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Left Ventricular Mechanics During Right Ventricular Apical or Left Ventricular-Based Pacing in Patients With Chronic Atrial Fibrillation After Atrioventricular Junction Ablation

Emmanuel N. Simantirakis, MD,* Konstantinos E. Vardakis, MD,* George E. Kochiadakis, MD,* Emmanuel G. Manios, MD,* Nikolaos E. Igoumenidis, MD,* Michele Brignole, MD,† Panos E. Vardas, MD, PHD, FACC*

Crete, Greece; and Lavagna, Italy

OBJECTIVES The aim of the study was to evaluate whether left ventricular (LV) mechanics are better under LV-based pacing than under right ventricular (RV) apical pacing in patients with permanent atrial fibrillation (AF) after atrioventricular junction (AVJ) ablation.

BACKGROUND "Ablate and pace" is an acceptable therapy for drug-refractory AF. However, the RV apical stimulation commonly used seems to interfere with the beneficial hemodynamic effect of regularization of heart rhythm.

METHODS The study included 12 patients (5 men, mean age 62 ± 8.3 years), 6 with impaired and 6 with normal LV systolic function. All of them had a biventricular pacemaker system implanted and underwent atrioventricular node ablation for drug-refractory chronic AF. Using a conductance catheter, we analyzed LV pressure–volume loops during routine coronary angiography in order to evaluate short-term changes in LV mechanics during RV apical and LV-based (LV free wall or biventricular) pacing.

RESULTS Compared with RV pacing, LV-based pacing significantly improved the indexes of LV systolic function (i.e., end-systolic pressure and volume, cardiac index, stroke work, preload recruitable stroke work, maximal rate of rise of LV pressure [dP/dt_{max}], LV ejection fraction, and end-systolic elastance). The LV diastolic filling indexes, end-diastolic pressure and volume, were better during LV-based pacing, whereas LV diastolic function indexes, $-dP/dt_{max}$, passive diastolic chamber stiffness, and time constant of LV isovolumic relaxation showed no clear change.

CONCLUSIONS In the short term, LV-based pacing is superior to RV apical pacing in terms of contractile function and LV filling after AVJ ablation for drug-refractory AF. (J Am Coll Cardiol 2004;43:1013–8) © 2004 by the American College of Cardiology Foundation

Atrioventricular junction (AVJ) ablation and ventricular pacing have been proposed as alternative treatments for patients with chronic atrial fibrillation (AF) in whom the ventricular rate cannot be controlled with drugs. The usual way of pacing in such treatment is from the right ventricular (RV) apex, mainly because it is easy and provides high stability. Right ventricular apical stimulation, however, leads to asynchronous ventricular contraction, which results in a decrease in cardiac performance (1,2). This could counteract the beneficial hemodynamic effect of regularization of heart rhythm and could be the reason why cardiac performance does not improve after "ablate and pace" treatment (3).

In some recent studies, it was found that left ventricular (LV) free wall pacing or biventricular pacing is a useful treatment in patients with severe heart failure, not only for those in sinus rhythm but also for patients with AF after AVJ ablation (4–7). However, the exact mechanism through which this treatment improves cardiac performance in these patients has not yet been studied, nor has the effect of LV-based pacing in patients with normal systolic LV function and an intact His-Purkinje system.

In this short-term study, we evaluated the LV mechanics under RV apical and LV free wall and biventricular pacing after ablation of the AVJ because of drug-refractory AF. We hypothesized that the hemodynamics of LV-based pacing would be superior to those under RV apical pacing.

METHODS

This study included 12 patients (5 men; mean age, 62 ± 8.3 years) who suffered from chronic AF with high ventricular response despite optimal treatment and where a clinical decision for AVJ ablation and pacing was made. In all cases, a biventricular pacing system was successfully implanted at least six weeks before the start of the study and was set to "off". The RV lead was implanted in the right ventricular apex in all cases, as it is the usual implantation site after His ablation. The target site for the LV lead was the mid-lateral cardiac vein. This was achieved in 10 patients, while in the remaining two patients the LV lead was implanted in the posterior cardiac vein.

According to the echocardiogram before the study, six patients had normal LV systolic function (i.e., LV ejection

From the *Cardiology Department, Heraklion University Hospital, Crete, Greece; and the †Arrhythmologic Centre, Department of Cardiology, Ospedali del Tigullio, Lavagna, Italy.

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Abbreviations and Acronyms

AF = atrial fibrillation
AVJ = atrioventricular junction
dP/dt_{max} = maximal rate of rise in left ventricular pressure
EDPVR = end-diastolic pressure–volume relation
LV = left ventricle/ventricular
P_{ED} = end-diastolic pressure
P_{ES} = end-systolic pressure
PRSW = preload recruitable stroke work
RV = right ventricle/ventricular
SW = stroke work
V_{ED} = end-diastolic volume
V_{ES} = end-systolic volume

fraction ≥40%), while in the remaining six it was impaired due to non-ischemic dilated cardiomyopathy. After AVJ ablation, echocardiograms were obtained and analyzed blindly by the study-independent echocardiogram laboratory personnel of our clinic to evaluate mitral valve regurgitation under different pacing modes. Before AVJ ablation, all patients had a native narrow QRS complex, as measured on a 12-lead surface electrocardiogram (50 mm/s speed) (Table 1). There were five hypertensive and three diabetic patients in our group. Medication remained unchanged throughout the study and included warfarin (all patients), angiotensin-converting enzyme inhibitors (10 patients), beta-blockers (9 patients), diuretics (8 patients), digitalis (4 patients), calcium channel blockers (4 patients), insulin (2 patients), oral antidiabetic treatment (1 patient).

All patients provided written, informed consent, and the experimental protocol was approved by the hospital ethics committee.

A short-term evaluation of left ventricular systolic and diastolic function was made 24 h after AVJ ablation, during routine coronary angiography, by pressure–volume relations obtained using the conductance catheter method during RV apical, LV free wall, and biventricular pacing.

The patients were alert, after an overnight fast, and were mildly sedated with diazepam orally on the day of evaluation. A conductance catheter (7F, Millar 572-7, Millar Instruments, Houston, Texas) was placed in the LV. For the production of pressure–volume curves under varying preload conditions, short-term preload reduction was achieved by transient occlusion of the inferior vena cava using a vascular occlusion balloon catheter (8F, STOP-FLOW catheter system, PFM, Cologne, Germany). Pressure–volume loops for final analysis were obtained from a set of cardiac cycles during preload reduction, starting at the beat just before the onset of the LV pressure decline and ending with the nadir of the pressure decline, while any extrasystoles that occurred during the transient preload reduction were excluded from analysis. To eliminate respiratory effects on pressure–volume curves, all measurements were performed during suspended ventilation at end expiration.

In all patients a Swan-Ganz catheter was positioned in the pulmonary artery; cardiac output (thermodilution technique) and mean pulmonary capillary wedge pressure were monitored continuously throughout the study. Pressure–volume loops were derived after 5-min pacing for each of the three pacing types, in random order. The same pacing rate (75 beats/min) was used throughout the study. To ensure synchronous activation during biventricular pacing, the LV-RV delay was programmed to 10 ms, which was the shortest available in the pacemakers we used in our study. We used a special adapter (Leycom CFL 512, Cardiodynamics BV, Zoetermeer, the Netherlands) to digitize and store the signals from the conductance catheter and special software (CONDUCT2000, Cardiodynamics BV) for data analysis.

Ventricular preload was defined as V_{ED}, measured by averaging volumes during the mid-portion of isovolumic contraction for the steady state pressure–volume loop. Systolic pump function parameters included cardiac index, stroke volume, stroke work (SW) (calculated as the integral of the area of the pressure–volume loop and measured automatically by the analysis software), LV ejection fraction,

Table 1. Echocardiographically Calculated Individual Left Ventricular Dimensions, Ejection Fraction, QRS Duration, and Mitral Valve Regurgitation Before AVJ Ablation

ID	Gender	LVEF (%)	LVEDD (mm)	LVESD (mm)	QRS (ms)	MVR
1	F	48	59	54	110	2
2	F	56	45	33	105	1
3	F	52	43	31	100	1
4	M	36	52	39	90	2
5	M	65	49	29	90	2
6	F	52	46	38	100	2
7	F	37	46	41	95	2
8	M	31	64	58	110	2
9	F	38	56	51	105	2
10	M	35	61	55	90	1
11	M	45	55	48	100	2
12	F	34	50	45	110	2

AVJ = atrioventricular junction; F = female; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; M = male; MVR = mitral valve regurgitation score, evaluated using the 1 (mild) to 4 (severe) scale.

end-systolic pressure (P_{ES}), and end-systolic volume (V_{ES}). Contractility change was assessed by four indexes: maximal rate of rise in LV pressure (dP/dt_{max}), slope of dP/dt_{max} to end-diastolic volume relation ($dP/dt_{max} - V_{ED}$), the slope of the SW-V_{ED} relation (PRSW), and the slope of the end-systolic pressure–volume relation line. The end-systolic pressure–volume relation line was determined from the set of pressure–volume points obtained at the end-systole (upper left corner of the pressure–volume loops) of 10 to 15 cardiac cycles before and immediately after mechanical obstruction of the inferior vena cava.

Diastolic performance parameters included V_{ED}, end-diastolic pressure (P_{ED}), negative dP/dt_{max}, end-diastolic pressure–volume relation (EDPVR), passive diastolic chamber stiffness (constant k), and the time constant of LV isovolumic relaxation. End-diastolic pressure–volume relation was determined similarly by the end-diastolic points of variably loaded pressure–volume loops produced by transient caval occlusion. The end-diastolic data were analyzed by exponential regression analysis to obtain the following equation: $P_{ED} = P_{ED}^{V0} \times \exp(k \times V_{ED}^{S})$, where P_{ED}^{V0} (mm Hg) is the LV end-diastolic pressure at zero volume and V_{ED}^{S} (ml) is the simultaneous LV end-diastolic volume. We defined the constant (k) (mm Hg/ml) in the equation as the passive diastolic chamber stiffness constant. The time constant was calculated by regressing LV pressure versus dP/dt during the isovolumic relaxation phase.

Statistics. Summary data are given as mean ± SD. Because of the small number of patients, parametric tests were not performed, because we could not reliably test the assumptions required for a repeated measures analysis of variance. The non-parametric Friedman test was used to compare the distributions of the various parameters of interest under the three pacing types. P values <5% were the criterion for significance. In case of a significant finding, post hoc, Bonferroni adjusted for three comparisons, Wilcoxon tests were performed to pinpoint differences.

RESULTS

Complete pressure–volume loop data sets were available from all patients. An example of pressure–volume loops obtained by transient occlusion of the inferior vena cava during three pacing modes is shown in Figure 1. Table 2 compares the values of systolic and diastolic performance under three types of pacing.

During LV-based pacing, load-dependent and load-independent indexes of contractile function improved in the short term, to a significant degree, compared with RV apical pacing (Table 2). The P_{ES} increased during LV-based pacing while V_{ES} decreased, both significantly, and this was represented by a leftward and upward shift of the end-systolic pressure–volume point in all patients (Fig. 2).

For LV diastolic filling, V_{ED} increased in the short term, whereas the P_{ED} decreased, both significantly. Mean pulmonary capillary wedge pressure and V-wave amplitude

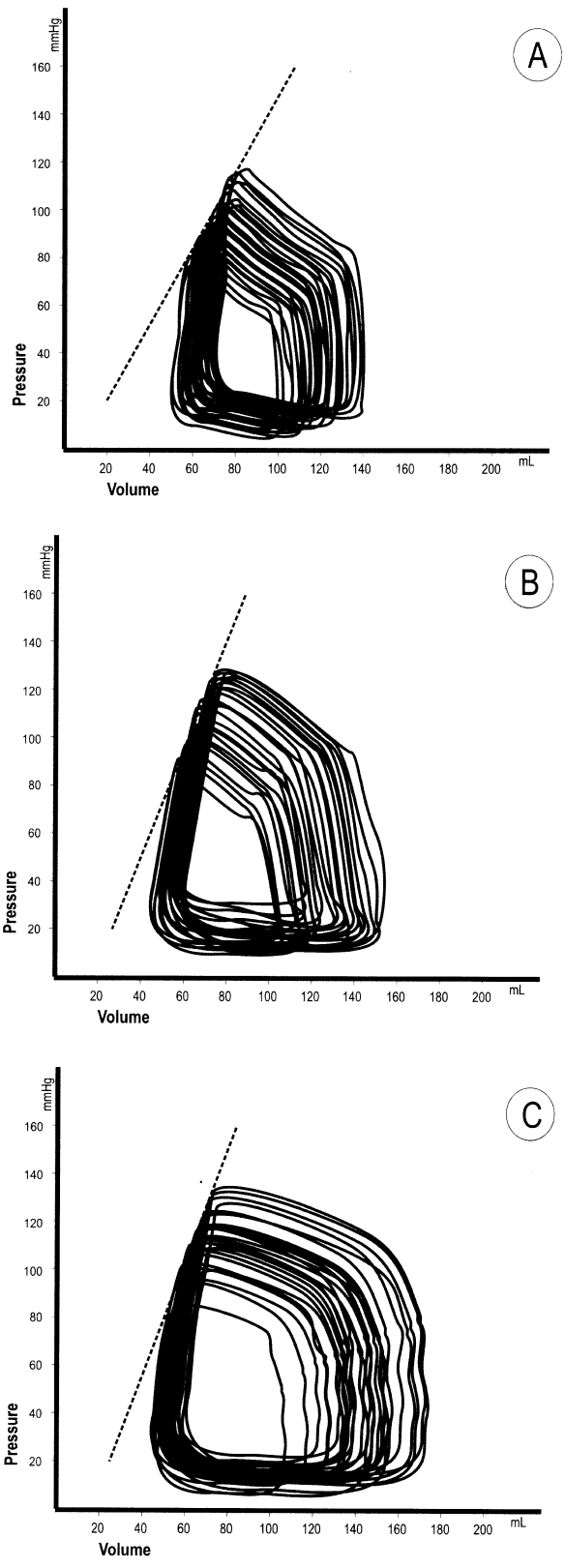

Figure 1. An example of pressure–volume loops obtained by transient occlusion of the inferior vena cava using a vascular occlusion balloon catheter during right ventricular apical **(A)**, left ventricular free wall **(B)**, and biventricular pacing **(C)** in one of our patients with normal left ventricular systolic function. The end-systolic pressure–volume relation line slope clearly increased during left ventricular free wall and biventricular pacing.

Table 2. Comparison of Parameters During Different Types of Pacing*

Parameters (n = 12)	RV Pacing	LV Pacing	BIV Pacing	Friedman p Value†
QRS duration (ms)	202 ± 12	206 ± 10	201 ± 7	0.526
End-systolic volume (ml)	75 ± 4	65 ± 4	63. ± 5	0.002
End-systolic pressure (mm Hg)	100 ± 9	109 ± 8	111 ± 10	0.010
End-diastolic volume (ml)	136 ± 18	149 ± 18	151 ± 18	0.002
End-diastolic pressure (mm Hg)	11 ± 1	9 ± 1	8. ± 1	0.002
Pulmonary capillary wedge pressure (mm Hg)	12 ± 2	9 ± 1	9 ± 1	0.010
V-wave amplitude (mm Hg)	27 ± 5	19 ± 4	19 ± 3	0.002
Stroke index (ml/m^2)	52 ± 4	58 ± 5	59 ± 5	0.008
Cardiac index (l/min·m^2)	3.1 ± 0.2	3.4 ± 0.2	3.4 ± 0.2	0.005
Ejection fraction (%)	40 ± 7	49 ± 8	49 ± 9	0.002
Stroke work (mm Hg·ml)	4,883 ± 382	5,190 ± 292	5,219 ± 320	0.002
Preload recruitable stroke work (mm Hg)	94 ± 9	108 ± 9	109 ± 10	0.002
dP/dt_{max} (mm Hg/s)	1,277 ± 151	1,378 ± 144	1,389 ± 151	0.002
$dP/dt_{max} - V_{ED}$ slope (mm Hg/s·ml^{-1})	75 ± 6	83 ± 5	83 ± 6	0.002
End-systolic elastance (mm Hg/ml)	2.23 ± 0.3	2.73 ± 0.3	2.81 ± 0.5	0.002
Negative dP/dt_{max} (mm Hg/s)	−1,340 ± 85	−1,378 ± 88	−1,382 ± 92	0.115
Passive diastolic LV stiffness (mm Hg/ml)	0.027 ± 0.01	0.026 ± 0.01	0.027 ± 0.01	0.920
Time constant of isovolumic relaxation (ms)	42.3 ± 3.1	42.4 ± 3.6	42.8 ± 3.6	0.882

*Values are expressed as mean ± SD; †According to post-hoc tests, all $p < 0.05$ are because of distinction between right ventricular (RV) pacing and both left ventricular (LV) free wall and biventricular pacing; no significant differences were noted between LV free wall and biventricular pacing.

BIV = biventricular; dP/dt_{max} = maximal rate of rise in LV pressure; V_{ed} = end-diastolic volume.

decreased dramatically during LV free wall or biventricular pacing. In contrast, LV diastolic relaxation indexes did not change during LV-based pacing compared with RV apical pacing. The passive diastolic chamber stiffness did not change significantly, and the EDPVR slope showed no clear change (Table 2). There were no significant differences in any of the measured parameters between LV free wall and biventricular pacing.

Angiography confirmed that all patients had mitral valve regurgitation, which improved dramatically during LV-based pacing compared with RV apical pacing; semiquantitative mitral valve regurgitation score decreased from 2.8 ± 0.3 to 1.2 ± 0.6 (1 to 4 score scale). These findings were in line with previous echocardiographic evaluation under various pacing modes in our patients (Table 3).

DISCUSSION

In this study we showed that LV-based pacing is superior to RV apical pacing in terms of LV contractile function and LV filling in patients with AF who had undergone AVJ ablation. In contrast, there were no significant differences in either systolic or diastolic function between LV free wall and biventricular pacing.

Biventricular or LV free wall pacing has already been examined in patients with AF and the "usual indications" for such pacing (i.e., dilated cardiomyopathy, severe heart failure, and interventricular conduction disturbances). Hemodynamics are improved in the short term during LV or biventricular pacing, regardless of whether the patients are in sinus rhythm or atrial fibrillation (4), while permanent biventricular pacing in such patients improves exercise tolerance (5). In a more recent study of patients with severe heart failure and RV apical pacing at least six months after AVJ ablation (6), upgrade to biventricular pacing was found to improve both LV function and symptoms. Finally, in the Multisite Stimulation in Cardiomyopathies Study (MUSTIC) study of patients with AF (7) biventricular pacing was found to increase exercise tolerance and to decrease the number of hospitalizations compared with VVIR pacing. The results of our study are consistent with those of the above clinical studies and provide the hemodynamic background to explain them.

Of particular importance is the fact that studying patients with AF is advantageous, because the impact of atrioventricular conduction can be eliminated as a complicating factor in the hemodynamic effects of LV-based pacing. Therefore, any changes in cardiac function during different modes of pacing may be attributed to a "pure" effect of pacing on LV function.

Furthermore, we included in our study consecutive patients with main criterion the indication for "ablate and pace" therapy. We selected the RV apex as the site of RV lead implantation as it is the usual position in this kind of therapy, in contrast with other studies where the RV lead site was chosen to be as far from the left lead as possible (7) or to ensure the shortest paced QRS duration (5). This difference, together with the shorter LV-RV delay in our study, could explain the absence of changes in QRS duration during biventricular compared with univentricular pacing from either ventricle in our patients.

Under these circumstances, we found that load-dependent and load-independent LV contractile function indexes were significantly improved in the short term during LV-based pacing compared with RV apical pacing. In contrast, indexes related to LV relaxation did not differ significantly between the three pacing types. However, V_{ED} was significantly higher and P_{ED} significantly lower during LV-based pacing, suggesting that the latter provides better LV diastolic filling. For patients in sinus rhythm with

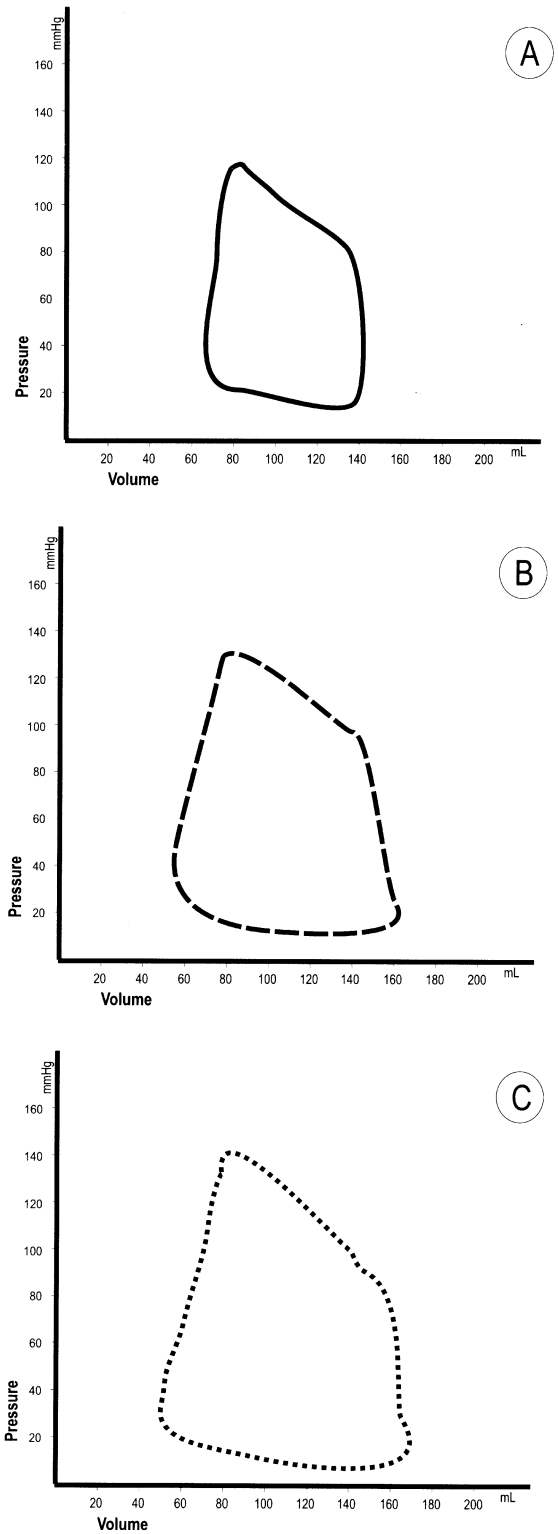

Figure 2. Signal-averaged data of left ventricular pressure–volume loops at baseline (before the beginning of the inflation of vascular occlusion balloon) during right ventricular apical **(A)**, left ventricular free wall **(B)**, and biventricular pacing **(C)** in the patient of Figure 1. Left ventricular–based pacing consistently shifted the end-systolic pressure–volume point upwards and to the left, and the end-diastolic pressure–volume point downwards and to the right. The area of the entire loop increased, indicating that left ventricular free wall and biventricular pacing produce a more effective contraction than does conventional right ventricular apical pacing.

dilated cardiomyopathy and ventricular conduction disturbances, LV-based pacing has been found to improve mainly LV systolic function, causing only minimal changes in LV filling (8). However, in another study that included congestive heart failure patients, with or without left bundle branch block, the hemodynamic improvement by LV pacing was mainly attributed to an improvement in LV filling rather than ventricular systolic resynchronization (9).

Although we describe the short-term improvement in LV diastolic filling during LV-based pacing compared with RV apical pacing for the first time in humans, this has previously been observed in closed-chest dogs (10) and might be attributable to several factors. A significant reduction of mitral valve regurgitation, which comes in agreement with recent studies (11–16), was observed in all our patients and could be considered as one of these factors. Left ventricular–based pacing might improve the competence of mitral valve closure through better timing of the motion of its leaflets and of papillary muscle contraction, both of which are affected by the degree of the ventricular wall synchronous depolarization (10). Ventricular interaction during RV apical and LV-based pacing, reflected by altered septal motion, might also affect V_{ED}. Previous studies have demonstrated that the volume in one ventricle affects the volume in the other (17,18). Therefore, preexcitation of the LV during LV-based pacing could result in an earlier start of LV filling compared with that of the RV. Under these circumstances, LV filling might be greater, as it would take place before the development of external restraint from the stretched pericardium and the increased volume (and pressure) of the RV. A transient inward end-systolic wall motion, continued until early diastole, has previously been described during RV pacing (19). This represents a shortening of late-activated regional LV segments and reflects an area of delayed depolarization that may cause impaired diastolic filling and, hence, a smaller V_{ED}.

In the present study, we also confirm the observation made in animals that the sequence of electrical activation rather than the synchrony is more important to preserve LV function (20). Thus, despite the fact that QRS duration (representative of the degree of synchrony) was not significantly different between RV apical and LV-based pacing, LV function was superior under the latter type of pacing. This could be due to the different number of hypocontractible regions produced by each type of pacing; RV apical pacing has been found to generate a larger number of such regions within the LV wall compared with LV lateral wall pacing, which seems to ensure a more "physiological" activation sequence (20).

Study limitations. In this study, we examined the short-term changes in LV mechanics during RV apical and LV-based pacing in patients with drug-refractory, chronic AF after AVJ ablation by means of pressure–volume relation analysis and hemodynamic evaluation. Under these conditions, no conclusions can be drawn about the long-term effects of permanent LV-based pacing in such patients. The

Table 3. Echocardiographic Evaluation of Mitral Valve Regurgitation, Using the 1 (Mild) to 4 (Severe) Scale, at Various Pacing Modes and Consequent QRS Durations

	RV Pacing		LV Pacing		BiV Pacing	
ID	QRS (ms)*	MVR†	QRS (ms)*	MVR†	QRS (ms)*	MVR†
1	210	2	200	1	205	1
2	200	3	190	1	210	1
3	230	3	220	2	200	1
4	200	2	200	1	190	1
5	200	4	210	2	200	2
6	190	3	220	1	200	1
7	200	3	210	1	200	1
8	210	2	200	1	210	1
9	190	3	200	1	200	1
10	210	4	220	2	200	2
11	190	3	200	1	210	1
12	190	3	200	2	190	2
Mean ± SD	202 ± 12	2.92 ± 0.7	206 ± 10	1.33 ± 0.5	201 ± 7	1.25 ± 0.5

*Measured on a 12-lead surface ECG (50 mm/s speed); †MVR = mitral valve regurgitation score.
BiV = biventricular; LV = left ventricular; RV = right ventricular.

size of the overall population included in our study was rather small. This was mainly because of the limited number of patients that met our inclusion criteria. In addition, our results should be interpreted in light of the hearts not being severely depressed, and it remains to be clarified whether this continues to apply in patients with severe systolic dysfunction.

Conclusions. In terms of LV mechanics, LV-based pacing is superior to RV apical pacing in the short term in patients with permanent AF after AVJ ablation. More studies are required to evaluate the long-term results of these different types of pacing in such patients.

Reprint requests and correspondence: Dr. Panos E. Vardas, Cardiology Department, Heraklion University Hospital, P.O. Box 1352 Stavrakia, Heraklion, Crete, Greece. E-mail: cardio@med.uoc.gr.

REFERENCES

1. Zile MR, Blaustein AS, Shimizu G, Gaasch WH. Right ventricular pacing reduces the rate of left ventricular relaxation and filling. J Am Coll Cardiol 1987;10:702–9.
2. Vanderheyden M, Goethals M, Anguera I, et al. Hemodynamic deterioration following radiofrequency ablation of the atrioventricular conduction system. Pacing Clin Electrophysiol 1997;20:2422–8.
3. 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.
4. Etienne Y, Mansourati J, Gilard M, et al. Evaluation of left ventricular based pacing in patients with congestive heart failure and atrial fibrillation. Am J Cardiol 1999;83:1138–40.
5. Leclercq C, Victor F, Alonso C, et al. Comparative effects of permanent biventricular pacing for refractory heart failure in patients with stable sinus rhythm or chronic atrial fibrillation. Am J Cardiol 2000;85:1154–6.
6. 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.
7. Leclercq C, Walker S, Linde C, et al. Comparative effects of permanent biventricular and right-univentricular pacing in heart failure patients with chronic atrial fibrillation. Eur Heart J 2002;23:1780–7.
8. Kass DA, Chen CH, Curry C, et al. Improved left ventricular mechanics from acute VDD pacing in patients with dilated cardiomyopathy and ventricular conduction delay. Circulation 1999;99:1567–73.
9. Morris-Thurgood JA, Turner MS, Nightingale AK, et al. Pacing in heart failure: improved ventricular interaction in diastole rather than systolic re-synchronization. Europace 2000;2:271–5.
10. Grover M, Glantz SA. Endocardial pacing site affects left ventricular end-diastolic volume and performance in the intact anesthetized dog. Circ Res 1983;53:72–85.
11. Yu CM, Fung WH, Lin H, et al. Predictors of left ventricular reverse remodeling after cardiac resynchronization therapy for heart failure secondary to idiopathic dilated or ischemic cardiomyopathy. Am J Cardiol 2002;91:684–8.
12. Erol-Yilmaz A, Tukkie R, Schrama TA, et al. Reversed remodelling of dilated left sided cardiomyopathy after upgrading from VVIR to VVIR biventricular pacing. Europace 2002;4:445–9.
13. Gras D, Leclercq C, Tang AS, et al. Cardiac resynchronization therapy in advanced heart failure: the multicenter InSync clinical study. Eur J Heart Fail 2002;4:311–20.
14. Yu CM, Chau E, Sanderson JE, et al. Tissue Doppler echocardiographic evidence of reverse remodeling and improved synchronicity by simultaneously delaying regional contraction after biventricular pacing therapy in heart failure. Circulation 2002;105:438–45.
15. Etienne Y, Mansourati J, Touiza A, et al. Evaluation of left ventricular function and mitral regurgitation during left ventricular-based pacing in patients with heart failure. Eur J Heart Fail 2001;3:441–7.
16. Kim WY, Sogaard P, Mortensen PT, et al. Three dimensional echocardiography documents haemodynamic improvement by biventricular pacing in patients with severe heart failure. Heart 2001;85:514–20.
17. Little WL, Reeves RC, Arciniegas J, et al. Mechanism of abnormal interventricular septal motion during delayed left ventricular activation. Circulation 1982;65:1486–91.
18. Bove AA, Santamore WP. Ventricular interdependence. Prog Cardiovasc Dis 1981;23:365–88.
19. Badke FR, Boinay P, Covell JW. Effects of ventricular pacing on regional left ventricular performance in the dog. Am J Physiol 1980;238:H858–67.
20. Prinzen FW, Peschar M. Relation between pacing induced sequence of activation and left ventricular pump function in animals. Pacing Clin Electrophysiol 2002;25:484–98.