

# Time Course of Hemodynamic Changes and Improvement of Exercise Tolerance After Cardioversion of Chronic Atrial Fibrillation Unassociated with Cardiac Valve Disease

Isabelle C. Van Gelder, MD, Harry J. G. M. Crijns, MD, Paul K. Blanksma, MD, Martin L. J. Landsman, MD, Jan L. Posma, MD, Maarten P. Van Den Berg, MD, Frits L. Meijler, MD, and Kong I. Lie, MD

**This study prospectively assessed the time course, magnitude and mechanism of the hemodynamic changes after restoration of sinus rhythm in patients with chronic atrial fibrillation (AF) unassociated with valvular disease. Severe cardiac dysfunction may occur after chronic supraventricular tachycardia in patients with and without underlying cardiac disease. Improvement may follow abolishment of the arrhythmia or adequate slowing of the ventricular rate. Eight patients were studied with a mean previous duration of AF of  $10 \pm 9$  months. Ejection fraction, exercise capacity and the atrial contribution to the left ventricular filling (only during sinus rhythm) were studied before cardioversion, after cardioversion and 1 week, 1 month and 6 months thereafter. A significant improvement in ejection fraction from  $36 \pm 13$  to  $53 \pm 8\%$  ( $p < 0.05$ ) occurred at 1 month after cardioversion. Concomitantly, peak oxygen consumption had increased at 1 month, from  $20.1 \pm 7$  to  $25.2 \pm 6$  ml/min/kg ( $p < 0.05$ ). Thereafter, no further improvement in hemodynamic parameters occurred. The atrial systole improved already at 1 week (from  $3 \pm 5$  to  $16 \pm 11\%$ ,  $p < 0.05$ ) and remained unchanged thereafter. Thus, restoration of sinus rhythm was associated with a delayed improvement in ejection fraction and maximal exercise capacity, preceded by an early restoration of atrial contractility and an acute slowing of the heart rate. The discrepancy in time course of restoration of atrial and ventricular function parameters suggests that an intrinsic left ventricular cardiomyopathy is present in patients with AF.**

(Am J Cardiol 1993;72:560-566)

The hemodynamic consequences of chronic atrial fibrillation (AF) include an impairment of left ventricular function at rest and during exercise.<sup>1,2</sup> This may be caused by a loss of atrial systole<sup>1-6</sup> and an inadequate ventricular rate response, especially during exercise.<sup>3,4,6-8</sup> Finally, this may result in a tachycardia-induced cardiomyopathy.<sup>9-18</sup> To reverse this process the general goal in these patients is to restore sinus rhythm. Recent studies, focusing primarily on improvement in exercise capacity, demonstrated an increase of maximal oxygen consumption at 1 month.<sup>5,6</sup> Other investigators studied the hemodynamic changes before and after cardioversion both at rest and during exercise, but follow-up was limited to 1 day.<sup>2,3,8</sup> Acute changes in postcardioversion exercise capacity were reported sporadically and there are only limited data concerning long-term changes in hemodynamic parameters. Therefore, this study evaluates the time-dependence of changes in hemodynamics and exercise tolerance after restoration of sinus rhythm in patients with chronic AF unassociated with cardiac valve disease over a time course of 6 months and tries to find evidence for a tachycardia-induced cardiomyopathy.

## METHODS

**Study patients:** Between January 1988 and January 1989, 120 patients with chronic AF underwent cardioversion in our institution. Sixteen initially entered the present study. Exclusion criteria were AF of <1 month or >24 months duration, valvular heart disease and New York Heart Association classification for exercise tolerance >II. The total follow-up was 6 months. Eight patients did not complete the study because of recurrence of AF in <6 months and were not evaluated. Patient characteristics are listed in Table I. Underlying heart disease was determined from the patient's history, physical examination, chest x-ray, 12-lead electrocardiogram, 2-dimensional echocardiogram, exercise test and if available, coronary angiogram. In all patients hyperthyroidism was excluded. "Lone" AF was diagnosed only in the absence of any demonstrable underlying heart disease.<sup>19</sup> Previous duration of the arrhythmia was determined by careful examination of the patient's medical record, by questioning the patient and by reviewing all previous electrocardiograms. A 24-hour Holter monitor

From the Department of Cardiology, Thoraxcenter, University Hospital Groningen, Groningen, and the Interuniversity Cardiology Institute, Utrecht, the Netherlands. Manuscript received February 4, 1993; revised manuscript received April 27, 1993, and accepted April 28.

Address for reprints: Isabelle C. Van Gelder, MD, Department of Cardiology, Thoraxcenter, Oostersingel 59, 9713 EZ Groningen, the Netherlands.

**TABLE I** Characteristics of Patients, Heart Rate at Rest, and Maximal Exercise, and Peak  $\text{VO}_2$ /Heart Rate at Peak  $\text{VO}_2$  Ratios at Different Times During Follow-Up

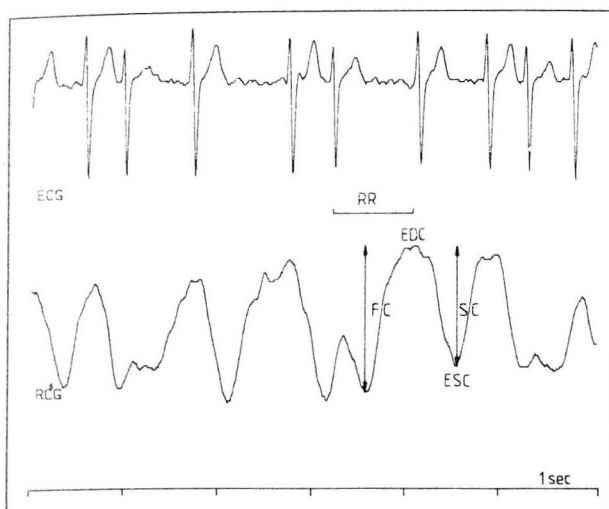
Patients	Age (yr) & Sex	Underlying Disease	Previous Duration (mos)	NYHA Class	LA Size (mm)	Before CV		After CV		One Week		One Month		Six Months	
						HR Rest Max. (beats/min)	$\text{PVO}_2/\text{HR}$ (ml/kg/beat)	HR Rest Max. (beats/min)	$\text{PVO}_2/\text{HR}$ (ml/kg/beat)	HR Rest Max. (beats/min)	$\text{PVO}_2/\text{HR}$ (ml/kg/beat)	HR Rest Max. (beats/min)	$\text{PVO}_2/\text{HR}$ (ml/kg/beat)	HR Rest Max. (beats/min)	$\text{PVO}_2/\text{HR}$ (ml/kg/beat)
1	40M	Lone AF	30	I	36	110	0.148	73	0.180	74	0.189	76	0.176	73	0.199
2	53F	Lone AF	2	II	60	195	0.080	170	0.10	170	0.110	182	0.112	198	0.110
3	60F	Lone AF	5	II	48	153	0.103	109	0.143	122	0.159	114	0.182	109	0.195
4	60M	Lone AF	3	I	43	212	0.110	66	0.186	174	0.189	57	0.236	176	0.210
5	62M	Lone AF	18	I	43	175	0.127	129	0.140	70	0.161	125	0.157	131	0.174
6	59F	HYT	5	II	37	160	0.063	73	0.100	80	0.110	57	0.118	56	0.126
7	78F	HYT	12	II	34	188	0.106	157	0.135	138	0.174	152	0.153	147	0.174
8	65M	CAD	3	I	36	172	0.120	101	0.167	147	0.2	104	0.207	92	0.221
						90		136		92		83		78	
						128		136		139		142		126	
						108		90		70		66		67	
						163		138		120		122		125	
Mean	60		10		43	Rest 123	0.107	81	0.144	85	0.162	79	0.168	76	0.176
±SD	± 10		± 9		± 8	± 28	± 0.02	± 16*	± 0.03*	± 19*	± 0.03*,†	± 19*	± 0.04*,†	± 16*	± 0.04*,†,‡
Mean						Max. 184		147		147		152		150	
±SD						± 31		± 14*		± 18*		± 21*		± 24*	

\*p &lt; 0.05 compared with value during atrial fibrillation.

†p &lt; 0.05 compared with value after cardioversion.

‡p &lt; 0.05 compared with 1 week after cardioversion.

AF = atrial fibrillation; CAD = coronary artery disease; CV = cardioversion; HR = heart rate; HYT = hypertension; LA = left atrial size, long axis; Max. = maximal exercise; NYHA = New York Heart Association;  $\text{PVO}_2/\text{HR}$  = peak oxygen consumption/heart rate at peak oxygen consumption;  $\text{VO}_2$  = oxygen consumption.



**FIGURE 1.** Example of a recording of the electrocardiogram (ECG) and radiocardiogram (RCG) with the use of a nuclear stethoscope. The minimum of the RCG was detected automatically and represents the end-systolic counts (ESC). The maximum of the RCG was taken at the R wave of the ECG and represents the end-diastolic counts (EDC). The ejection fraction was defined as  $([EDC-ESC]/EDC) \times 100\%$ . FC = filling counts; SC = stroke counts.

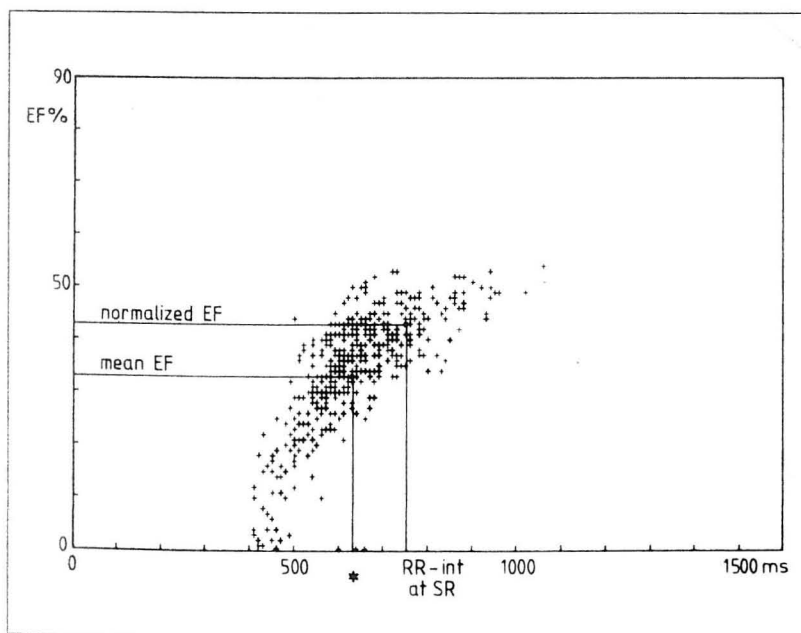
before electrical cardioversion was performed to assure that AF occurred without intercurrent sinus rhythm. During AF all patients were treated with digoxin (0.25 mg) and verapamil (240 to 360 mg) to control the ventricular response. The protocol for direct-current electrical cardioversion has been described previously.<sup>20</sup> According to the protocol digitalis was withheld for >5 days and verapamil for >1 day before the cardioversion. After the shock, chronic antiarrhythmic drug treatment was instituted in 5 of the 8 patients completing the study, depending on the patient's arrhythmia history. The only drug used was flecainide. During follow-up therapy was left unchanged. Patients were followed in the outpatient department 1 week, 1 month and 6 months after the

shock. All patients gave written informed consent and the study was approved by the Medical Ethics Committee of the University Hospital Groningen.

**Measurement of ejection fraction and atrial contribution to ventricular filling with the nuclear stethoscope:** The nuclear stethoscope is a computerized non-imaging probe (Nuclear Stethoscope, Bios Inc., Valhalla, New York). It consists of a single crystal detector, mounted on a flexible arm. The output of the nuclear stethoscope is fed into a computer system together with the electrocardiogram. The electrocardiogram and the radiocardiogram are displayed in real-time. During the display of the electrocardiogram and the radiocardiogram the RR interval and the ejection fraction are calculated and stored in a buffer<sup>21,22</sup> (Figure 1). Measurements were performed before cardioversion and <4 hours after the shock using a single dose of technetium-99m. Thereafter, the studies were repeated 1 week, 1 month and 6 months after the cardioversion. The ejection fraction was determined according to its definition: end-diastolic counts minus end-systolic counts (= stroke counts)/end-diastolic counts. During AF the "normalized" ejection fraction was determined and used for comparison with values during sinus rhythm. The normalized ejection fraction during AF was defined as the mean of all separate ejection fractions found at the RR intervals with the same length ( $\pm 20$  ms) as that during sinus rhythm immediately after the shock. Figure 2 gives a graphic representation of the normalized ejection fraction and the mean ejection fraction during AF. AF measurements were recorded during 500 cardiac cycles. During sinus rhythm recordings were made during 40 seconds and the mean values of the ejection fraction and RR interval were determined.

Figure 3 shows the method of assessment of the atrial contribution to the ventricular filling (% atrial systole) using the same equipment.

**Exercise capacity assessment:** The exercise studies were performed on the same day as the measure-



**FIGURE 2.** Plot of the left ventricular ejection fraction (EF) versus the immediately preceding RR interval (RR-int) in 1 patient. This figure shows 500 separate measurements. Mean EF was 34%, found at an RR interval of 633 ms. The normalized EF, at the RR interval during sinus rhythm (SR) after the cardioversion (758 ms), was 43%. Asterisk indicates the RR interval at the mean EF during atrial fibrillation.

ments with the nuclear stethoscope, except for the investigations after the shock. Postshock exercise testing was performed on the day after the cardioversion (<24 hours after the shock).

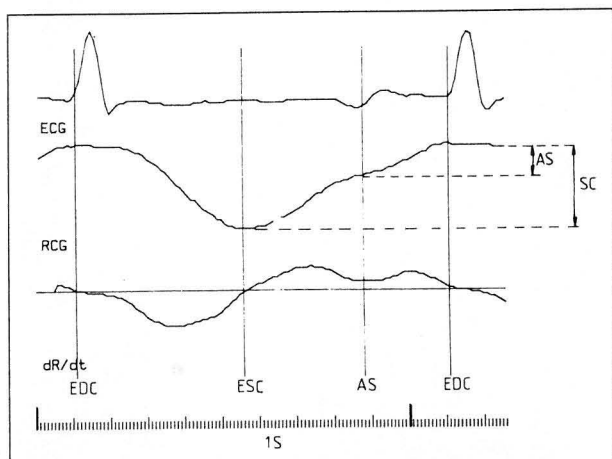
Exercise testing with respiratory gas exchange measurements was performed while patients exercised on a treadmill according to a modified Naughton protocol.<sup>23</sup> Oxygen consumption, carbon dioxide production and respiratory exchange ratios were measured continuously during exercise using an automated gas exchange measuring system (Sensormedics system 2900, Sensor Medics Corporation, Anaheim, California). Values were recorded at 20-second intervals through an on-line computer assembly (IBM computer systems, IBM Corporation, Austin, Texas). The electrocardiogram was monitored continuously with a computer-assisted system (Marquette Electronics Inc., Milwaukee, Wisconsin). Patients were familiar with exercise testing and they were encouraged to exercise until symptoms forced them to

stop. All patients terminated the test because of dyspnea or fatigue, and in all patients the gas exchange anaerobic threshold (the point at which carbon dioxide production increased disproportionately in relation to oxygen consumption) and a respiratory exchange ratio >1 were reached. Peak oxygen consumption rate ( $\text{VO}_2$ ) was defined as oxygen consumption (ml/min/kg) at peak exercise calculated as the mean of values during the last minute of exercise. Efficiency of exercise was expressed as the ratio of peak  $\text{VO}_2$  divided by the heart rate at peak  $\text{VO}_2$ .

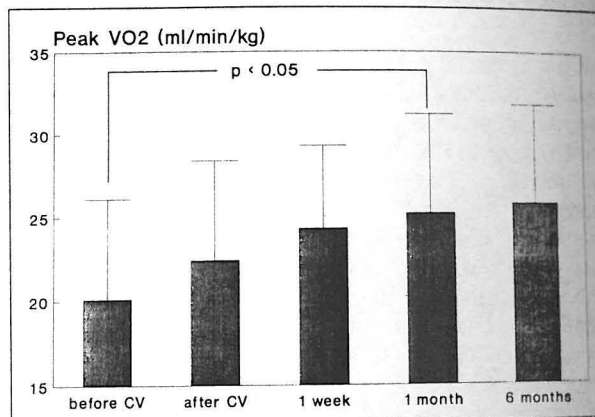
**Statistical analysis:** Values are expressed as mean  $\pm$  SD. A p value <0.05 was considered to indicate statistical significance. Measurements during the course of the study were compared by a repeated-measures analysis of variance. If significant overall effects were found, the Bonferroni multiple-comparison method was used to determine where the differences occurred.<sup>24</sup>

## RESULTS

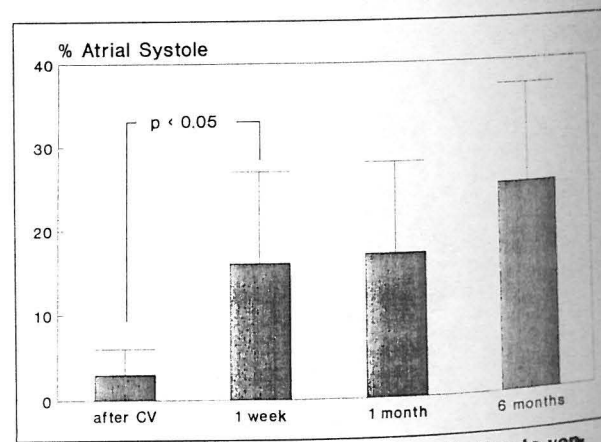
**Ejection fraction:** Figure 4 shows the changes in ejection fraction in the course of time. Before cardiover-



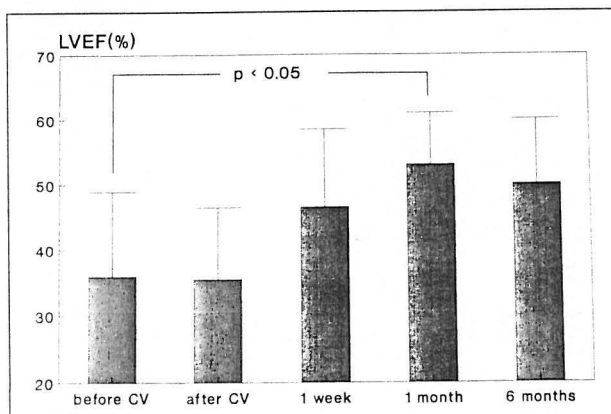
**FIGURE 3.** Example of measurement of atrial contribution to left ventricular filling (expressed as percent atrial systole [AS]) with the nuclear stethoscope in a patient having maintained sinus rhythm for 1 month. The percent atrial systole was defined as  $(\text{AS}/\text{SC}) \times 100\%$ . The beginning of the atrial systole was defined as the point where the first derivative of the radiocardiogram ( $dR/dt$ ) changed polarity. Its end was found at the maximum of the radiocardiogram (RCG). S = second; other abbreviations as in Figure 1.



**FIGURE 5.** Serial peak oxygen consumption ( $\text{VO}_2$ ) measurements during treadmill exercise testing (mean  $\pm$  SD). Note that the increase paralleled that found for left ventricular ejection fraction and reached statistical significance after 1 month maintenance of sinus rhythm. CV = cardioversion.



**FIGURE 6.** Mean percentages of atrial contribution to ventricular filling during follow-up. Improvement in atrial function occurred earlier than improvement in left ventricular systolic function or in exercise capacity, after 1 week maintenance of sinus rhythm. CV = cardioversion.



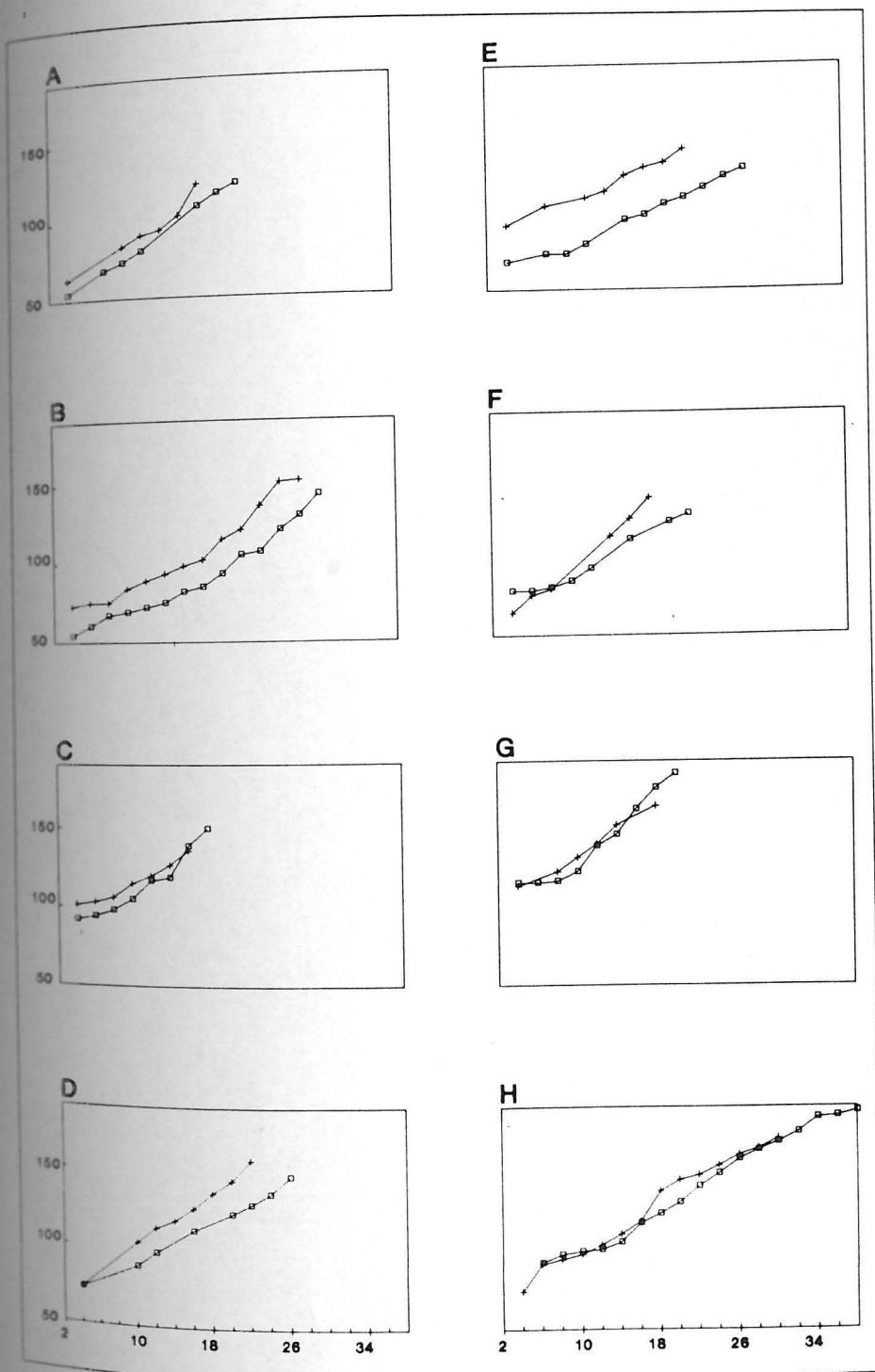
**FIGURE 4.** Changes in left ventricular ejection fraction (LVEF) during follow-up (mean  $\pm$  1 SD). The Bonferroni multiple comparison method indicated that the ejection fraction had increased significantly 1 month after cardioversion (CV).

sion it was  $36 \pm 13\%$ . The ejection fraction showed a small and not significant improvement 1 week after the cardioversion, but only after 1 month there was a significant increase to  $53 \pm 8\%$  ( $p < 0.05$ ). Thereafter it remained constant. An improvement occurred in all patients.

**Peak oxygen consumption:** Figure 5 shows the assessments of the peak oxygen consumption. It was unchanged at 1 day and 1 week after cardioversion but increased significantly from  $20.1 \pm 7$  ml/min/kg before cardioversion to  $25.2 \pm 6$  ml/min/kg 1 month after car-

dioversion ( $p < 0.05$ ), and remained unchanged thereafter.

**Percent atrial systole:** Figure 6 shows the changes in percent atrial systole from 4 hours after the cardioversion until 6 months thereafter as measured with the nuclear stethoscope. The mean atrial systole for all patients was  $3 \pm 5\%$  on day 1 and increased significantly 1 week after the cardioversion to  $16 \pm 11\%$ . Thereafter no further significant improvement occurred. Only 2 patients showed a detectable atrial systole (13 and 7%, respectively) immediately after the shock. At the end of



**FIGURE 7.** Relation between oxygen consumption (x axis, ml/min/kg) and heart rate response (y axis, beats/min) during exercise testing in all patients A to H, at 1 day (plus signs) and 6 months after cardioversion (open squares). Resting heart was lower in 4 patients at 6 months after cardioversion. Peak heart rate was higher at 6 months in 4 patients, whereas the other 4 had a lower heart rate. Efficiency of exercise was higher in 5 patients at all stages of exercise 6 months after cardioversion.



follow-up, 1 patient did not have a return of the atrial contraction. This patient had a considerably enlarged left atrium (51 mm, long-axis view).

**Heart rate responses during exercise:** At rest and during exercise, heart rates were significantly higher during AF than at different times after restoration of sinus rhythm (Table I). This table also presents the values for the peak  $\text{VO}_2$ /heart rate at peak  $\text{VO}_2$  ratio. This ratio shows a significant improvement after restoration of sinus rhythm. To illustrate the change in the efficiency of exercise the heart rate was plotted against the  $\text{VO}_2$  at 1 day and 6 months after cardioversion (Figure 7). Resting heart rate was unchanged in 3 and lower in 4 patients at 6 months after cardioversion. Peak heart rate was higher in 4 patients at 6 months. In 5 patients the  $\text{VO}_2$ /heart rate ratio was higher at all stages of exercise 6 months after the cardioversion.

## DISCUSSION

Severe cardiac dysfunction can develop in association with a chronic supraventricular tachycardia. Many studies have shown a significant improvement after abolishment of the arrhythmia or after adequate slowing of the ventricular rate.<sup>5,6,9-18</sup> Most investigations concerned arrhythmias other than AF. In addition, those studying AF after cardioversion had a limited follow-up. This study presents the exact time course of systolic and diastolic hemodynamic changes in relation to changes in exercise tolerance in patients with AF after cardioversion. It shows maximal improvement in ventricular systolic function at 1 month, preceded by restoration of atrial systolic function (and hence normalization of diastolic filling) at 1 week after restoration of sinus rhythm, and obviously also by an acute slowing of the heart rate. Furthermore, it shows that the increase in exercise tolerance assessed from the peak  $\text{VO}_2$  follows the same time course as the improvement in left ventricular ejection fraction.

**Delayed improvement in left ventricular function:** Improvement in ejection fraction and peak  $\text{VO}_2$  occurred during the first month after restoration of sinus rhythm. After 1 month both parameters remained unaltered. The late amelioration is in accordance with previous studies on changes in exercise capacity.<sup>5,6</sup> Because of the frequency of repeated investigations we could show that improvement in cardiac function stabilizes after 1 month. Whether a complete restoration of cardiac function has been attained at that time remains difficult to establish, since a comparison with the clinical situation before AF is impossible. However, one animal study suggests incomplete restoration after recovery from a tachycardiomyopathy induced by pacing.<sup>18</sup>

**Evidence for tachycardia-induced cardiomyopathy in the present study and possible underlying mechanisms:** The dissociation between (sub)acute normalization of the ventricular rate and the atrial kick on the one hand, and the late improvement in left ventricular function and exercise tolerance on the other, suggests that an intrinsic cardiomyopathy plays an important role in AF. This is also suggested by typical changes in heart rate response with exercise early versus late after cardioversion (Figure 7). Compared with normal subjects,

patients with heart failure have a reduced efficiency in exercise at any given  $\text{VO}_2$  (i.e., a high heart rate in relation to the corresponding  $\text{VO}_2$ ), a reduced peak  $\text{VO}_2$  and a lower peak heart rate.<sup>25</sup> Figure 7 shows that 1 day after cardioversion most of our patients exhibited a pattern similar to that found in patients with heart failure, with a significant improvement in  $\text{VO}_2$ /heart rate ratio at 6 months. The same holds for the peak  $\text{VO}_2$ /heart rate ratios presented in Table I. Although our patients did not have overt heart failure, these findings still support the notion that an intrinsic left ventricular cardiomyopathy may be present in the majority of patients with chronic AF.

Tachycardia itself seems to be the most likely trigger leading to this cardiomyopathy. Chronically maintained high ventricular rates (as are intermittently present in patients with AF despite treatment with digoxin and verapamil) may lead to intracellular energy depletion and cell dysfunction that is not necessarily due to ischemia.<sup>11,26</sup> One alternative arrhythmia-related mechanism may be the presence of mitral regurgitation due to the irregular ventricular rate, which may cause ventricular dilatation. However, during AF its hemodynamic importance is supposed to be minimal, in particular if there is no primary mitral valve disease,<sup>27</sup> which was not the case in our patients. Another possible mechanism relates to ischemia, which may be caused by an increased rate-pressure product or by attenuation of myocardial blood flow, both due to tachycardia. Attenuation of blood flow has been suggested in an experimental tachycardia model.<sup>18</sup> However, ischemia may be a pathophysiologic mechanism on its own, especially in patients with significant coronary artery disease. Only 1 of our patients had coronary artery disease; therefore ischemia should be considered a secondary mechanism, at least in this study. Because of the above-mentioned findings, we believe that a high ventricular rate plays a key role in the development of a cardiomyopathy in patients with AF, and that its abolishment may lead to its reversal. The elucidation of specific mechanisms leading to this intrinsic tachycardiomyopathy deserves further attention, since these may become important therapeutic targets in the management of AF. Our results cannot be translated to the general population with chronic AF, especially to patients with significant coronary artery or mitral valve disease, who may have a more marked cardiomyopathy because their underlying disease adds to the negative effects of the chronic tachycardia.

**Study limitations:** Five patients received flecainide after cardioversion. This drug may cause negative inotropic effects, which may have masked further improvement in cardiac function. Nevertheless, all patients showed improvement in cardiac function without an apparent difference between treated and untreated patients. These data cannot determine to what extent withdrawal of the negative inotropic verapamil influenced the course of hemodynamic changes. However, it appears extremely unlikely that the withdrawal of verapamil played a role in the improvement late (at 1 month) after cardioversion. Withdrawal of the positive inotropic digitalis before shock could not have significantly influenced the outcome of the present study; if it had any effect, it

would have been in worsening of the hemodynamic situation.

**Clinical implications:** Our data suggest that chronic AF unassociated with cardiac valve disease may lead to a slowly progressive intrinsic cardiomyopathy. Left ventricular dysfunction and a decreased exercise capacity may develop independent of the loss of the atrial kick and may be related to the chronic tachycardia present during AF. Early cardioversion after establishment of AF seems mandatory to prevent reversible or irreversible myocardial damage. Alternatively, abolishment of the tachycardia by adequate rate control of the AV conduction with drugs or His bundle ablation seems important. How far these treatment modalities are comparable with respect to reversion of tachycardiomyopathy needs further investigation.

1. Braunwald E. Symposium on cardiac arrhythmias: introduction with comments on the hemodynamic significance of atrial systole. *Am J Med* 1964;37:665-669.
2. Morris JJ Jr, Entman M, North WC, Kong Y, McIntosh H. The changes in cardiac output with reversion of atrial fibrillation to sinus rhythm. *Circulation* 1965;31:670-678.
3. Resnekov L. Hemodynamic studies before and after electrical conversion of atrial fibrillation and flutter to sinus rhythm. *Br Heart J* 1967;29:700-708.
4. Khaja F, Parker JO. Hemodynamic effects of cardioversion in chronic atrial fibrillation. *Arch Intern Med* 1972;132:433-440.
5. Lipkin DP, Frenneaux M, Stewart R, Joshi J, Lowe T, McKenna WJ. Delayed improvement in exercise capacity after cardioversion of atrial fibrillation to sinus rhythm. *Br Heart J* 1988;59:572-577.
6. Arwood JE, Myers J, Sullivan M, Forbes S, Sandhu S, Callahan P, Froelicher V. The effect of cardioversion on maximal exercise capacity in patients with chronic atrial fibrillation. *Am Heart J* 1989;118:913-918.
7. Cramer G. Early and late results of conversion of atrial fibrillation with quinidine. *Acta Med Scand* 1968;490:1-102.
8. Killip T, Baer RA. Hemodynamic effects after reversion from atrial fibrillation to sinus rhythm by precordial shock. *J Clin Invest* 1966;45:658-671.
9. Grogan M, Smith HC, Gersh BJ, Wood DL. Left ventricular dysfunction due to atrial fibrillation in patients initially believed to have idiopathic dilated cardiomyopathy. *Am J Cardiol* 1992;69:1570-1573.
10. Heinz G, Siostroznek P, Kreiner G, Gössinger H. Improvement in left ventricular systolic function after successful radiofrequency His bundle ablation for drug refractory, chronic atrial fibrillation and recurrent atrial flutter. *Am J Cardiol* 1992;69:489-492.

11. Packer DL, Bardy GH, Worley SJ, Smith MS, Cobb FR, Coleman RE, Gallagher JJ, German LD. Tachycardia-induced cardiomyopathy: a reversible form of left ventricular dysfunction. *Am J Cardiol* 1986;57:563-570.
12. Lemery R, Brugada P, Chierix E, Wellens HJJ. Reversibility of tachycardia-induced left ventricular dysfunction after closed-chest catheter ablation of the atrioventricular junction for intractable atrial fibrillation. *Am J Cardiol* 1987;60:1406-1408.
13. Peters KG, Kienle MG. Severe cardiomyopathy due to chronic rapidly conducted atrial fibrillation: complete recovery after restoration of sinus rhythm. *Am J Med* 1988;85:242-244.
14. Gillette PC, Wampler DG, Garson A, Zinner A, Ott D, Cooley D. Treatment of atrial automatic tachycardia by ablation procedures. *J Am Coll Cardiol* 1985;6:405-409.
15. McLaran CJ, Gersh BJ, Sugrue DD, Hammill SC, Seward JB, Holmes DR. Tachycardia induced myocardial dysfunction. A reversible problem? *Br Heart J* 1985;53:323-327.
16. Cruz FES, Chierix EC, Smeets JLRM, Atié J, Peres AK, Penn OCKM, Brugada P, Wellens HJJ. Reversibility of tachycardia-induced cardiomyopathy after cure of incessant supraventricular tachycardia. *J Am Coll Cardiol* 1990;16:739-744.
17. Tomita M, Spinale FG, Crawford FA, Zile MR. Changes in left ventricular volume, mass and function during the development and regression of supraventricular tachycardia-induced cardiomyopathy. *Circulation* 1991;83:635-644.
18. Spinale FG, Tanaka R, Crawford FA, Zile MR. Changes in myocardial blood flow during development of and recovery from tachycardia-induced cardiomyopathy. *Circulation* 1992;85:717-729.
19. Evans W, Swann P. Lone auricular fibrillation. *Br Heart J* 1954;16:189-194.
20. Van Gelder IC, Crijns HJ, Van Gilst WH, Verwer R, Lie KI. Prediction of uneventful cardioversion and maintenance of sinus rhythm from direct current electrical cardioversion of chronic atrial fibrillation and flutter. *Am J Cardiol* 1991;68:41-46.
21. Wagner HN, Wake R, Nickoloff E, Natarajan TK. The nuclear stethoscope: a simple device for generation of left ventricular volume curves. *Am J Cardiol* 1977;38:79-82.
22. Berger HJ, Davies RA, Batsford WP, Hoffer PB, Gottschalk A, Zaret BL. Beat-to-beat left ventricular performance assessed from equilibrium cardiac blood pool using a computerized nuclear probe. *Circulation* 1981;63:133-142.
23. Patterson JA, Naughton J, Pietras RJ, Gunnar RM. Treadmill exercise in assessment of functional capacity of patients with cardiac disease. *Am J Cardiol* 1972;30:757-762.
24. Wallenstein S, Zucker CL, Fleiss JL. Some statistical methods useful in circulation research. *Circ Res* 1980;47:1-9.
25. Francis GS. Hemodynamic and neurohumoral responses to dynamic exercise: normal subjects versus patients with heart disease. *Circulation* 1987;76(suppl VI):VI-11-VI-17.
26. Armstrong PW, Stopps TP, Ford SE, De Bold AJ. Rapid ventricular pacing in the dog: pathophysiologic studies of heart failure. *Circulation* 1986;74:1075-1084.
27. Naito M, Dreifus LS, Mardelli TJ, Chen CC, David D, Michelson EL, Marcy V, Morganroth J. Echocardiographic features of atrioventricular and ventriculoatrial conduction. *Am J Cardiol* 1980;46:625-633.

Reprinted from the September 1, issue of **The American Journal of Cardiology**, A Yorke Medical Journal, Published by Cahners Publishing Company, a Division of Reed Publishing USA, 249 West 17th Street, New York, N.Y., 10011. Copyright 1993. All rights reserved. Printed in the U.S.A.