessitating the implantation of a permanent pacemaker; 32 of the 35 events were adjudicated as serious (7 in patients who underwent mitral-valve surgery alone and 25 in patients who underwent mitral-valve surgery plus ablation). A total of 33 events were adjudicated as probably or possibly related to the surgical procedure or surgical ablation (7 in patients who underwent mitral-valve surgery alone and 26 in patients who underwent mitral-valve surgery plus ablation). The proportion of patients who required a permanent pacemaker within 30 days after randomization was 5.5% (7 patients) with mitral-valve surgery alone and 17.3% (23 patients) with mitral-valve surgery plus ablation (P=0.003).

§ The values for all serious adverse events exclude the 3 nonserious conduction-abnormality events necessitating implantation of a permanent pacemaker.

pathways needed for maintenance of the arrhythmia.[27,28] Most retrospective observational studies suggest that in patients with persistent or long-standing persistent atrial fibrillation, pulmonary-vein isolation is inferior to the biatrial maze procedure.[29] We found no significant difference in freedom from atrial fibrillation between the two groups. The trial was not planned to have the

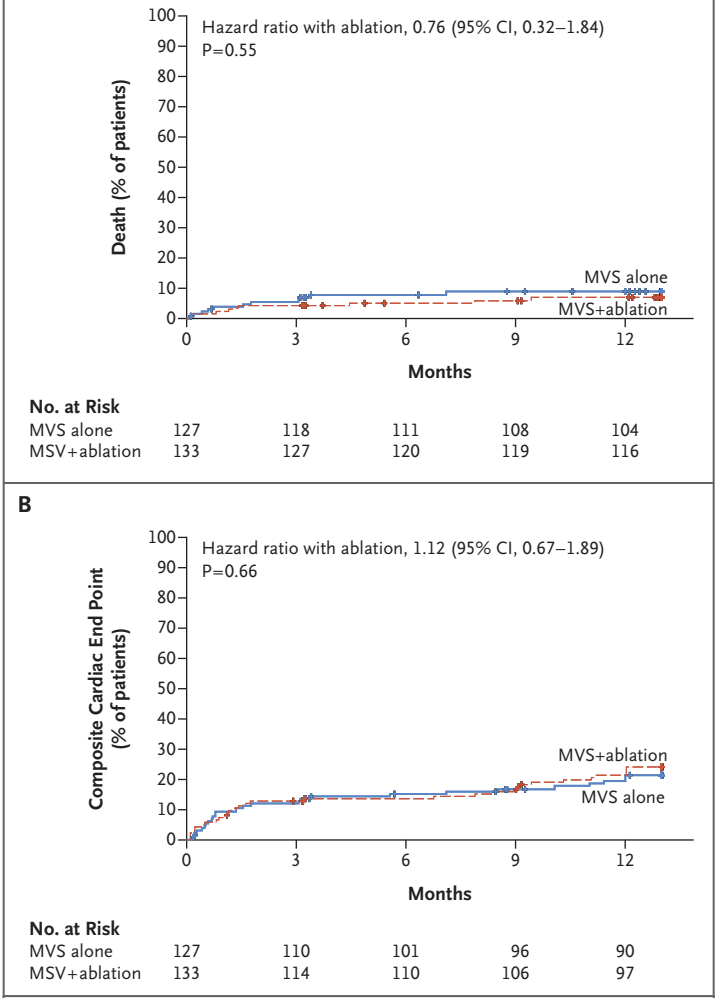

Figure 2. Time-to-Event Curves for Death and Composite Cardiac End Point.
The composite end point of major cardiac or cerebrovascular adverse events included death, stroke, hospitalization for heart failure, worsening heart failure (as defined by an increase of one or more classes in the New York Heart Association classification), or mitral-valve reintervention. Tick marks represent patients with censored data.

power to distinguish between these two methods, however, and it is possible that a larger trial might identify a clinically meaningful difference. Unlike most previous trials, our trial confirmed conduction block at the pulmonary-vein level, when feasible, in patients undergoing either type of ablation procedure. This confirmation may have contributed to the relatively good results in those undergoing pulmonary-vein isolation.

Atrial fibrillation, which is common among patients undergoing mitral-valve surgery, is a risk factor for death and illness.[1,2,7-10] These observations suggest that ablation of atrial fibrillation at the time of surgery may improve long-term outcomes. However, at 1 year, the increased rate of freedom from atrial fibrillation in the ablation group in our trial was not associated with a decrease in the rate of major cardiac or cerebrovascular adverse events in general or stroke in particular. The trial was not planned to have the power to show a benefit with respect to these outcomes, and a single year of follow-up is unlikely to provide definitive evidence in this regard. Moreover, the performance of left atrial appendage occlusion in all patients in this trial, which reduced the risk of stroke, may have further limited our ability to detect a benefit of ablation on cardiovascular outcomes.[30-32]

Ablation was associated with a significant increase in the need for implantation of a permanent pacemaker. The proportion of patients who had received a permanent pacemaker at 30 days was 17%, a proportion higher than the 5 to 10% reported in most studies[33] but similar to that observed in a recent study.[34] This relatively higher rate may be attributable in part to the fact that approximately 50% of the patients who underwent ablation had multivalve surgery, which increases the risk of atrioventricular block. Moreover, approximately 40% of the patients who underwent ablation had valve-replacement surgery, and more than 50% of the patients who underwent ablation were 70 years of age or older, factors that also increase the risk of postoperative atrioventricular block.

This trial has several limitations in addition to those mentioned above. First, 20% of the patients did not complete the primary end-point assessment at both 6 months and 12 months, although the rate was similar in the two groups. Second, the definition of persistent atrial fibrillation in the guidelines was revised after the trial completed enrollment; however, this change affected only a small percentage of trial participants. Finally, our patient population included mostly older persons with persistent or long-standing persistent atrial fibrillation; the results may not apply to younger patients or those with paroxysmal atrial fibrillation.

In this trial involving patients with persistent or long-standing persistent atrial fibrillation, the addition of surgical ablation at the time of mi-

Table 3. Quality of Life and Functional Status of Patients at 1 Year.*

Measure	Mitral-Valve Surgery Alone	Mitral-Valve Surgery plus Ablation	P Value
SF-12†			
Physical function			0.38
Patients evaluated — no./total no. (%)	97/116 (83.6)	111/124 (89.5)	
Score	45.3±7.9	44.3±9.0	
Mental function			0.56
Patients evaluated — no./total no. (%)	97/116 (83.6)	111/124 (89.5)	
Score	48.5±6.5	48.0±6.3	
AFSS‡			
Frequency of atrial fibrillation			<0.001
Patients evaluated — no./total no. (%)	93/116 (80.2)	101/124 (81.5)	
At least once daily	42/93 (45.2)	20/101 (19.8)	
Present Life Rating			0.45
Patients evaluated — no./total no. (%)	96/116 (82.8)	108/124 (87.1)	
Median score (interquartile range)	8.0 (7.0–9.0)	8.0 (7.0–9.0)	
NYHA class — no./total no. (%)			0.17
Patients evaluated	102/116 (87.9)	114/124 (91.9)	
Class III or IV	3/102 (2.9)	8/114 (7.0)	

* Plus–minus values are means ±SD. For all scores, values exclude patients who died by month 12.
† Scores on the Medical Outcomes Study 12-Item Short Form Health Survey (SF-12) range from 0 to 100, with higher scores indicating a better outcome.
‡ The frequency of atrial fibrillation was determined by patients' responses to question 3 on the Atrial Fibrillation Severity Scale (AFSS) questionnaire. Scores on the Present Life Rating range from 1 to 10, with higher scores indicating better perspective on present life.

tral-valve surgery significantly increased the rate of freedom from atrial fibrillation at 1 year. Ablation was associated with an increased risk of implantation of a permanent pacemaker. There was no significant difference between study groups in the rate of major cardiac or cerebrovascular adverse events at 1 year. Establishing the effects of ablation on long-term survival, stroke incidence, the need for rehospitalization, repeat rhythm procedures, and freedom from anticoagulation therapy requires further study.

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APPENDIX

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