

# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

DECEMBER 2, 2004

VOL. 351 NO. 23

## Catheter Ablation for Atrial Fibrillation in Congestive Heart Failure

Li-Fern Hsu, M.B., B.S., Pierre Jaïs, M.D., Prashanthan Sanders, M.B., B.S., Ph.D., Stéphane Garrigue, M.D., Ph.D.,  
Mélèze Hocini, M.D., Frédéric Sacher, M.D., Yoshihide Takahashi, M.D., Martin Rotter, M.D.,  
Jean-Luc Pasquié, M.D., Ph.D., Christophe Scavée, M.D., Pierre Bordachar, M.D., Jacques Clémenty, M.D.,  
and Michel Haïssaguerre, M.D.

### ABSTRACT

#### BACKGROUND

Congestive heart failure and atrial fibrillation often coexist, and each adversely affects the other with respect to management and prognosis. We prospectively evaluated the effect of catheter ablation for atrial fibrillation on left ventricular function in patients with heart failure.

#### METHODS

We studied 58 consecutive patients with congestive heart failure and a left ventricular ejection fraction of less than 45 percent who were undergoing catheter ablation for atrial fibrillation. We selected as controls 58 patients without congestive heart failure who were undergoing ablation for atrial fibrillation, matched according to age, sex, and classification of atrial fibrillation. We evaluated the patients' left ventricular function and dimensions, symptom score, exercise capacity, and quality of life at baseline and at months 1, 3, 6, and 12.

#### RESULTS

After a mean ( $\pm$ SD) of  $12\pm 7$  months, 78 percent of the patients with congestive heart failure and 84 percent of the controls remained in sinus rhythm ( $P=0.34$ ) (69 percent and 71 percent, respectively, were in sinus rhythm without the administration of antiarrhythmic drugs). The patients with congestive heart failure had significant improvement in left ventricular function (increases in the ejection fraction and fractional shortening of  $21\pm 13$  percent and  $11\pm 7$  percent, respectively;  $P<0.001$  for both comparisons), left ventricular dimensions (decreases in the diastolic and systolic diameters of  $6\pm 6$  mm and  $8\pm 7$  mm, respectively;  $P=0.03$  and  $P<0.001$ , respectively), exercise capacity, symptoms, and quality of life. The ejection fraction improved significantly not only in patients without concurrent structural heart disease ( $24\pm 10$  percent,  $P<0.001$ ) and those with inadequate rate control before ablation ( $23\pm 10$  percent,  $P<0.001$ ), but also in those with coexisting heart disease ( $16\pm 14$  percent,  $P<0.001$ ) and adequate rate control before ablation ( $17\pm 15$  percent,  $P<0.001$ ).

#### CONCLUSIONS

Restoration and maintenance of sinus rhythm by catheter ablation without the use of drugs in patients with congestive heart failure and atrial fibrillation significantly improve cardiac function, symptoms, exercise capacity, and quality of life.

From Hôpital Cardiologique du Haut-Lévêque and Université Victor Ségalen, Bordeaux II, Bordeaux-Pessac, France. Address reprint requests to Dr. Jaïs at Hôpital Cardiologique du Haut-Lévêque, Ave. de Magellan 33604, Bordeaux-Pessac, France, or at pierre.jais@chu-bordeaux.fr.

N Engl J Med 2004;351:2373-83.

Copyright © 2004 Massachusetts Medical Society.

**C**ONGESTIVE HEART FAILURE AND ATRIAL fibrillation, the two “epidemics” of cardiovascular disease,<sup>1</sup> are major health problems. They often coexist, and the intersection of the two conditions creates a vicious circle, with congestive heart failure promoting the development of atrial fibrillation and vice versa.<sup>2,3</sup> In addition, each increases the morbidity and mortality associated with the other.<sup>4,5</sup>

Among patients with congestive heart failure, maintaining sinus rhythm with the use of antiarrhythmic drugs is challenging, owing to the limited efficacy and potentially deleterious effects of the drugs.<sup>6-10</sup> This finding has led to renewed interest in rate control, stimulated by reports on several important studies,<sup>11-13</sup> particularly the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)<sup>11</sup> and the Rate Control versus Electrical Cardioversion (RACE)<sup>12</sup> trials, both of which suggested an equivalent outcome for strategies involving pharmacologic rhythm and rate control. However, recent evidence from the AFFIRM investigators, in addition to confirming the adverse prognostic effects of congestive heart failure, highlights the potential benefit of maintaining sinus rhythm if it could be achieved without the adverse effects of antiarrhythmic drugs.<sup>14</sup>

Curative catheter ablation for atrial fibrillation has been established as an effective therapeutic option for atrial fibrillation that is resistant to pharmacologic rhythm or rate control, with successful long-term maintenance of sinus rhythm in the absence of treatment with antiarrhythmic drugs reported in the majority of patients.<sup>15-18</sup> We evaluated the effects of restoration and maintenance of sinus rhythm by catheter ablation for atrial fibrillation on left ventricular function in patients with congestive heart failure.

## METHODS

### STUDY POPULATION

In this prospective study, we enrolled 58 consecutive patients with congestive heart failure from any cause who were undergoing curative ablation for atrial fibrillation that was resistant to at least two antiarrhythmic drugs. All patients with symptomatic congestive heart failure, defined as New York Heart Association (NYHA) class II or higher that was associated with a left ventricular ejection fraction of less than 45 percent, were included. The definition and classification of atrial fibrillation used in this

study were based on published guidelines from the American College of Cardiology–American Heart Association and the European Society of Cardiology.<sup>6</sup> No patients meeting the above criteria were excluded. In the case of patients with hypotension or NYHA class IV symptoms, the procedure was performed after the patients’ condition stabilized. Fifty-eight patients, matched for age, sex, and classification of atrial fibrillation, were selected as procedural controls from a total of 591 patients without congestive heart failure who underwent ablation during the same period. Written informed consent was obtained from all patients, and the study protocol was approved by the research committee at our institution. The study took place from March 2001 to March 2004.

### BASELINE EVALUATION AND DATA COLLECTION

Patients were routinely admitted two days before the ablation procedure for baseline evaluation. Treatment with oral anticoagulants, taken by all the patients, was stopped on admission, and treatment with all antiarrhythmic drugs, except amiodarone, was stopped for an appropriate period before ablation. Heart rate and rhythm were monitored with the use of 48-hour ambulatory electrocardiography. Transesophageal echocardiography was performed to rule out atrial thrombi, and transthoracic echocardiography was performed to evaluate cardiac structure and function. Echocardiographic measurement of the left ventricular ejection fraction was standardized with the use of Simpson’s biplane method for all patients during the initial hospitalization and subsequent visits. Arrhythmia-related symptoms were assessed with the Symptom Checklist–Frequency and Severity Scale,<sup>19</sup> and health-related quality of life was assessed with the 36-item Short-Form General Health Survey (SF-36) questionnaire.<sup>20</sup>

### ELECTROPHYSIOLOGICAL STUDY AND RADIOFREQUENCY CATHETER ABLATION

The ablation procedure, based on electrical isolation of the pulmonary veins in all patients,<sup>16</sup> with additional left atrial linear ablation when necessary, has been described previously.<sup>21</sup> In brief, after the administration of heparin to maintain anticoagulation, pulmonary-vein isolation was performed, guided by a circumferential deca-polar mapping catheter (Lasso, Biosense Webster) positioned within the target pulmonary vein. Radiofrequency energy, with power and temperature limited to 25 to

30 W and 50°C, respectively, was delivered proximal to the pulmonary-vein ostia with the use of a 4-mm ablation catheter with an irrigated tip (Celsius Thermocool, Biosense Webster). The end point of ablation was electrical isolation of all the pulmonary veins, manifested by the disappearance or dissociation of pulmonary-vein potentials. Then linear ablation, with power limited to 40 W or less, was performed in most patients. This procedure involved the creation of one or more linear lesions bridging the two superior pulmonary veins or extending from a pulmonary vein to the mitral annulus to form a complete obstacle to electrical conduction, as demonstrated by established electrophysiological criteria.<sup>21</sup>

After ablation, anticoagulation therapy was reinitiated, and ambulatory electrocardiographic monitoring continued for at least three days in the hospital. In the absence of concurrent indications, all antiarrhythmic-drug treatment was stopped. In the event of an early recurrence of atrial fibrillation or atrial flutter, patients were offered either further ablation during their index hospitalization or a trial of antiarrhythmic drugs. A bicycle-ergometer stress test, with the use of a standard protocol of 30-W increments in exercise intensity every three minutes, was performed within three days after the procedure in order to assess baseline exercise capacity.

#### FOLLOW-UP

Patients were rehospitalized 1, 3, 6, and 12 months after the last procedure for follow-up evaluation involving clinical interviews, 48-hour ambulatory electrocardiographic monitoring, transthoracic echocardiography, and exercise testing. Anticoagulation therapy was stopped if sinus rhythm had been maintained for three to six months, unless otherwise indicated. Symptoms and quality of life were reevaluated at 3 and 12 months. If patients remained in sinus rhythm after 12 months, they were discharged to their own cardiologists for further follow-up.

#### DEFINITIONS AND OUTCOMES

Before ablation, adequate rate control was defined in patients with persistent and permanent atrial fibrillation as a mean ventricular rate of less than 80 beats per minute at rest,<sup>6</sup> the mean ventricular rate being the average of the number of ventricular beats per minute during the 48-hour electrocardiographic monitoring period before the procedure was performed. Ablation was considered to be successful if sinus rhythm was maintained with no symptomatic

or documented episodes of atrial fibrillation or atrial flutter. A marked improvement in left ventricular function was defined as an increase of 20 percent or more in the left ventricular ejection fraction or a value of 55 percent or more.

#### STATISTICAL ANALYSIS

Continuous variables, expressed as means  $\pm$ SD, and their distribution were analyzed with the Shapiro-Wilks test of normality. A comparison between the groups was performed with Student's t-test or the nonparametric Wilcoxon rank-sum test, as appropriate. Sequential data measurements were analyzed by repeated-measures analysis of variance, and differences between measures were evaluated with Fisher's least-significant-difference test for post hoc comparisons. Categorical variables, expressed as numbers and percentages, were compared with Fisher's exact test. The relationship between clinical variables and significant improvement in left ventricular function was assessed with a descending stepwise Cox proportional-hazards model, and the results are reported as relative risks with 95 percent confidence intervals. All tests of significance were two-tailed, and a P value of less than 0.05 was considered to indicate statistical significance.

## RESULTS

#### PATIENTS AND PROCEDURAL OUTCOME

The characteristics of the patients and the procedural outcomes are presented in Table 1. All patients with congestive heart failure had symptoms in NYHA class II or higher, despite treatment with angiotensin-converting-enzyme or angiotensin II-receptor blockers in 72 percent of the patients, beta-blockers in 97 percent, and digoxin in 29 percent. Nine patients (16 percent) had had at least one episode of class IV symptoms within the previous six months. Treatment with amiodarone was initiated in 93 percent of the patients but because of adverse effects or intolerance was continued in only 71 percent at the time of ablation. Fifty-three patients (91 percent) had persistent or permanent atrial fibrillation, and 38 (66 percent) had a left ventricular ejection fraction of less than 40 percent. Three patients awaiting cardiac transplantation were referred for ablation of atrial fibrillation to ameliorate symptoms.

During a mean of  $12 \pm 7$  months of follow-up (range, 3 to 34 months) after the final procedure (50 percent of patients with congestive heart failure and

**Table 1. Baseline Characteristics of the Patients with and Those without Congestive Heart Failure.\***

Variable	CHF (N=58)	No CHF (N=58)	P Value
<b>Clinical characteristics</b>			
Age — yr	56±10	56±10	0.94
Male sex — no. (%)	51 (88)	51 (88)	1.00
Classification of atrial fibrillation — no. (%)			
Permanent	43 (74)	43 (74)	1.00
Persistent	10 (17)	10 (17)	1.00
Paroxysmal	5 (9)	5 (9)	1.00
Duration of atrial fibrillation — mo	80±45	79±53	0.85
Previous electrical cardioversion — no. (%)	47 (81)	35 (60)	0.01
No. of antiarrhythmic drugs tried	3±1	3±1	0.61
Treatment with amiodarone — no. (%)	41 (71)	45 (78)	0.43
Hypertension — no. (%)	18 (31)	16 (28)	0.68
<b>Associated heart disease</b>			
Dilated cardiomyopathy alone — no. (%)	32 (55)	2 (3)	<0.001
Concurrent structural heart disease — no. (%)†			
Coronary artery disease	12 (21)	5 (9)	0.07
Valvular disease	9 (16)	3 (5)	0.13
Congenital heart disease	2 (3)	0	0.50
Hypertrophic cardiomyopathy	4 (7)	2 (3)	0.68
NYHA functional class	2.3±0.5	1.3±0.5	<0.001
Left ventricular ejection fraction — %	35±7	66±7	<0.001
Left ventricular fractional shortening — %	20±5	35±4	<0.001
Left ventricular dimensions— mm			
End-diastolic	60±8	53±5	<0.001
End-systolic	46±9	33±5	<0.001
Left atrial parasternal dimension — mm	50±7	46±6	0.004
<b>Procedure and outcome</b>			
All pulmonary veins isolated — no. (%)	58 (100)	58 (100)	1.00
Additional left atrial linear ablation — no. (%)	53 (91)	54 (93)	1.00
Total duration of radiofrequency ablation — min	69±27	78±29	0.15
Total duration of fluoroscopy — min	64±24	72±36	0.20
Total duration of procedure — min	218±65	232±90	0.39
Serious complications — no. (%)			
Tamponade	1 (2)	1 (2)	0.74
Stroke	1 (2)	0	
Repeated ablation — no. (%)	29 (50)	27 (47)	0.55
Overall success — no. (%)‡			
Without drugs	40 (69)	41 (71)	0.84
With drugs	45 (78)	49 (84)	0.34
Length of follow-up since last procedure — mo	12±7	12±6	0.98

\* Plus-minus values are means ±SD. CHF denotes congestive heart failure, and NYHA New York Heart Association. Because of rounding, not all values sum to the totals shown.

† Some patients had more than one coexisting heart disease.

‡ Success was defined as maintenance of sinus rhythm during the follow-up period without symptomatic or documented asymptomatic atrial fibrillation or flutter.

47 percent of patients in the control group underwent a second procedure), 78 percent of patients with congestive heart failure and 84 percent of patients in the control group were in sinus rhythm ( $P=0.34$ ); among the patients who were not taking antiarrhythmic drugs, 69 percent of those with congestive heart failure and 71 percent of those in the control group were in sinus rhythm. Pericardial tamponade requiring percutaneous drainage occurred in one patient in each group, and one patient with congestive heart failure had a stroke during the procedure. One patient with severe congenital heart disease and congestive heart failure who was being considered for heart transplantation had a recurrence of atrial fibrillation one month after ablation and died after three months from worsening congestive heart failure. The condition of the other two patients who were being evaluated for transplantation improved sufficiently to merit their removal from the transplant waiting list (i.e., the symptoms of both patients improved by one NYHA class, and the left ventricular ejection fraction increased by 8 percent in one patient and 12 percent in the other).

#### **SYMPTOMS, QUALITY OF LIFE, AND EXERCISE CAPACITY**

In the group with congestive heart failure, the NYHA class improved from a mean of  $2.3\pm 0.5$  before ablation to  $1.4\pm 0.5$  at 1 month and remained close to the 1-month level at 12 months ( $P<0.001$ ). No changes were observed in the control group. The Symptom Checklist–Frequency and Severity scores and SF-36 quality-of-life measures improved significantly in both groups. In patients with congestive heart failure, the SF-36 summary scores on the physical component and the mental component increased by  $24\pm 21$  and  $21\pm 19$  points, respectively ( $P<0.001$  for both comparisons); for patients in the control group, the scores on the two components increased by  $18\pm 17$  ( $P=0.003$ ) and  $14\pm 19$  ( $P=0.004$ ), respectively.

Exercise time and capacity also increased significantly in both groups. In the group with congestive heart failure, exercise time increased from  $11\pm 4$  to  $14\pm 5$  minutes ( $P<0.001$ ) and maximal capacity from  $123\pm 44$  to  $144\pm 55$  W ( $P<0.001$ ), whereas in the control group, the numbers increased from  $14\pm 4$  to  $16\pm 5$  minutes ( $P=0.001$ ) and from  $145\pm 44$  to  $158\pm 52$  W ( $P<0.001$ ) during the follow-up period.

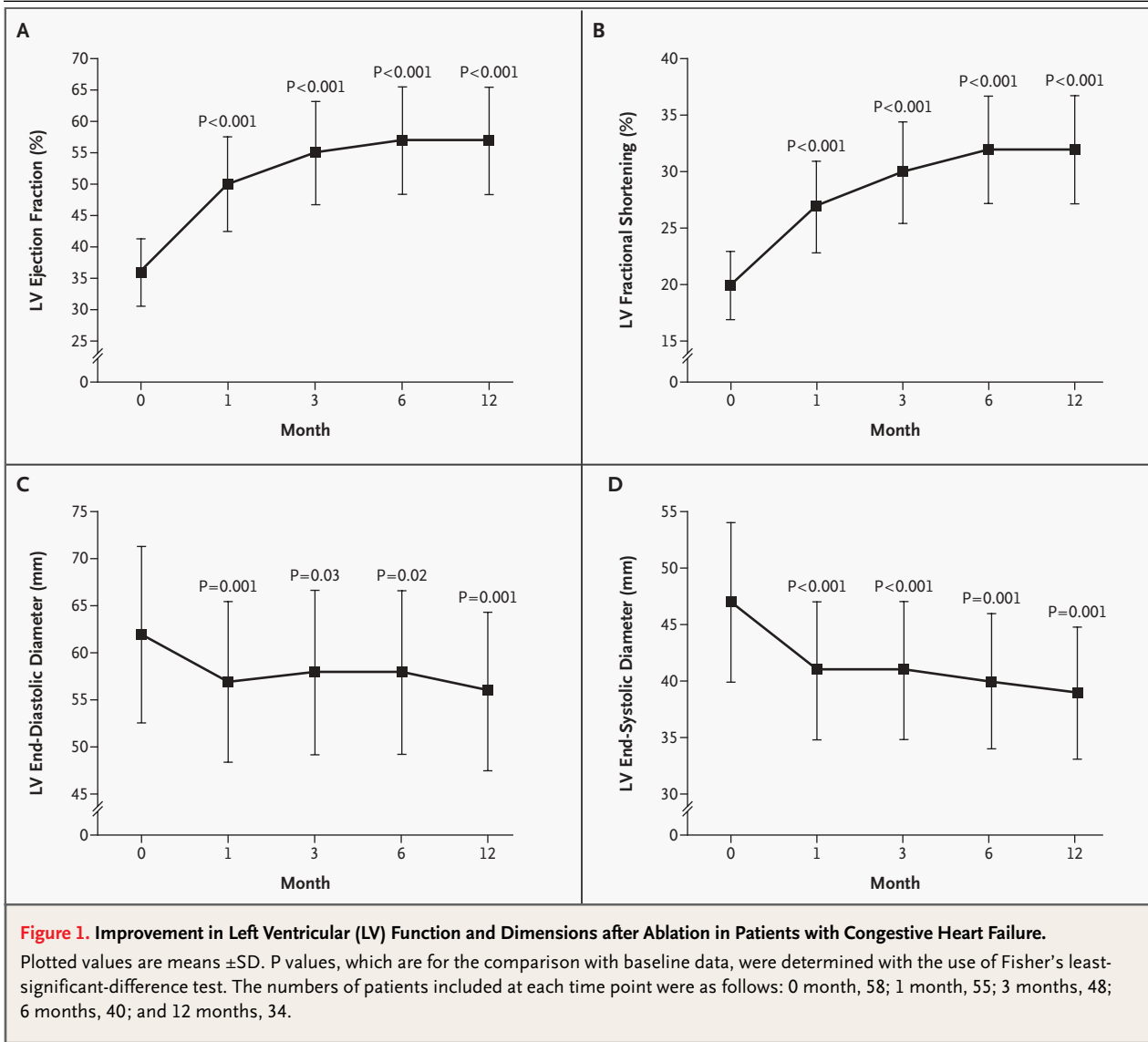
#### **LEFT VENTRICULAR FUNCTION**

Changes in left ventricular function and dimensions in the patients with congestive heart failure are shown in Figure 1. The left ventricular ejection fraction increased by a mean of  $21\pm 13$  percent and left ventricular fractional shortening by  $11\pm 7$  percent ( $P<0.001$  for both comparisons), with the greatest improvement observed within the first three months. Concurrently, left ventricular dilatation was reduced: end-diastolic diameter by  $6\pm 6$  mm ( $P=0.03$ ), and end-systolic diameter by  $8\pm 7$  mm ( $P<0.001$ ).

Marked improvement of the left ventricular ejection fraction (i.e., an increase of 20 percent or more or to a value of 55 percent or more) was observed in 42 patients (72 percent). Recurrence of arrhythmia despite the use of antiarrhythmic drugs was the only variable negatively affecting the recovery of the left ventricular ejection fraction (Table 2). However, among the 12 patients in whom arrhythmia recurred despite the use of drugs, left ventricular function was still significantly improved in 4 patients in whom ablation had converted permanent atrial fibrillation to paroxysmal fibrillation.

#### **CONCURRENT STRUCTURAL HEART DISEASE**

The presence of concurrent structural heart disease other than isolated dilated cardiomyopathy did not significantly affect the outcome of ablation. Sinus rhythm was maintained in 73 percent of patients with coexisting heart disease (66 percent without antiarrhythmic therapy), as compared with 81 percent of patients with isolated dilated cardiomyopathy (73 percent without antiarrhythmic therapy) ( $P=0.46$ ). The left ventricular function increased significantly in both groups after ablation (Fig. 2A and 2B). In the absence of concurrent structural heart disease, the left ventricular ejection fraction increased by  $24\pm 10$  percent ( $P<0.001$ ), and 28 of 32 patients who were studied (88 percent) had a marked increase (i.e., an increase of 20 percent or more or to a value of 55 percent or more). Three of the four patients without improvement had a recurrence of persistent atrial fibrillation; of those, two had suboptimal rate control despite drug therapy (mean ventricular rate, 94 and 98 beats per minute). In patients with concurrent structural heart disease, the left ventricular ejection fraction increased by  $16\pm 14$  percent ( $P<0.001$ ), and 14 of 26 patients who were studied (54 percent) had a marked increase in the left ventricular ejection fraction ( $P=0.007$  for the



comparison with those without concurrent heart disease).

**PREABLATION RATE CONTROL AND TACHYCARDIA-MEDIATED CARDIOMYOPATHY**

The characteristics of the subgroup of 53 patients with persistent or permanent atrial fibrillation and congestive heart failure are shown in Table 3. Seventy-five percent of patients in whom rate control was adequate had concurrent structural heart disease. Both groups had significant improvement in left ventricular function after ablation (Fig. 2C and 2D), with the left ventricular ejection fraction increasing by a mean of  $23 \pm 10$  percent in patients with

poor rate control ( $P < 0.001$ ) and by  $17 \pm 15$  percent in those with adequate rate control ( $P < 0.001$ ). No statistically significant differences were observed between the groups. A marked increase in the left ventricular ejection fraction was observed in 86 percent of patients with poor rate control, as compared with 54 percent of those with adequate rate control ( $P = 0.02$ ).

Regardless of the presence or absence of concurrent heart disease or rate-controlled arrhythmia, the left ventricular ejection fraction improved significantly, with the greatest improvement ( $24 \pm 8$  percent) in patients with poor rate control who did not have coexisting heart disease. In this group, in

**Table 2. Variables Affecting Marked Improvement in Left Ventricular Function in Patients with Congestive Heart Failure.\***

Variable	Marked Improvement in LV Function†		Hazard Ratio (95% CI)	P Value
	Yes (N=42) no. (%)	No (N=15) no. (%)		
Age ≤55 yr	24 (57)	4 (27)	0.76 (0.38–1.56)	0.46
Coexisting heart disease	14 (33)	11 (73)	1.11 (0.52–2.44)	0.78
Valvular heart disease	4 (10)	4 (27)	1.35 (0.47–3.85)	0.58
Hypertrophic cardiomyopathy	1 (2)	3 (20)	4.17 (0.58–33.33)	0.16
Recurrent atrial fibrillation				
Without drugs	7 (17)	10 (67)	1.54 (0.44–5.56)	0.50
With drugs	4 (10)	8 (53)	3.23 (1.15–9.09)	0.03

\* Marked improvement of left ventricular (LV) function was defined as an increase in the left ventricular ejection fraction of 20 percent or more or to a value of 55 percent or more, as measured on transthoracic echocardiography with the use of Simpson's biplane method. CI denotes confidence interval.

† Of the 58 patients in the study, data were analyzed for only 57 because 1 died during the study.

which congestive heart failure could be attributed to tachycardia-mediated cardiomyopathy alone, 92 percent of the patients had marked improvement in the left ventricular ejection fraction.

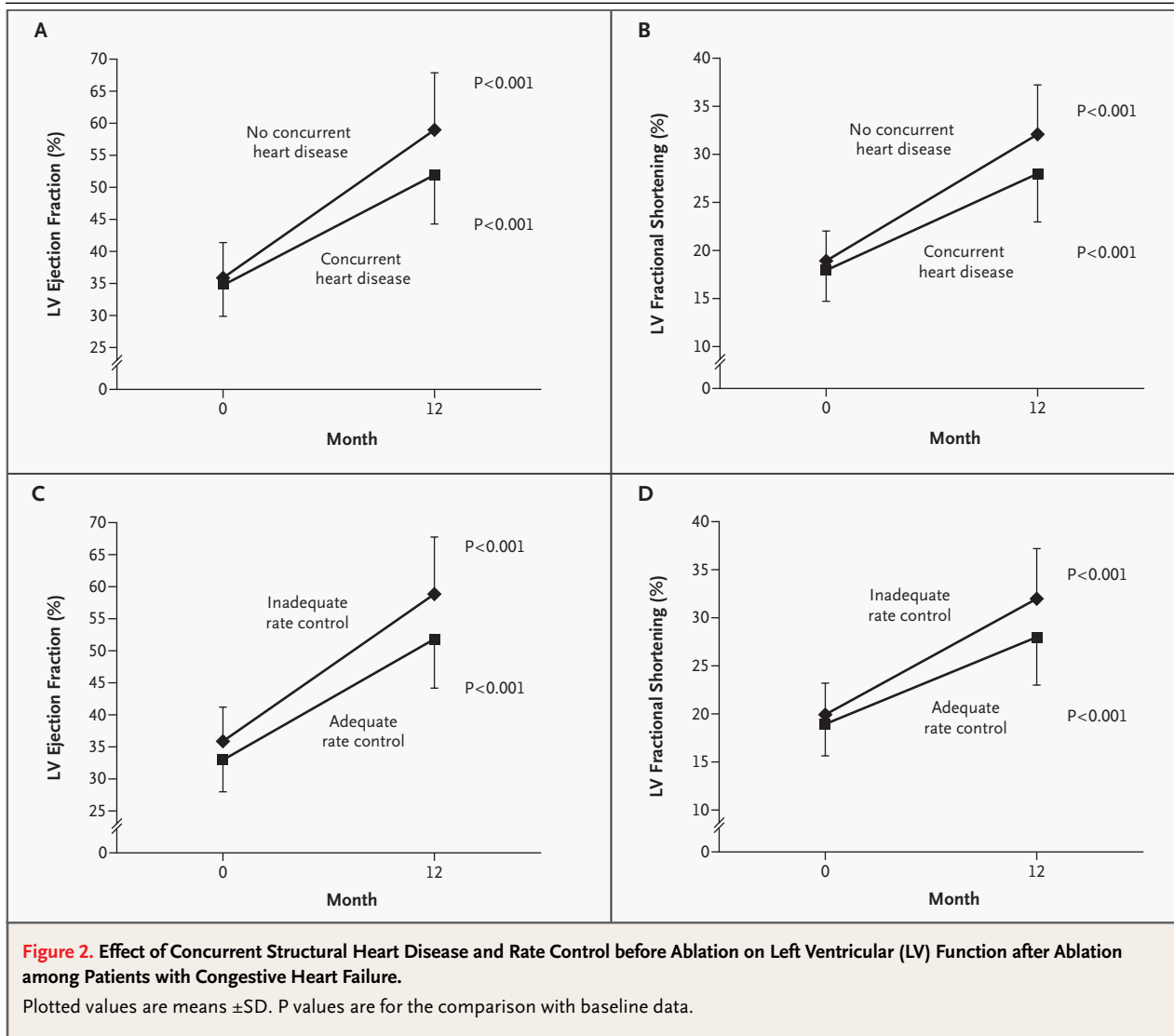
#### DISCUSSION

This study presents new information on the detrimental effects of atrial fibrillation in patients with congestive heart failure and the treatment of these patients. After catheter ablation for atrial fibrillation, long-term restoration of sinus rhythm, without the use of antiarrhythmic drugs in most patients, resulted in significant improvement in left ventricular function, exercise capacity, symptoms, and quality of life, even in the presence of concurrent structural heart disease and adequate ventricular rate control before ablation.

Cardiomyopathy due to a rapid ventricular response has been implicated as the main mechanism by which atrial fibrillation results in congestive heart failure.<sup>22</sup> However, impaired atrial contractile function, loss of atrioventricular synchrony, and an irregular ventricular rhythm have also been shown to have adverse effects on cardiac output.<sup>2,22-24</sup> In our study, restoration of sinus rhythm resulted in an overall increase in the left ventricular ejection fraction of 21 percent in patients with congestive heart failure. More modest improvements in the left ventricular ejection fraction were observed in studies using the clinically proven and effective "ablate and pace" strategy for rate control, comprising creation of atrioventricular block by catheter ablation, fol-

lowed by permanent implantation of a pacemaker.<sup>25-29</sup> Though this strategy provides effective rate control and regularization of ventricular rhythm, it does not restore atrial contraction or atrioventricular or interventricular synchrony. In addition, the benefit of rhythm regularization is negated by the adverse hemodynamic effects of right ventricular pacing, which is commonly used in such patients.<sup>28</sup> The use of left ventricular or biventricular pacing, associated with a more favorable hemodynamic profile,<sup>30</sup> may circumvent this problem, as demonstrated clinically by the recently completed Post AV Node Ablation Evaluation (PAVE) trial.<sup>31</sup>

The striking improvement in left ventricular function after restoration of sinus rhythm in 92 percent of the patients in our study who had inadequate rate control without coexisting heart disease suggests that congestive heart failure was attributable primarily to tachycardia-mediated cardiomyopathy in this group of patients. This high incidence suggests that in previous studies, tachycardia-related cardiomyopathy in association with atrial fibrillation may have been underestimated, possibly because of the use of antiarrhythmic drugs.<sup>29,32</sup> Patients with adequate rate control and coexisting heart disease, including some with severe congestive heart failure who were being considered for cardiac transplantation, also benefited from ablation, though to a lesser extent, a finding that demonstrates the additional hemodynamic benefits of the restoration of sinus rhythm as compared with pharmacologic rate control. These results highlight the important contribution of atrial contraction and



atrioventricular synchrony to the total cardiac output and their role, in addition to a rapid ventricular rate, in the pathogenesis of left ventricular dysfunction in atrial fibrillation.

A recent retrospective study examined the effect of catheter ablation of atrial fibrillation on left ventricular function in 94 patients with impaired left ventricular function. The study showed a nonsignificant overall increase of 5 percent in the left ventricular ejection fraction after ablation, on the basis of a single echocardiographic examination performed approximately six months after the initial ablation procedure.<sup>33</sup> The smaller improvement that was observed in this recent study could be attributed to differences in the study design and also in the patient

population, since a preponderance of the patients had paroxysmal atrial fibrillation and concurrent structural heart disease. However, most patients with concurrent heart disease in our study also had significant improvement in left ventricular function after restoration of sinus rhythm.

Our study was not powered to assess mortality, owing to the small number of patients with congestive heart failure, which reflects the current pattern of referrals for ablation in most centers. However, several randomized trials have shown improved survival among patients with congestive heart failure and atrial fibrillation who had a reversion to sinus rhythm.<sup>34,35</sup> Since a reduced left ventricular ejection fraction is an important predictor of mortality

**Table 3. Characteristics of the Patients with Congestive Heart Failure, According to the Adequacy of Ventricular Rate Control.\***

Variable	Ventricular Rate Control		P Value
	Inadequate (N=29)	Adequate (N=24)	
<b>Clinical characteristics</b>			
Age — yr	56±9	56±12	0.71
Male sex — no. (%)	26 (90)	21 (88)	1.00
Duration of atrial fibrillation — mo	89±53	76±32	0.28
Ventricular rate before ablation — beats/min			
Average	103±14	72±6	<0.001
Maximal	180±23	122±37	<0.001
Previous electrical cardioversion — no. (%)	26 (90)	20 (83)	0.69
No. of antiarrhythmic drugs tried	4±1	3±1	0.28
<b>Associated heart disease</b>			
Dilated cardiomyopathy alone — no. (%)	23 (79)	6 (25)	<0.001
Concurrent structural heart disease — no. (%)†	6 (21)	18 (75)	<0.001
Coronary artery disease	3 (10)	9 (38)	0.02
Valvular disease	2 (7)	5 (21)	0.23
Congenital heart disease	0	2 (8)	0.20
Hypertrophic cardiomyopathy	1 (3)	3 (12)	0.32
NYHA functional class	2.2±0.4	2.5±0.6	0.01
Left ventricular ejection fraction — %	36±7	36±9	0.93
Left ventricular fractional shortening — %	20±6	20±5	0.91
Left ventricular dimensions — mm			
End-diastolic	59±8	61±9	0.50
End-systolic	44±9	48±10	0.18
Left atrial parasternal dimension — mm	49±7	51±6	0.28
<b>Outcome</b>			
Length of follow-up since last procedure — mo	12±7	12±6	0.98
Overall success — no. (%)‡			
Without drugs	19 (66)	17 (71)	0.68
With drugs	23 (79)	18 (75)	0.75
Marked improvement in left ventricular function — no. (%)§	25 (86)	13 (54)	0.02

\* Plus-minus values are means ±SD. Adequate ventricular rate control was defined as a mean ventricular rate of less than 80 beats per minute without exercise, the mean ventricular rate being the average of the number of ventricular beats per minute during 48 hours of electrocardiographic monitoring before ablation. Because of rounding, not all values sum to the totals shown.

† Some patients had more than one coexisting heart disease.

‡ Success was defined as maintenance of sinus rhythm during the follow-up period without symptomatic or documented asymptomatic atrial fibrillation or flutter.

§ Marked improvement in left ventricular function was defined as an increase in the left ventricular ejection fraction of 20 percent or more or to a value of 55 percent or more as measured on transthoracic echocardiography with the use of Simpson's biplane method.

ty,<sup>36</sup> the significant improvement in left ventricular function after ablation could be important in improving survival. In the recently reported substudy of the AFFIRM trial, restoration and maintenance of sinus rhythm were associated with a 47 percent reduction in the risk of death, as compared with that

of patients who were in atrial fibrillation, whereas the use of antiarrhythmic drugs and the presence of congestive heart failure significantly increased the risk of death, by 49 percent and 57 percent, respectively, thereby reversing the benefit of the restoration of sinus rhythm.<sup>14</sup> The maintenance of sinus

rhythm without antiarrhythmic drugs may thus be of critical importance and can now be achieved through curative ablation with the use of catheter or surgical techniques.

Our study is limited by the relatively small sample and the nonrandomized design, partly imposed by the characteristics of patients referred for atrial fibrillation ablation. We tried to minimize bias by including a control group of patients without congestive heart failure who were matched for age, sex, and classification of atrial fibrillation. All clinical characteristics except those related to cardiac function were also identical. Since no patients with symptomatic congestive heart failure from any cause were excluded, the results, including procedural rates of success and complications, are likely to represent the clinical situation and be applicable to most patients with congestive heart failure and atrial fibrillation.

Though the results of catheter ablation for atrial fibrillation have been steadily improving, with the rate of success often reported as more than 80 percent for paroxysmal atrial fibrillation,<sup>16-18</sup> ablation of permanent atrial fibrillation has been more difficult and has required more extensive atrial ablation and often multiple procedures.<sup>18,37</sup> Complications have been infrequent (usually occurring in less than 1 percent of patients) but have included pericardial tamponade and stroke. The results can be expected to improve with a better understanding of the sub-

strate maintaining atrial fibrillation and with the development of more effective techniques.

Curative ablation for atrial fibrillation offers the unique opportunity to maintain sinus rhythm without antiarrhythmic drugs, which can have deleterious effects. Our study shows that restoration and long-term maintenance of sinus rhythm are associated with significant improvement in cardiac function, symptoms, exercise capacity, and quality of life in patients with congestive heart failure, even in the presence of concurrent heart disease and adequate rate control.

Dr. Hsu is the recipient of a Health Manpower Development Program fellowship funded by the Ministry of Health, Singapore. Dr. Sanders is the recipient of a Neil Hamilton Fairley and Ralph Reader Fellowship, jointly funded by the National Health and Medical Research Council and the National Heart Foundation of Australia. Dr. Rotter is the recipient of a grant from the Swiss National Foundation for Scientific Research, Bern.

Dr. Hsu reports having received lecture fees from Biosense Webster; Dr. Jaïs having received consulting and lecture fees from Biosense Webster; Dr. Sanders having served on the advisory board of and having received lecture fees from Biosense Webster and Endocardial Solutions; Dr. Garrigue having received consulting fees from Medtronic, St. Jude Medical, and Sorin and lecture fees from St. Jude Medical and Sorin; Dr. Hocini having received lecture fees from Biosense Webster and Bard Electrophysiology; Dr. Pasquié having received consulting fees from Medtronic; and Dr. Haïssaguerre having received consulting and lecture fees from Biosense Webster. A U.S. patent entitled "Catheter Having Mapping Assembly (6711428)" was issued on March 23, 2004; Dr. Haïssaguerre is one of the inventors. The patent is owned by Biosense Webster. A European patent entitled "Steerable Catheter with Fixed Curve (EPO 839547)" was issued on September 24, 2003; Dr. Haïssaguerre is one of the inventors. The patent is owned by Bard Electrophysiology.

#### REFERENCES

- Braunwald E. Shattuck Lecture — cardiovascular medicine at the turn of the millennium: triumphs, concerns, and opportunities. *N Engl J Med* 1997;337:1360-9.
- Stevenson WG, Stevenson LW. Atrial fibrillation in heart failure. *N Engl J Med* 1999;341:910-1.
- Ehrlich JR, Nattel S, Hohnloser SH. Atrial fibrillation and congestive heart failure: specific considerations at the intersection of two common and important cardiac disease sets. *J Cardiovasc Electrophysiol* 2002;13:399-405.
- Middlekauff HR, Stevenson WG, Stevenson LW. Prognostic significance of atrial fibrillation in advanced heart failure: a study of 390 patients. *Circulation* 1991;84:40-8.
- Wang TJ, Larson MG, Levy D, et al. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: the Framingham Heart Study. *Circulation* 2003;107:2920-5.
- Fuster V, Ryden LE, Asinger RW, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients with Atrial Fibrillation) developed in collaboration with the North American Society of Pacing and Electrophysiology. *Circulation* 2001;104:2118-50.
- Torp-Pedersen C, Møller M, Bloch-Thomsen PE, et al. Dofetilide in patients with congestive heart failure and left ventricular dysfunction. *N Engl J Med* 1999;341:857-65.
- Roy D, Talajic M, Dorian P, et al. Amiodarone to prevent recurrence of atrial fibrillation. *N Engl J Med* 2000;342:913-20.
- Falk RH. Atrial fibrillation. *N Engl J Med* 2001;344:1067-78. [Erratum, *N Engl J Med* 2001;344:1876.]
- The AFFIRM First Antiarrhythmic Drug Substudy Investigators. Maintenance of sinus rhythm in patients with atrial fibrillation: an AFFIRM substudy of the first antiarrhythmic drug. *J Am Coll Cardiol* 2003;42:20-9.
- The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002;347:1825-33.
- Van Gelder IC, Hagens VE, Bosker HA, et al. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. *N Engl J Med* 2002;347:1834-40.
- Hohnloser SH, Kuck KH, Lillenthal J. Rhythm or rate control in atrial fibrillation — Pharmacological Intervention in Atrial Fibrillation (PIAF): a randomized trial. *Lancet* 2000;356:1789-94.
- Corley SD, Epstein AE, DiMarco JP, et al. Relationships between sinus rhythm, treatment, and survival in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Study. *Circulation* 2004;109:1509-13.
- Haïssaguerre M, Jaïs P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;339:659-66.

16. Haissaguerre M, Jais P, Shah DC, et al. Electrophysiological end point for catheter ablation of atrial fibrillation initiated from multiple pulmonary venous foci. *Circulation* 2000;101:1409-17.
17. Pappone C, Oreto G, Rosanio S, et al. Atrial electroanatomic remodeling after circumferential radiofrequency pulmonary vein ablation: efficacy of an anatomic approach in a large cohort of patients with atrial fibrillation. *Circulation* 2001;104:2539-44.
18. Oral H, Knight BP, Tada H, et al. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. *Circulation* 2002;105:1077-81.
19. Bubien RS, Knotts-Dolson SM, Plumb VJ, Kay GN. Effect of radiofrequency catheter ablation on health-related quality of life and activities of daily living in patients with recurrent arrhythmias. *Circulation* 1996;94:1585-91.
20. Ware JE. SF-36 physical and mental summary scales: a user's manual. Boston: Health Institute, New England Medical Center, 1994.
21. Jais P, Hocini M, Hsu LF, et al. Technique and result of linear ablation at the mitral isthmus. *Circulation* 2004;110:2996-3002.
22. Shinbane JS, Wood MA, Jensen DN, Ellenbogen KA, Fitzpatrick AP, Scheinman MM. Tachycardia-induced cardiomyopathy: a review of animal models and clinical studies. *J Am Coll Cardiol* 1997;29:709-15.
23. Pozzoli M, Cioffi G, Traversi E, Pinna GD, Cobelli F, Tavazzi L. Predictors of primary atrial fibrillation and concomitant clinical and hemodynamic changes in patients with chronic heart failure: a prospective study in 344 patients with baseline sinus rhythm. *J Am Coll Cardiol* 1998;32:197-204.
24. Clark DM, Plumb VJ, Epstein AE, Kay GN. Hemodynamic effects of an irregular sequence of ventricular cycle lengths during atrial fibrillation. *J Am Coll Cardiol* 1997;30:1039-45.
25. 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.
26. Ozcan C, Jahangir A, Friedman PA, et al. Long-term survival after ablation of the atrioventricular node and implantation of a permanent pacemaker in patients with atrial fibrillation. *N Engl J Med* 2001;344:1043-51.
27. Wood MA, Brown-Mahoney C, Kay GN, Ellenbogen KA. Clinical outcomes after ablation and pacing therapy for atrial fibrillation: a meta-analysis. *Circulation* 2000;101:1138-44.
28. 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.
29. Ozcan C, Jahangir A, Friedman PA, et al. Significant effects of atrioventricular node ablation and pacemaker implantation on left ventricular function and long-term survival in patients with atrial fibrillation and left ventricular dysfunction. *Am J Cardiol* 2003;92:33-7.
30. Leon AR, Greenberg JM, Kanuru N, et al. Cardiac resynchronization in patients with congestive heart failure and chronic atrial fibrillation: effect of upgrading to biventricular pacing after chronic right ventricular pacing. *J Am Coll Cardiol* 2002;39:1258-63.
31. Doshi R, Daoud E, Fellows C, Turk K, Duran A, Hamdan M. PAVE: the first prospective, randomized study evaluating biventricular pacing after ablate and pace therapy. Presented at the American College of Cardiology Annual Scientific Session 2004, New Orleans, March 7-10, 2004. (Accessed November 3, 2004, at <http://www.acc04online.org>.)
32. Redfield MM, Kay GN, Jenkins LS, Mi-anulli M, Jensen DN, Ellenbogen KA. Tachycardia-related cardiomyopathy: a common cause of ventricular dysfunction in patients with atrial fibrillation referred for atrioventricular ablation. *Mayo Clin Proc* 2000;75:790-5.
33. Chen MS, Marrouche NF, Khaykin Y, et al. Pulmonary vein isolation for the treatment of atrial fibrillation in patients with impaired systolic function. *J Am Coll Cardiol* 2004;43:1004-9.
34. Pedersen OD, Bagger H, Keller N, Marchant B, Kober L, Torp-Pedersen C. Efficacy of dofetilide in the treatment of atrial fibrillation-flutter in patients with reduced left ventricular function: a Danish Investigations of Arrhythmia and Mortality ON Dofetilide (DIAMOND) substudy. *Circulation* 2001;104:292-6.
35. Deedwania PC, Singh BN, Ellenbogen K, Fisher S, Fletcher R, Singh SN. Spontaneous conversion and maintenance of sinus rhythm by amiodarone in patients with heart failure and atrial fibrillation: observations from the Veterans Affairs Congestive Heart Failure Survival Trial of Antiarrhythmic Therapy (CHF-STAT). *Circulation* 1998;98:2574-9.
36. Vasan RS, Larson MG, Benjamin EJ, Evans JC, Reiss CK, Levy D. Congestive heart failure in subjects with normal versus reduced left ventricular ejection fraction: prevalence and mortality in a population-based cohort. *J Am Coll Cardiol* 1999;33:1948-55.
37. Kanagaratnam L, Tomassoni G, Schweikert R, et al. Empirical pulmonary vein isolation in patients with chronic atrial fibrillation using a three-dimensional nonfluoroscopic mapping system: long-term follow-up. *Pacing Clin Electrophysiol* 2001;24:1774-9.

Copyright © 2004 Massachusetts Medical Society.

CLINICAL PROBLEM-SOLVING SERIES

The *Journal* welcomes submissions of manuscripts for the Clinical Problem-Solving series. This regular feature considers the step-by-step process of clinical decision making. For more information, please see <http://authors.nejm.org>.