

LONG-TERM SURVIVAL AFTER ABLATION OF THE ATRIOVENTRICULAR NODE AND IMPLANTATION OF A PERMANENT PACEMAKER IN PATIENTS WITH ATRIAL FIBRILLATION

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ABSTRACT

Background In patients with atrial fibrillation that is refractory to drug therapy, radio-frequency ablation of the atrioventricular node and implantation of a permanent pacemaker are an alternative therapeutic approach. The effect of this procedure on long-term survival is unknown.

Methods We studied all patients who underwent ablation of the atrioventricular node and implantation of a permanent pacemaker at the Mayo Clinic between 1990 and 1998. Observed survival was compared with the survival rates in two control populations: age- and sex-matched members of the Minnesota population between 1970 and 1990 and consecutive patients with atrial fibrillation who received drug therapy in 1993.

Results A total of 350 patients (mean [\pm SD] age, 68 ± 11 years) were studied. During a mean of 36 ± 26 months of follow-up, 78 patients died. The observed survival rate was significantly lower than the expected survival rate based on the general Minnesota population ($P < 0.001$). Previous myocardial infarction ($P < 0.001$), a history of congestive heart failure ($P = 0.02$), and treatment with cardiac drugs after ablation ($P = 0.03$) were independent predictors of death. Observed survival among patients without these three risk factors was similar to expected survival ($P = 0.43$). None of the 26 patients with lone atrial fibrillation died during follow-up (37 ± 27 months). The observed survival rate among patients who underwent ablation was similar to that among 229 controls with atrial fibrillation (mean age, 67 ± 12 years) who received drug therapy ($P = 0.44$).

Conclusions In the absence of underlying heart disease, survival among patients with atrial fibrillation after ablation of the atrioventricular node is similar to expected survival in the general population. Long-term survival is similar for patients with atrial fibrillation, whether they receive ablation or drug therapy. Control of the ventricular rate by ablation of the atrioventricular node and permanent pacing does not adversely affect long-term survival. (N Engl J Med 2001;344:1043-51.)

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ATRIAL fibrillation is associated with increased morbidity and mortality¹⁻⁵ and is an independent risk factor for stroke.^{6,7} Although the association between atrial fibrillation and mortality has been debated, a recent report showed that atrial fibrillation was associated with a mortality rate that was higher by a factor of 1.5 to 1.9 than the rate expected in the general population, after adjustment for other cardiovascular conditions.¹

The optimal goal in treating atrial fibrillation is to restore and maintain sinus rhythm — often a formidable task. Despite therapy with antiarrhythmic drugs, studies have reported recurrence rates of 50 to 60 percent during a mean follow-up of one to two years.⁸⁻¹² In patients with severe symptoms in whom drug therapy fails, ablation of the atrioventricular node and permanent pacing are effective in controlling the ventricular rate.¹³⁻¹⁶ Although ablation of the atrioventricular node does not eliminate atrial fibrillation, it alleviates symptoms and improves the quality of life, exercise tolerance, and left ventricular function.¹⁷⁻²⁰ Despite the effectiveness of this treatment in relieving symptoms, its effect on long-term survival in patients with severe symptoms in whom drug therapy has failed is unknown. The potentially deleterious effect on survival of the creation of permanent atrioventricular block and the resulting lifelong commitment to the use of a pacemaker is a serious concern.

We assessed long-term survival and predictors of death after the ablation of the atrioventricular node and the implantation of a permanent pacemaker in 350 patients with atrial fibrillation. To test the hypothesis that this treatment has an adverse effect on long-term survival, we compared the observed survival with expected survival calculated on the basis of age- and sex-specific mortality rates in the Minnesota population and with the observed survival of a group of consecutive patients who received pharmacologic therapy for atrial fibrillation.

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METHODS

Study Population

All patients with atrial fibrillation who underwent radio-frequency ablation of the atrioventricular node and implantation of a permanent pacemaker at the Mayo Clinic between July 1990 and December 1998 were included in the study. Patients with indications for ablation were those with symptomatic paroxysmal or chronic atrial fibrillation that was refractory to drug therapy aimed at controlling the ventricular rate or maintaining sinus rhythm. None of the 350 patients we studied underwent direct-current ablation. The potential risks of the procedure were explained, and oral informed consent was obtained from all patients.

Control Groups

The first control group was constructed on the basis of the age and sex of all patients who underwent ablation, and the expected survival rate was calculated on the basis of age- and sex-specific mortality rates in the Minnesota population for the period between 1970 and 1990.²¹ We assumed that the expected survival rate accounts for the effects of cardiovascular and other medical conditions according to their known prevalence in the reference population.

The second control group was selected from a group of consecutive patients who received drug therapy for atrial fibrillation at the Mayo Clinic in 1993. These patients were selected from an existing data base as members of the control group because they had clinical characteristics and follow-up that were similar, although not identical, to those of the patients who underwent ablation.

Data Collection

Data were collected from a centralized system that contained complete records of all patients treated and followed at the Mayo Clinic and its hospitals. These records provide a detailed history and diagnosis for all outpatient encounters, including emergency room visits and home and nursing home visits, as well as data recorded during inpatient care, death certificates, and autopsy reports.

Follow-up

The follow-up period for the patients who underwent ablation began at the time of the procedure; the follow-up period for the controls treated with drugs began in 1993. For both groups, follow-up ended in January 1999 or at the time of death. Patients who underwent ablation had follow-up visits in the pacemaker clinic every three months for the first year and were surveyed annually thereafter. Causes of death were determined by a review of hospital records and death certificates and by telephone interviews of local physicians or family members. All patients in both groups who entered the study had at least one follow-up visit.

Atrioventricular-Node Ablation and Pacemaker Implantation

Radio-frequency ablation of the atrioventricular node was performed by standard techniques.^{22,23} Complete atrioventricular block was achieved in all patients. Seven patients (2 percent of those enrolled) required a left-sided approach to achieve complete block, and 24 patients (7 percent) required a second or third procedure because of recurrent atrioventricular conduction after the first attempt.

A rate-responsive ventricular pacemaker was implanted if the patient was in atrial fibrillation at the time of the procedure and if attempts to restore and maintain sinus rhythm by means of cardioversion were not performed. A dual-chamber, rate-adaptive pacemaker was implanted if the patient was in sinus rhythm at the time of the procedure.

Statistical Analysis

Survival of the patients who underwent ablation and the controls treated with drugs was estimated by the Kaplan–Meier method. For each person who underwent ablation, the expected survival

was calculated on the basis of age- and sex-specific mortality rates in the Minnesota population during the period between 1970 and 1990.²¹ The observed and expected survival rates were compared by means of the one-sample log-rank test.²⁴ All three survival curves were compared by means of the two-sample log-rank test. Categorical variables were compared between groups with use of the chi-square test for independence. Continuous variables were compared with the use of the Wilcoxon rank-sum test. Univariate and multivariate associations between base-line variables and survival were assessed by means of the log-rank test and a Cox regression model.²⁵ The following variables were considered as potential prognostic factors: demographic features (age and sex), clinical history (syncope, angina, and congestive heart failure), and the presence of heart disease (ischemic heart disease, cardiomyopathy, and valvular heart disease) and associated clinical conditions (diabetes mellitus, chronic obstructive pulmonary disease, cerebrovascular disease, hypertension, and cancer). Treatment with cardiac medications after ablation was also included as a variable in the analysis. Multivariate models are presented in the form of point estimates of the risk ratios, with 95 percent confidence intervals.

RESULTS

Demographic Characteristics

A total of 350 patients with atrial fibrillation (185 men and 165 women) who underwent ablation and had a pacemaker implanted at the Mayo Clinic between 1990 and 1998 were included in the study. A single-chamber ventricular pacemaker was implanted in 55 percent of the patients, and a dual-chamber pacemaker in 45 percent.

The base-line characteristics of the patients who underwent ablation are summarized in Table 1. Drugs used to control the ventricular rate or to maintain sinus rhythm before ablation included digoxin (used by 87 percent of patients), a calcium-channel blocker (82 percent), a beta-blocker (56 percent), quinidine (43 percent), procainamide (30 percent), disopyramide (18 percent), propafenone (47 percent), flecainide (20 percent), encainide (6 percent), sotalol (13 percent), and amiodarone (41 percent). After ablation, 188 patients (54 percent) continued to take one or more cardiac drugs because of preexisting cardiovascular disease. These drugs included digoxin, calcium-channel blockers, beta-blockers, angiotensin-converting-enzyme inhibitors, nitrates, diuretics, and antiarrhythmic agents (propafenone, sotalol, amiodarone, and mexiletine). At the time of the ablation, 11 percent of patients were in New York Heart Association functional class III or IV, and 37 percent had a reduced left ventricular ejection fraction (a fraction of 40 percent or lower).

Sixty-eight patients (19 percent) had a history of a cerebrovascular accident or transient ischemic attack, and eight patients (2 percent) had peripheral arterial embolism before ablation. During follow-up, a cerebrovascular accident or transient ischemic attack occurred in 15 patients (of whom 6 [40 percent] had had a previous such event), and 3 had peripheral arterial embolism. At the time of embolic complications, all patients except one were receiving warfarin therapy. The mean (\pm SD) international normalized ratio was

TABLE 1. BASE-LINE CHARACTERISTICS OF PATIENTS WITH ATRIAL FIBRILLATION WHO UNDERWENT ABLATION OF THE ATRIOVENTRICULAR NODE AND IMPLANTATION OF A PACEMAKER BETWEEN 1990 AND 1998.*

CHARACTERISTIC	ALL PATIENTS (N=350)	PATIENTS WHO SURVIVED (N=272)	PATIENTS WHO DIED (N=78)
Sex (no.)			
Male	185	135	50
Female	165	137	28
Age at time of ablation (yr)	68±11	68±11	69±10
Duration of arrhythmia (yr)	7±18	8±8	5±5
Duration of follow-up (mo)	36±26	38±26	27±25
Type of atrial fibrillation (%)			
Chronic	50	49	54
Paroxysmal	45	47	41
Atrial flutter	5	4	5
Lone	7	10	0
No. of antiarrhythmic drugs	4.3±2.0	4.3±2.0	4.5±2.0
Left ventricular ejection fraction (%)	47±17	49±17	41±17
NYHA functional class	1.3±0.7	1.2±0.7	1.6±0.9
Medical history and conditions (%)			
Coronary-artery bypass graft	18	16	27
Cardiac-valve surgery	17	15	24
Coronary artery disease	45	38	67
Previous myocardial infarction	27	19	58
Congestive heart failure†	21	17	36
Left ventricular hypertrophy	10	10	12
Nonischemic cardiomyopathy	16	15	42
Syncope	17	8	28
Previous cerebrovascular accident or transient ischemic attack	19	18	26
Hypertension	46	45	50
Hyperlipidemia	36	33	47
Diabetes mellitus	20	16	33
Chronic obstructive lung disease	32	25	56
Cancer	21	19	31
Renal disease	12	8	27
Liver failure	3	3	4
Smoking	53	50	67

*Plus-minus values are means ±SD. NYHA denotes New York Heart Association.

†Congestive heart failure was defined as NYHA class II or higher.

2.1±1.0 (range, 1.0 to 4.5) immediately before the thromboembolic event. The clinical characteristics of the patients who underwent ablation and the controls treated with drugs are summarized in Table 2.

Overall Survival

The observed survival among the patients who underwent ablation is shown in Figure 1A, along with the expected survival for age- and sex-matched members of the Minnesota population. The observed survival was significantly worse than the expected survival ($P<0.001$). The survival curve of the controls treated with drugs is also shown in Figure 1A. The observed survival rates of the patients who underwent ablation and the controls treated with drugs were not significantly different ($P=0.44$; risk ratio for the ab-

TABLE 2. CLINICAL CHARACTERISTICS OF THE PATIENTS WHO UNDERWENT ABLATION AT THE TIME OF THE PROCEDURE AND OF THE CONTROLS TREATED WITH DRUGS AT THE TIME OF IN-HOSPITAL THERAPY.*

CHARACTERISTIC	ABLATION (N=350)	DRUG THERAPY (N=229)	P VALUE
Age (yr)	68±11	67±13	0.97
Male sex (%)	53	66	0.003
Duration of follow-up (mo)	36±26	48±23	
Coronary-artery bypass graft (%)	18	17	0.77
Cardiac-valve surgery (%)	17	13	0.25
Coronary artery disease (%)	45	36	0.07
Previous myocardial infarction (%)	27	17	0.006
Congestive heart failure (%)†	21	16	0.13
Left ventricular ejection fraction (%)	47±17	49±16	0.17
NYHA functional class	1.3±0.7	1.2±0.6	0.07
Nonischemic cardiomyopathy (%)	16	15	0.67
Diabetes mellitus (%)	20	17	0.49
Previous cerebrovascular accident (%)	19	17	0.38
Hypertension (%)	46	38	0.04
No. of antiarrhythmic drugs	4.3±2.0	2.0±1.0	<0.001

*Plus-minus values are means ±SD. NYHA denotes New York Heart Association.

†Congestive heart failure was defined as NYHA class II or higher.

lation group as compared with the controls, 1.14; 95 percent confidence interval, 0.81 to 1.60).

Overall Survival with Coexisting Heart Disease

In subgroup analyses, the survival rate among 115 patients with atrial fibrillation and congestive heart failure who underwent ablation was compared with that among 58 controls with the same indications who were treated with drugs (Fig. 1B). The difference in survival between the groups was not significant ($P=0.75$; risk ratio, 1.09; 95 percent confidence interval, 0.66 to 1.79). Survival was similar for 156 patients with coronary artery disease who underwent ablation and 83 controls with coronary artery disease who were treated with drugs ($P=0.85$; risk ratio, 0.96; 95 percent confidence interval, 0.60 to 1.52) (Fig. 1C). When patients with a history of congestive heart failure and previous myocardial infarction were excluded from the analysis, survival among the 194 patients who underwent ablation was similar to that among the 144 controls who were treated with drugs ($P=0.13$; risk ratio, 1.57; 95 percent confidence interval, 0.88 to 2.81).

Univariate and multivariate predictors of death, with associated risk ratios, 95 percent confidence intervals, and P values, are summarized in Table 3. Multivariate analysis showed that previous myocardial infarction ($P<0.001$), a history of congestive heart failure ($P=0.02$), and use of cardiac drugs after the

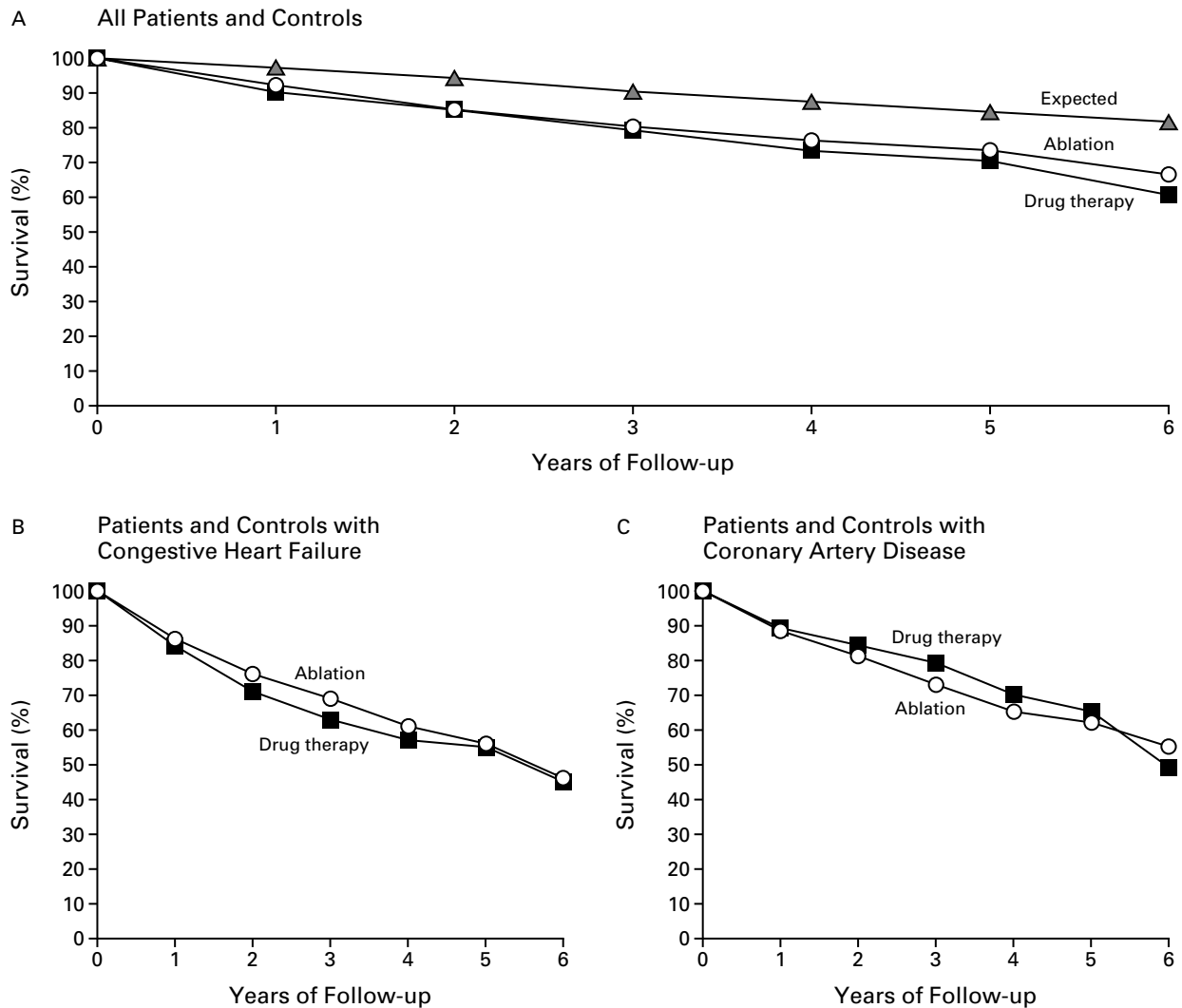


Figure 1. Observed Survival among Patients Who Underwent Ablation of the Atrioventricular Node and among Controls Treated with Drugs for Atrial Fibrillation, and Expected Survival Rates Based on Mortality in an Age- and Sex-Matched General Population. As shown in Panel A, observed survival among patients who underwent ablation of the atrioventricular node and implantation of a permanent pacemaker for atrial fibrillation between 1990 and 1998 was worse than the expected survival based on mortality among age- and sex-matched members of the Minnesota population ($P < 0.001$); however, it was similar to the survival among controls treated with drugs for atrial fibrillation ($P = 0.44$). In the subgroup of patients with congestive heart failure (Panel B), the survival among the 115 patients who underwent ablation was similar to that among the 58 controls treated with drugs ($P = 0.75$). In the subgroup with coronary artery disease (Panel C), the survival rates were not significantly different for the 156 patients who underwent ablation and the 83 controls treated with drugs ($P = 0.85$).

ablation ($P = 0.03$) were independent predictors of death (Table 3). Cumulative survival rates were significantly worse than expected survival rates for patients who had a history of myocardial infarction or congestive heart failure or who received cardiac-drug therapy after ablation (Fig. 2). The observed survival rates among patients without a history of myocardial infarction were not significantly different from the expected survival rates ($P = 0.07$); the same was true for

those who did not receive cardiac-drug therapy after ablation ($P = 0.32$). The observed survival among patients without congestive heart failure was worse than the expected survival rate ($P = 0.05$), but 17 percent of the patients with a history of congestive heart failure also had a history of myocardial infarction, and 42 percent of the patients with a history of congestive heart failure were taking cardiac drugs after ablation. For the 121 patients without any of the three

TABLE 3. PREDICTORS OF DEATH IN PATIENTS WITH ATRIAL FIBRILLATION AFTER ABLATION OF THE ATRIOVENTRICULAR NODE AND PERMANENT PACING.*

VARIABLE	RISK RATIO (95% CI)	P VALUE
Univariate predictors		
Previous myocardial infarction	3.67 (2.34–5.75)	<0.001
History of congestive heart failure	2.88 (1.84–4.52)	<0.001
Cardiac-drug therapy after ablation	2.72 (1.63–4.53)	<0.001
Diabetes mellitus	2.52 (1.56–4.06)	<0.001
Coronary artery disease	2.34 (1.46–3.75)	<0.001
NYHA functional class \geq II	1.59 (1.23–2.05)	<0.001
Dilated cardiomyopathy	2.00 (1.27–3.16)	0.003
Longer duration of arrhythmia	0.91 (0.85–0.97)	0.006
Smoking	1.78 (1.12–2.85)	0.02
Left ventricular ejection fraction <40%	0.59 (0.37–0.96)	0.03
Older age (each 10-year increase)	1.28 (1.02–1.61)	0.03
Multivariate predictors		
Previous myocardial infarction	2.70 (1.65–4.28)	<0.001
History of congestive heart failure	1.72 (1.11–2.94)	0.02
Cardiac-drug therapy after ablation	1.81 (1.05–3.08)	0.03

*CI denotes confidence interval, and NYHA New York Heart Association.

independent risk factors, the observed survival was similar to the expected survival ($P=0.43$) (Fig. 3).

Lone Atrial Fibrillation

In our study, patients were considered to have lone atrial fibrillation if they did not have ischemic heart disease, hyperthyroidism, congestive heart failure, cardiomyopathy, hypertension, chronic obstructive pulmonary disease, previous cardiac surgery, or potentially life-shortening noncardiac disease (diabetes or cancer). There was no age restriction. Twenty-six patients met the criteria for lone atrial fibrillation (14 men and 12 women; mean age, 64 ± 13 years; range, 41 to 83 years); none of them died during a mean follow-up period of 37 ± 27 months.

Mortality and Causes of Death

At the latest assessment, 78 patients had died (mean follow-up, 27 ± 25 months; range, 3 days to 88 months) (Table 1). Their mean age at the time of ablation was 69 ± 10 years (range, 39 to 95). The causes of death are summarized in Table 4.

DISCUSSION

In this long-term follow-up study, we assessed the survival of patients who presented with symptomatic atrial fibrillation that was refractory to medical therapy and who then underwent ablation of the atrioventricular node and implantation of a permanent pacemaker. Among the patients who underwent ablation, the observed overall survival was significantly worse than the expected survival for age- and sex-matched members of the Minnesota population. The

observed survival among patients who underwent ablation for atrial fibrillation was similar to that among controls treated with drugs for atrial fibrillation. In the absence of previous myocardial infarction, previous congestive heart failure, and treatment with cardiac medications after ablation, the observed survival among patients who underwent ablation was similar to the expected survival for age- and sex-matched members of the Minnesota population. None of the 26 patients with lone atrial fibrillation died during a mean follow-up period of 37 ± 27 months.

Our observations confirm that the presence of pre-existing cardiac disease is the main determinant of long-term survival in patients with atrial fibrillation who undergo ablation of the atrioventricular node. More important, the normal survival rate among patients without clinically significant heart disease, the excellent survival rate among patients with lone atrial fibrillation, and the similar survival rates for the patients who underwent ablation and the controls with atrial fibrillation who were treated with drugs suggest that controlling the ventricular rate and alleviating symptoms by ablation of the atrioventricular node and permanent pacing do not have an adverse effect on long-term survival in this patient population.

Survival data from epidemiologic studies have demonstrated higher mortality among patients with atrial fibrillation than among patients in sinus rhythm.^{1,2,4,26-28} Data from the Framingham Heart Study showed that the risk-factor-adjusted odds ratio for mortality was 1.5 for men and 1.9 for women with atrial fibrillation, as compared with subjects in sinus rhythm.¹ In some patients, atrial fibrillation may be a marker of atherosclerosis, older age, and loss of vascular compliance (all of which could be associated with a higher risk of stroke and death); nevertheless, the evidence supports the conclusion that atrial fibrillation is an independent predictor of poor long-term survival.

Results from observational studies¹⁷⁻²⁰ and randomized trials^{29,30} have demonstrated that ablation of the atrioventricular node and permanent pacing are effective in controlling the ventricular rate, alleviating symptoms, and improving the quality of life, exercise tolerance, and left ventricular function. However, there is concern that the creation of complete atrioventricular block that is inherent in this approach and the requirement for permanent pacing to which it leads may have an adverse effect on survival. According to the Framingham Heart Study, overall mortality for men between 65 and 74 years old is 20.8 percent at one year and 48.2 percent at five years; for women in the same age group, overall mortality is 18.2 percent at one year and 38.9 percent at five years.¹ The mean age of our study population was 68 ± 11 years, and overall mortality was 8 percent at one year and 27 percent at five years; these rates compare favorably with those in the Framingham Heart Study, in which

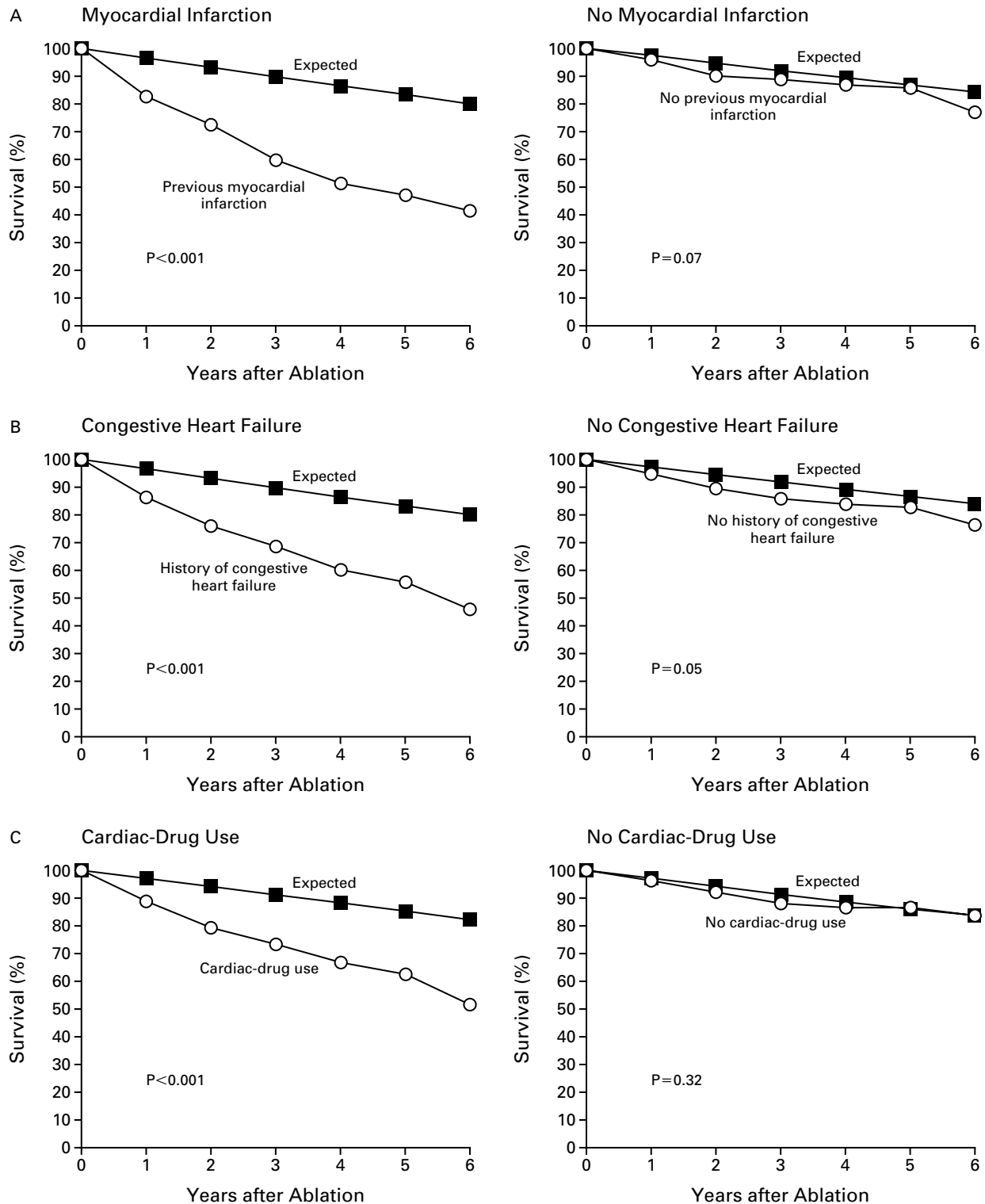


Figure 2. Cumulative Survival for Subgroups of Patients Who Underwent Ablation of the Atrioventricular Node and Implantation of a Permanent Pacemaker between 1990 and 1998 and Expected Survival Based on Mortality among Age- and Sex-Matched Controls. Panel A shows the survival curves for those with a history of myocardial infarction (left-hand side) and those without such a history (right-hand side), Panel B for those with and those without a history of congestive heart failure (CHF), and Panel C for those with and those without cardiac-drug use after ablation.

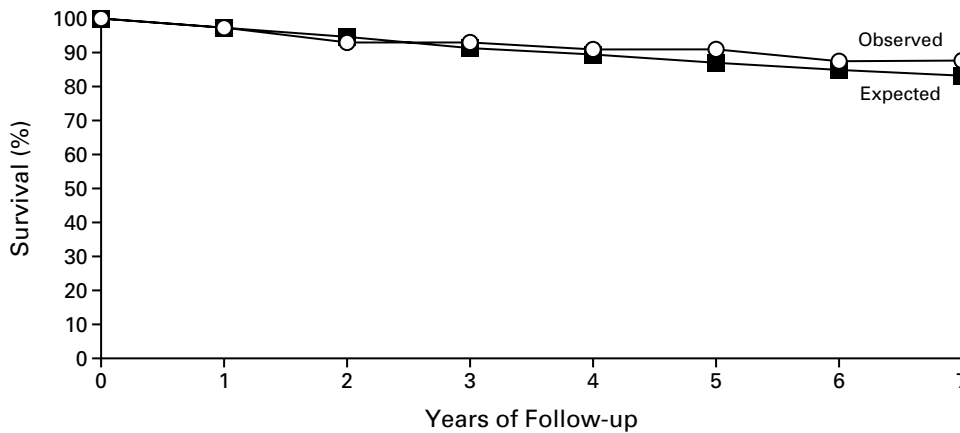


Figure 3. Observed Survival among 121 Patients Who Underwent Ablation of the Atrioventricular Node and Implantation of a Permanent Pacemaker for Atrial Fibrillation but Who Had No History of Congestive Heart Failure or Myocardial Infarction and No Cardiac-Drug Use after Ablation, as Compared with the Expected Survival Based on Mortality in an Age- and Sex-Matched Control Population.

In this subgroup of patients, the observed survival and the expected survival were not significantly different ($P=0.43$).

most cases of atrial fibrillation were managed medically. Although direct comparisons cannot be made between our data and data from the Framingham Heart Study, because of differences in the study populations, the methods of analysis, and the timing of the studies, it is encouraging to note that overall mortality was lower among the patients in our study who underwent ablation of the atrioventricular node and permanent pacing than it was among patients in the Framingham Heart Study.

The safety of ablation for controlling the ventricular rate is confirmed by the similar long-term survival in a group of consecutive patients receiving medical treatment for atrial fibrillation. Because the controls who were treated with drugs were identified retrospectively, the clinical characteristics of the two groups are not identical, but the survival rate in this group was similar to that among patients who underwent ablation, despite the fact that the ablation group had higher proportions of men, of patients with myocardial infarction and hypertension, and of patients in whom previous drug treatment had failed.

Our study confirmed that preexisting cardiovascular disease and coexisting medical conditions are predictors of a higher risk of death in patients with atrial fibrillation. The mode of pacing and the type of atrial fibrillation (chronic or paroxysmal) were not independent predictors of long-term survival. The observation that survival was normal among patients without a history of myocardial infarction or congestive heart failure who were not taking cardiac medications after ablation suggests that in addition to having beneficial effects on symptoms, as demonstrated by other studies, this therapy is unlikely to have a negative ef-

TABLE 4. PRIMARY CAUSES OF DEATH AMONG PATIENTS WHO UNDERWENT ABLATION OF THE ATRIOVENTRICULAR NODE AND PERMANENT PACING FOR ATRIAL FIBRILLATION.

CAUSE OF DEATH	NO. OF PATIENTS (%)
Cardiac causes	49 (63)
Congestive heart failure	26 (33)
Myocardial infarction	10 (13)
Sudden death	5 (6)
Other	8 (10)
Noncardiac causes	24 (31)
Stroke	2 (3)
Respiratory failure	8 (10)
Cancer	7 (9)
Infection	3 (4)
Other	4 (5)
Unknown cause	5 (6)
Total	78 (100)

fect on long-term survival. The observation of similar rates of survival in subgroups of patients with coronary artery disease or congestive heart failure whether they were treated medically or with ablation indicates that ablation of the atrioventricular node is as safe as conventional medical treatment for atrial fibrillation in patients with underlying heart disease.

The clinical features of patients with lone atrial fibrillation have been highlighted by epidemiologic

studies such as the Framingham Heart Study³¹ and a study from Olmsted County, Minnesota,³² which found a low risk of stroke and a low rate of mortality overall. In our study, the indications in 26 patients (7 percent) met the definition of lone atrial fibrillation, and none of them had died by the end of the study, further supporting the conclusion that ablation of the atrioventricular node and permanent pacing do not negatively affect long-term survival in the absence of clinically significant heart disease.

During follow-up, 49 of the 78 patients who died (63 percent) died of cardiac causes. This high proportion is probably the result of the prevalence of cardiovascular diseases in our study population (Table 1). Five patients (1 percent of all the patients who underwent ablation) had sudden death from cardiac causes, and in four of them, underlying heart disease with left ventricular dysfunction had previously been documented. Earlier studies from a registry of patients who underwent direct-current ablation of the atrioventricular node estimated that the prevalence of sudden death from cardiac causes after ablation is between 2.04 percent and 3.70 percent.^{22,33} Most sudden deaths occurred in patients with preexisting heart disease.

Our observations and conclusions should be interpreted in the light of the limitations imposed by a retrospective study design. All the information was obtained from original hospital records of the Mayo Clinic. Although these records were interpreted and transferred into a standard data format, most of the information was qualitative. The multivariate model was used to minimize the effect of base-line differences. Selection of the study patients and the control population was not random, but the inclusion of consecutive patients minimized selection bias. Although the relative benefit of ablation of the atrioventricular node and permanent pacing, as compared with other methods of treatment, can be determined only by prospective, randomized trials, it is unlikely that such studies will be conducted, given the difficulties in maintaining sinus rhythm and controlling the ventricular rate by other medical and nonmedical methods, the diverse population of patients, and the high rate of crossover that would be expected.

Although the observed overall survival among the patients in our study who underwent ablation was significantly worse than the expected survival among matched controls from the Minnesota population, the observed survival among patients without overt heart disease was similar to that of the general-population controls, and no deaths occurred during follow-up among patients with lone atrial fibrillation. Survival rates were similar in the group receiving medical treatment for atrial fibrillation and the group that underwent ablation of the atrioventricular node. These observations suggest that permanent atrioventricular block and implantation of a pacemaker after ablation

of the atrioventricular node do not have an important adverse effect on survival, thus reassuring patients and physicians that ablation of the atrioventricular node is an acceptable treatment option for symptomatic atrial fibrillation that is refractory to medical therapy.

REFERENCES

1. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation* 1998;98:946-52.
2. Lake FR, Cullen KJ, de Klerk NH, McCall MG, Rosman DL. Atrial fibrillation and mortality in an elderly population. *Aust N Z J Med* 1989; 19:321-6.
3. Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation: the Framingham Study. *N Engl J Med* 1982;306:1018-22.
4. Gajewski J, Singer RB. Mortality in an insured population with atrial fibrillation. *JAMA* 1981;245:1540-4.
5. Phillips SJ, Whisnant JP, O'Fallon WM, Frye RL. Prevalence of cardiovascular disease and diabetes mellitus in residents of Rochester, Minnesota. *Mayo Clin Proc* 1990;65:344-59.
6. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991;22:983-8.
7. 2000 Heart and stroke statistical update. Dallas: American Heart Association, 1999.
8. Nemeč J, Shen W-K. Pharmacotherapy of atrial fibrillation. *Expert Opin Pharmacother* 1999;1:81-96.
9. Antman EM, Beamer AD, Cantillon C, McGowan N, Friedman PL. Therapy of refractory symptomatic atrial fibrillation and atrial flutter: a staged care approach with new antiarrhythmic drugs. *J Am Coll Cardiol* 1990;15:698-707.
10. Pritchett ELC. Management of atrial fibrillation. *N Engl J Med* 1992; 326:1264-71.
11. Zehender M, Hohnloser S, Muller B, Meinertz T, Just H. Effects of amiodarone versus quinidine and verapamil in patients with chronic atrial fibrillation: results of a comparative study and a 2-year follow-up. *J Am Coll Cardiol* 1992;19:1054-9.
12. Crijns HJ, Van Gelder IC, Van Gilst WH, Hillege H, Gosselink AM, Lie KI. Serial antiarrhythmic drug treatment to maintain sinus rhythm after electrical cardioversion for chronic atrial fibrillation or atrial flutter. *Am J Cardiol* 1991;68:335-41.
13. Prystowsky EN, Benson DW Jr, Fuster V, et al. Management of patients with atrial fibrillation: a statement for healthcare professionals: from the Subcommittee on Electrocardiography and Electrophysiology, American Heart Association. *Circulation* 1996;93:1262-77.
14. Touboul P. Atrioventricular nodal ablation and pacemaker implantation in patients with atrial fibrillation. *Am J Cardiol* 1999;83:241D-245D.
15. Brignole M, Menozzi C. Control of rapid heart rate in patients with atrial fibrillation: drugs or ablation? *Pacing Clin Electrophysiol* 1996;19: 348-56.
16. Brignole M. Ablate and pace: a pragmatic approach to paroxysmal atrial fibrillation not controlled by antiarrhythmic drugs. *Heart* 1998;79:531-3.
17. Twidale N, Sutton K, Bartlett L, et al. Effects on cardiac performance of atrioventricular node catheter ablation using radiofrequency current for drug-refractory atrial arrhythmias. *Pacing Clin Electrophysiol* 1993;16: 1275-84.
18. Marshall HJ, Harris ZI, Griffith MJ, Gammage MD. Atrioventricular nodal ablation and implantation of mode switching dual chamber pacemakers: effective treatment for drug refractory paroxysmal atrial fibrillation. *Heart* 1998;79:543-7.
19. Kay GN, Ellenbogen KA, Giudici M, et al. The Ablate and Pace Trial: a prospective study of catheter ablation of the AV conduction system and permanent pacemaker implantation for treatment of atrial fibrillation. *J Interv Card Electrophysiol* 1998;2:121-35.
20. Fitzpatrick AP, Kourouyan HD, Siu A, et al. Quality of life and outcomes after radiofrequency His-bundle catheter ablation and permanent pacemaker implantation: impact of treatment in paroxysmal and established atrial fibrillation. *Am Heart J* 1996;131:499-507.
21. Therneau T, Sicks J, Bergstralh E, Offord J. Expected survival based on hazard rates. Technical report series. No. 52. Section of biostatistics. Rochester, Minn.: Mayo Clinic, March 1994.
22. Trohman RG, Simmons TW, Moore SL, Firstenberg MS, Williams D, Maloney JD. Catheter ablation of the atrioventricular junction using radiofrequency energy and a bilateral cardiac approach. *Am J Cardiol* 1992;70: 1438-43.

23. Olgin JE, Scheinman MM. Comparison of high energy direct current and radiofrequency catheter ablation of the atrioventricular junction. *J Am Coll Cardiol* 1993;21:557-64.
24. Peto R, Peto J. Asymptotically efficient rank invariant test procedures. *J R Stat Soc [A]* 1972;135:185-206.
25. Cox DR. Regression models and life-tables. *J R Stat Soc [B]* 1972;34:187-220.
26. Krahn AD, Manfreda J, Tate RB, Mathewson FA, Cuddy TE. The natural history of atrial fibrillation: incidence, risk factors, and prognosis in the Manitoba Follow-Up Study. *Am J Med* 1995;98:476-84.
27. Dries DL, Exner DV, Gersh BJ, Domanski MJ, Waclawiw MA, Stevenson LW. Atrial fibrillation is associated with an increased risk for mortality and heart failure progression in patients with asymptomatic and symptomatic left ventricular systolic dysfunction: a retrospective analysis of the SOLVD trials: Studies of Left Ventricular Dysfunction. *J Am Coll Cardiol* 1998;32:695-703.
28. Wolf PA, Mitchell JB, Baker CS, Kannel WB, D'Agostino RB. Impact of atrial fibrillation on mortality, stroke, and medical costs. *Arch Intern Med* 1998;158:229-34.
29. Brignole M, Menozzi C, Gianfranchi L, et al. Assessment of atrioventricular junction ablation and VVIR pacemaker versus pharmacological treatment in patients with heart failure and chronic atrial fibrillation: a randomized, controlled study. *Circulation* 1998;98:953-60.
30. Brignole M, Gianfranchi L, Menozzi C, et al. Assessment of atrioventricular junction ablation and DDDR mode-switching pacemaker versus pharmacological treatment in patients with severely symptomatic paroxysmal atrial fibrillation: a randomized controlled study. *Circulation* 1997;96:2617-24.
31. Brand FN, Abbott RD, Kannel WB, Wolf PA. Characteristics and prognosis of lone atrial fibrillation: 30-year follow-up in the Framingham Study. *JAMA* 1985;254:3449-53.
32. Kopecky SL, Gersh BJ, McGoon MD, et al. The natural history of lone atrial fibrillation: a population-based study over three decades. *N Engl J Med* 1987;317:669-74.
33. Scheinman MM, Morady F, Hess DS, Gonzalez R. Catheter-induced ablation of the atrioventricular junction to control refractory supraventricular arrhythmias. *JAMA* 1982;248:851-5.

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