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Long-Term Benefits of Biventricular Pacing in Congestive Heart Failure: Results From the MUltisite STimulation In Cardiomyopathy (MUSTIC) Study

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OBJECTIVES The main objective of this study was to assess if the benefits of biventricular (BiV) pacing observed during the crossover phase were sustained over 12 months.

BACKGROUND MUltisite STimulation In Cardiomyopathies (MUSTIC) is a randomized controlled study intended to evaluate the effects of BiV pacing in patients with New York Heart Association (NYHA) class III heart failure and intraventricular conduction delay.

METHODS Of 131 patients included, 42/67 in sinus rhythm (SR) and 33/64 in atrial fibrillation (AF) were followed up longitudinally at 9 and 12 months by 6-min walked distance, peak oxygen uptake (peak VO_2), quality of life by the Minnesota score, NYHA class, echocardiography, and left ventricular ejection fraction by radionuclide technique.

RESULTS At 12 months, all SR and 88% of AF patients were programmed to BiV pacing. Compared with baseline, the 6-min walked distance increased by 20% (SR) ($p = 0.0001$) and 17% (AF) ($p = 0.004$); the peak VO_2 by 11% (SR) and 9% (AF); quality of life improved by 36% (SR) ($p = 0.0001$) and 32% (AF) ($p = 0.002$); NYHA class improved by 25% (SR) ($p = 0.0001$) and 27% (AF) ($p = 0.0001$). The ejection fraction improved by 5% (SR) and 4% (AF). Mitral regurgitation decreased by 45% (SR) and 50% (AF).

CONCLUSIONS The clinical benefits of BiV pacing appeared to be significantly maintained over a 12-month follow-up period. (J Am Coll Cardiol 2002;40:111–8) © 2002 by the American College of Cardiology Foundation

Despite recent advances in drug treatment for heart failure (HF) (1–3), many patients are not sufficiently improved by drug treatment. Previously, these patients could be offered only heart transplantation or a cardiac assist. In recent years, biventricular (BiV) pacing has emerged as a promising therapeutic addition in a subset of these patients.

It is estimated that 30% of patients with severe HF have intraventricular conduction disturbances characterized electrically by wide QRS complexes and characterized mechanically by a discoordinated ventricular contraction and relaxation pattern (4). This electromechanical delay in ventricular activation may be partially overcome by BiV pacing. Acute hemodynamic studies and uncontrolled studies of permanent implants in these patients suggest that BiV pacing significantly improves hemodynamics, symptoms, exercise tolerance, and quality of life (5–8). The MUltisite STimulation In Cardiomyopathies (MUSTIC) study is a randomized trial designed to assess the clinical efficacy of BiV pacing in this subset of HF patients. We have previously reported substantial symptomatic relief from the crossover phase of this study (9,10). These improvements were, however, observed over a three-month period. The long-term effects of BiV pacing remain to be determined. The aim of the present study was to assess the one-year results of the MUSTIC study.

METHODS

Patient selection. All patients had chronic severe HF due to idiopathic or ischemic left ventricular (LV) systolic dysfunction, with an ejection fraction <35% as measured by radionuclides and an LV end-diastolic diameter >60 mm at echocardiography. Patients were stabilized in New York Heart Association (NYHA) functional class III HF for at least one month before inclusion and were receiving opti-

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Abbreviations and Acronyms

ACE	= angiotensin-converting enzyme
AF	= atrial fibrillation
AV	= atrioventricular
BiV	= biventricular
BP	= blood pressure
CT	= cardiothoracic
HF	= heart failure
HR	= heart rate
LV	= left ventricle/ventricular
MUSTIC	= MUltisite STimulation In Cardiomyopathies
NYHA	= New York Heart Association
RV	= right ventricle/ventricular
SR	= sinus rhythm
VVIR	= rate adaptive ventricular inhibited pacing

mized drug treatment that included at least diuretics and angiotensin-converting enzyme (ACE) inhibitors at the maximum tolerated dose. The 6-min walked distance had to <450 m. Patients with sinus rhythm (SR) did not have a conventional indication for pacing and a QRS duration >150 ms. The atrial fibrillation (AF) patients had persistent (>3 months) AF requiring permanent ventricular pacing due to slow ventricular rate, either spontaneous or induced by atrioventricular (AV) node junction ablation. For these, a paced QRS duration >200 ms during right ventricular (RV) pacing was required. Exclusion criteria and pacemaker implantation technique have been described previously (9,10).

Study design. This European multicenter trial involved 16 centers in six countries (9). The study was approved by the local ethics committee of all centers, and all patients gave their written informed consent before inclusion. Inclusion began in March 1998 and was completed 15 months later. The study began with a single-blind crossover comparison of three months each of BiV pacing and inactive pacing (SR group) or BiV compared with right univentricular rate adaptive ventricular inhibited pacing (VVIR) pacing (AF group) followed by a longitudinal follow-up. At the end of the crossover phase, patients were asked which of the three-month periods they preferred and were programmed accordingly. If no preference was expressed, the programming was made according to the physician's judgment. Thereafter, the patients were followed up every three months. This article is a 12-month intra-patient long-term comparison for patients programmed to BiV pacing at the end of the crossover phase. Thus, baseline and 12-month follow-up parameters are compared. Data concerning the crossover phase in BiV pacing at six months and the follow-up phase at nine months are reported for descriptive purposes.

Evaluated parameters. Patients were evaluated with the 6-min walked distance, the peak VO_2 by cardio-pulmonary exercise test, quality of life, NYHA class, systolic and diastolic blood pressure (BP), body-weight, 12-lead surface electrocardiogram (ECG), 24-h Holter monitoring and Doppler echocardiography. Heart rate (HR) was calculated from the ECG, and the systolic and diastolic BPs were measured by a cuff manometer after 10 min of supine rest. The QRS duration was measured during BiV pacing and during spontaneous rhythm (SR group) or RV-VVIR with a basic rate of 70 beats/min (AF group). The LV ejection fraction by ^{99m}Tc and the cardiothoracic (CT) ratio by chest X-ray were calculated at baseline and after 12 months.

The 6-min walk test was carried out according to Guyatt's recommendation (11). Quality of life was evaluated with the Minnesota-Living with Heart Failure questionnaire (12). The higher the score, the poorer the quality of life. Hospitalizations, mortality, and pacemaker complications were monitored at each follow-up and classified by an independent safety committee.

Statistical analysis. Values are presented as mean ± SD. The calculation of the sample size based solely on the crossover phase of the study has previously been described (9). All statistical tests are intra-patient comparisons independently performed for each group between parameters evaluated at 12 months compared with randomization (SR group) or baseline (AF group). To correct for incomplete follow-up data, the values in each individual at the BiV crossover phase at months 6, 9, and 12 were always related to the same patients at baseline. The Student paired *t* test was performed for paired comparisons. In order to adjust for multiple analysis comparisons, the Bonferroni method has been applied to the four main efficacy criteria defined in the study protocol (6-min walked distance, peak VO_2, quality-of-life score, and NYHA class). Therefore, the threshold of significance was set at 0.0125 for individual comparisons to comply with a global significance level of 0.05.

All analyses for mortality and hospitalizations were based on the intention-to-treat principle, thus encompassing the total of 131 patients in the SR and AF groups included.

RESULTS

The study profile is shown in Figure 1. A total of 131 patients consented to participate in the study. Eighty-seven patients completed both crossover phases: 48 in the SR-group and 41 in the AF group. At that time, significantly more patients in both groups preferred BiV pacing: 41/48 or 85% in the SR group ($p < 0.001$) and 35/41 or 85% ($p < 0.001$) in the AF group.

In the SR group, five additional patients were programmed to BiV pacing according to the physician's judgment, whereas two preferred the period corresponding to VVI 40, and another was erroneously programmed to the VVI 40 mode and programmed correctly back to BiV pacing at the nine-month follow-up.

In the AF group, four patients preferred the period corresponding to RV-VVIR and were programmed accordingly. Thus, at the 9- and 12-month follow-ups, all patients in

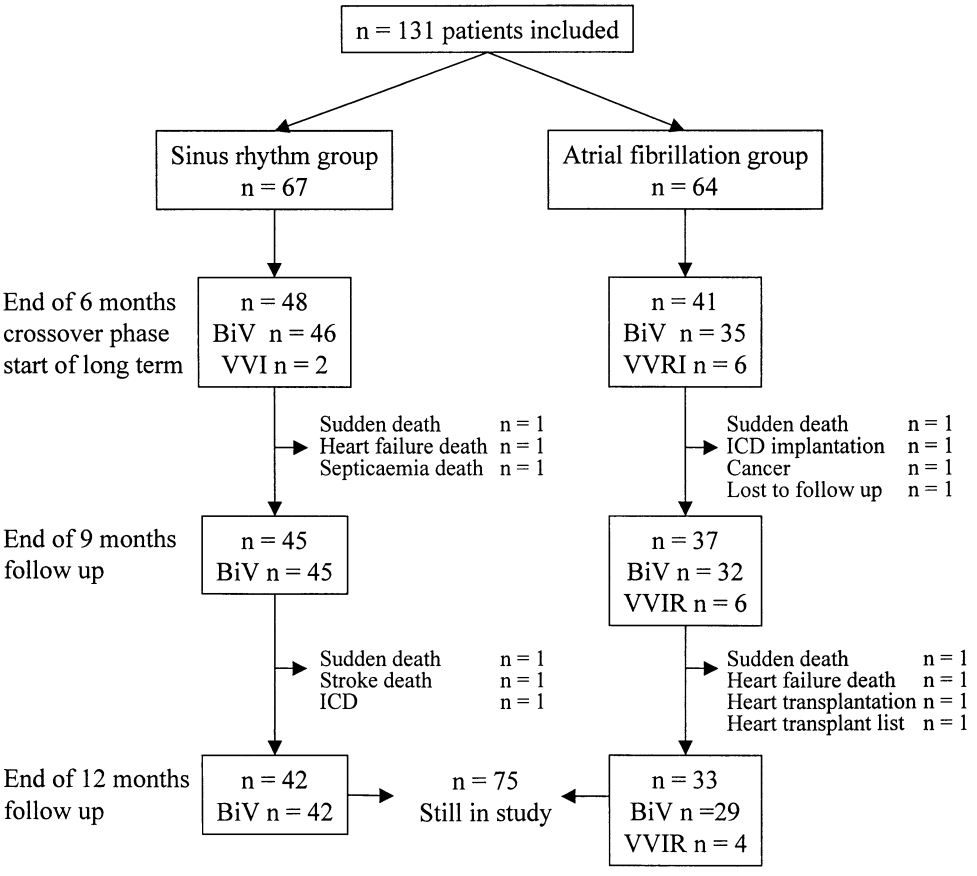

Figure 1. Study profile. Number of patients active in the study at each follow-up between inclusion and the 12 months in the sinus rhythm (**left side**) and atrial fibrillation (**right side**) groups. The reasons for study exits during the crossover phase of the study have been published elsewhere (9). BiV = biventricular; ICD = implantable cardioverter defibrillator; VVIR = rate adaptive ventricular inhibited pacing.

SR and 86 (88%) in the AF group were programmed to BiV pacing. The reason for reprogramming was deterioration in the heart failure condition.

Pacemaker performance. One case of transient elevation of LV threshold was seen. No other complications related to the LV lead were found between the 6- and 12-month follow-up. Thus, at the end of the 12-month follow-up, all LV leads were fully functional.

Clinical characteristics of patients at the time of inclusion. The clinical characteristics at the time of inclusion are presented in Table 1. Sixty-three percent of the patients in the AF group had undergone a previous AV junction ablation. Moreover, 36% of AF patients had a previous pacemaker before entering the study.

QRS duration over time. The QRS duration during BiV pacing and during spontaneous rhythm (SR group) or right ventricular pacing (VVIR) with a basic rate of 70 beats/min (AF group) is given in Figure 2. As evidence that BiV pacing had been delivered, a significant decrease in QRS width of 8% to 14% in the SR group and 14% to 24% in the AF group was seen at all times of observation. No signs of an incremental decrease by time were observed in either of the two groups. The duration of the spontaneous QRS remained unchanged over time.

Six-min walked distance, peak VO_2, quality of life, and NYHA class. The results of the 6-min walked distance, peak VO_2, and quality of life are given in Table 2. To correct for incomplete follow-up data, the values in each individual at the BiV crossover phase at months 6, 9, and 12 were always compared with the same number of patients at baseline.

In the SR group by the 12-month follow-up, a mean improvement in 6-min walked distance of 70 meters, or 20% compared with baseline, was found with highly statistically significant improvements between baseline and the 6-, 9-, and 12-month follow-ups. There was, however, no evidence of an incremental improvement over the 12-month follow-up period. In the AF group, the mean improvement at 12 months was 55 meters or 17%.

The peak VO_2 at 12 months had increased by 1.7 ml/min/kg or 11% (p = NS) in the SR group and 1.1 ml/kg/min or 9% (p = NS) in the AF group compared with baseline. At the same time, there was mean reduction in the Minnesota score of 17 points or 36% in the SR group and of 14 points or 32% in the AF group. The NYHA class improved by 0.7 in the SR group and 0.8 in the AF group. Thus, maintained benefits without incremental change were observed in the 12-month follow-up.

Table 1. Baseline Characteristics

Demography and Clinical Characteristics	Sinus Rhythm Group (n = 67)	Atrial Fibrillation Group (n = 64)
Mean age (yrs)	63 ± 10	65 ± 9
Gender (male/female)	50 (75%)/17 (25%)	52 (81%)/12 (19%)
NYHA III	67 (100%)	64 (100%)
Ischemic/Nonischemic	25 (37%)/42 (63%)	17 (27%)/47 (73%)
Drug treatment		
Ace inhibitor or AII blocker	64 (96%)	64 (100%)
Diuretics	63 (94%)	63 (98%)
Cardiac glycoside	32 (48%)	36 (57%)
Beta-blockers	19 (28%)	14 (22%)
Spironolactone	15 (22%)	10 (15%)
Amiodarone	21 (31%)	14 (22%)
Mean measurements		
LVEF (%)	22 ± 8	26 ± 10
LVEDD (mm)	73 ± 10	68 ± 7
MR area (cm^2)	7.4 ± 6.8	10.5 ± 13.7
DFT (ms)	376 ± 134	349 ± 95
ECG measurements		
Heart rate (beats/min)	75 ± 13	74 ± 5
QRS duration (ms)	176 ± 19	206 ± 19
LBBB	58 (87%)	NA
PR interval (ms)	215 ± 43	NA
6-min walked distance (m)	320 ± 97	328 ± 80
Peak VO_2 (ml/min/kg)	13.6 ± 3.8	12.7 ± 3.9
SBP (mm Hg)	117 ± 14	120 ± 21
DBP (mm Hg)	74 ± 9	72 ± 12
Weight (kg)	79 ± 19	76 ± 14

DBP = diastolic blood pressure; DFT = diastolic filling time; LBBB = left bundle branch block; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; NA = not applicable; SBP = systolic blood pressure.

Systolic and diastolic BP, body weight, and HR. For both groups of patients, the systolic and diastolic BP and pulse pressure remained unchanged over time. Body weight did not change. The HR decreased in the SR group from 75 ± 13 at baseline to 71 ± 12 at 6 months, 68 ± 11 at 9 months, and 70 ± 10 at 12 months, with no statistically progressive change observed over time.

Echocardiographic data, ejection fraction, and CT ratio. The LV echocardiographic data over time is presented in Table 3. For the SR group, improvements in LV dimensions had already been observed after the crossover phase in BiV pacing, with sustained effects over time. Mitral regurgitation had decreased markedly by 24% at 6 months, by 39% at 9 months, and by 45% at 12 months. Diastolic filling

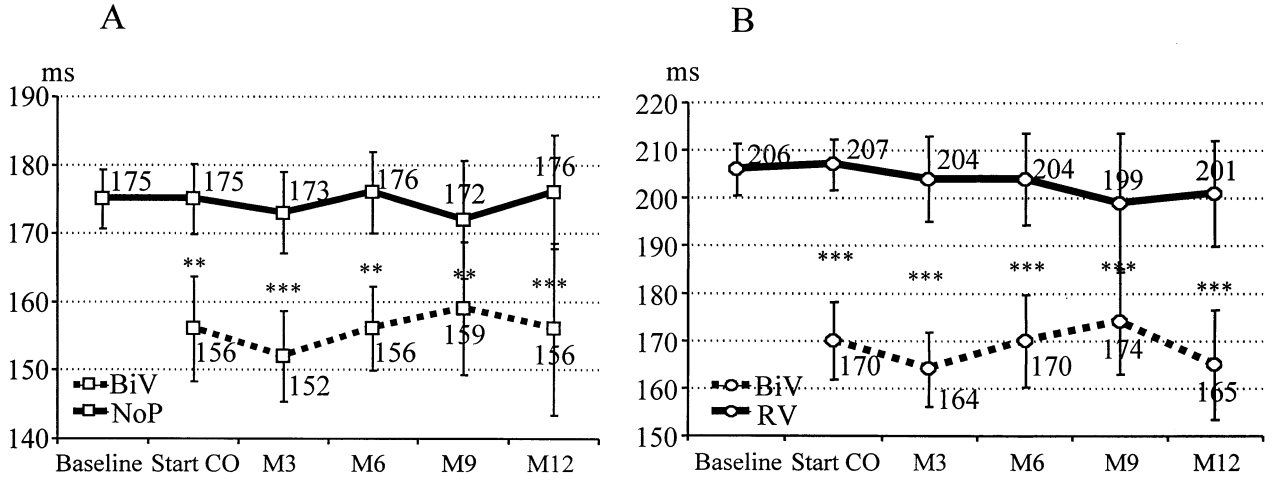

Figure 2. The QRS duration over time. **(A) Solid lines** represent values during spontaneous rhythm and **dotted lines** those during biventricular (BiV) pacing in the sinus rhythm group. **(B)** For the atrial fibrillation group, **solid lines** represent values during right ventricular pacing at a rate of 70 beats/min and **dotted lines** those during BiV pacing. CO = cardiac output; M3 = three months; M6 = six months; M9 = nine months; M12 = 12 months; NoP = inactive pacing; RV = right ventricle.

Table 2. The Evolution of the 6-min Walked Distance, Peak VO_2, QoL and NYHA Class at M6, M9 and M12

	Sinus Rhythm Group			
	Randomization	**M6**	**M9**	**M12**
6-min walked distance (m)	354 ± 92 (n = 43)	396 ± 104 (n = 43)		
	346 ± 96 (n = 38)		411 ± 113 (n = 38)	
	348 ± 98 (n = 38)			418 ± 112 (n = 38)
				p = 0.0001
Peak VO_2 (ml/kg/min)	14.2 ± 4.6 (n = 41)	15.5 ± 4.6 (n = 41)	NA	
	14.9 ± 4.7 (n = 32)			16.6 ± 3.6 (n = 32)
				p = NS
QoL score (0–105)	47 ± 22 (n = 46)	31 ± 22 (n = 46)		
	45 ± 21 (n = 41)		30 ± 20 (n = 41)	
	47 ± 23 (n = 41)			30 ± 22 (n = 41)
				p = 0.0001
NYHA (I–IV)	2.8 ± 0.4 (n = 46)	2.1 ± 0.5 (n = 46)		
	2.8 ± 0.4 (n = 40)		2.1 ± 0.4 (n = 40)	
	2.8 ± 0.4 (n = 41)			2.1 ± 0.5 (n = 41)
				p = 0.0001
	Atrial Fibrillation Group			
	Randomization	**M6**	**M9**	**M12**
6-min walked distance (m)	338 ± 87 (n = 37)	363 ± 101 (n = 37)		
	320 ± 82 (n = 27)		368 ± 97 (n = 27)	
	315 ± 80 (n = 27)			370 ± 87 (n = 27)
				p = 0.004
Peak VO_2 (ml/kg/min)	12.8 ± 4.7 (n = 37)	14.3 ± 4.1 (n = 37)	NA	
	12.8 ± 3.6 (n = 24)			13.9 ± 3.5 (n = 24)
				p = NS
QoL score (0–105)	44 ± 22 (n = 40)	34 ± 20 (n = 40)		
	45 ± 22 (n = 31)		34 ± 22 (n = 31)	
	45 ± 23 (n = 28)			31 ± 17 (n = 28)
				p = 0.002
NYHA (I–IV)	3.0 ± 0 (n = 38)	2.3 ± 0.5 (n = 38)		
	3.0 ± 0 (n = 29)		2.1 ± 0.4 (n = 29)	
	3.0 ± 0 (n = 28)			2.2 ± 0.5 (n ± 28)
				p = 0.0001

M6 = six months; M9 = nine months; M12 = 12 months; NA = not applicable; NS = nonsignificant (p > 0.0125 Bonferroni adjustment); NYHA = New York Heart Association; QoL = quality of life.

time increased by 13% to 27%. For the AF group, no changes in LV dimensions were observed. Mitral regurgitation decreased by 35% at 9 months and 50% by 12 months compared with baseline values.

Mortality. The intention-to-treat analysis of the one-year survival rate in the global population of 131 patients was 83% (85% in SR and 81% in AF). Of 23 deaths, nine were sudden (SR, n = 5; AF, n = 4). There were nine deaths from HF (SR, n = 4; AF, n = 5): two from stroke (1 in each group), and three from non-cardiovascular causes (2 from cancer and 1 from infection). No deaths were attributed to the pacemaker system.

Hospitalizations for HF. To compensate for the twice-as-long time spent in BiV pacing compared with VVI 40 (SR group) or RV-VVIR pacing (AF group) in the study, we calculated the individual monthly rate of HF-related hospitalizations (Table 4). During this 12-month follow-up, there were seven times fewer hospitalizations for HF during BiV pacing in the SR group and four times fewer in the AF group.

DISCUSSION

This is the first study to show favorable one-year results in exercise tolerance and quality of life by BiV pacing in patients with severe HF and intraventricular conduction disturbances. In addition, improvements in LV function and a decrease in HF-related hospitalizations were found. A placebo effect of pacemaker implantation has previously been shown in patients treated with AV synchronous pacing for hypertrophic obstructive cardiomyopathy (13). Such a placebo effect wanes over the course of time. Therefore, the present sustained benefits can be presumed to be actual treatment effects of BiV pacing.

Patient material. The patients in this study were selected for having stable NYHA III HF despite optimized medical treatment. This implied the use of ACE inhibitors or equivalents at an optimal dose but not beta-blockers or aldosterone antagonists, because the results from the beta-blocker trials (14) and the Randomized Aldactone Evaluation Study (RALES) (3) trial were not available at the time

Table 3. Echocardiographic Data and Ejection Fraction for the Sinus Rhythm Group and the Atrial Fibrillation Group at M6, M9 and M12

	Sinus Rhythm Group			
	Randomization	**M6**	**M9**	**M12**
LVEDD (mm)	74 ± 9 (n = 46)	69 ± 11 (n = 46)		
	73 ± 9 (n = 42)		68 ± 10 (n = 42)	
	74 ± 10 (n = 40)			67 ± 12 (n = 40)
LVESD (mm)	64 ± 10 (n = 46)	58 ± 12 (n = 46)		
	64 ± 10 (n = 42)		57 ± 11 (n = 42)	
	63 ± 10 (n = 40)			58 ± 12 (n = 40)
MR area (cm^2)	7.4 ± 6.8 (n = 44)	5.6 ± 8.3 (n = 44)		
	8.0 ± 7.8 (n = 39)		4.9 ± 4.6 (n = 39)	
	7.8 ± 7.8 (n = 39)			4.3 ± 4.0 (n = 39)
DFT (ms)	376 ± 134 (n = 44)	430 ± 137 (n = 44)		
	372 ± 132 (n = 42)		471 ± 154 (n = 42)	
	375 ± 136 (n = 40)			425 ± 129 (n = 40)
LVEF (%) radionuclides		NA		
			NA	
	24.5 ± 7.8 (n = 26)			30.0 ± 12.1 (n = 26)
CT ratio	0.60 ± 0.07 (n = 41)	0.60 ± 0.07 (n = 41)		
	0.59 ± 0.07 (n = 34)		0.56 ± 0.06 (n = 34)	
	0.60 ± 0.07 (n = 36)			0.56 ± 0.06 (n = 36)
	Atrial Fibrillation Group			
	Randomization	**M6**	**M9**	**M12**
LVEDD (mm)		NA		
	69 ± 8 (n = 28)		68 ± 10 (n = 28)	
	70 ± 9 (n = 28)			68 ± 8 (n = 28)
LVESD (mm)		NA		
	59 ± 9 (n = 28)		56 ± 11 (n = 28)	
	60 ± 10 (n = 28)			58 ± 9 (n = 28)
MR area (cm^2)		NA		
	10.2 ± 13.7 (n = 27)		6.4 ± 6.2 (n = 27)	
	10.8 ± 13.7 (n = 26)			5.4 ± 3.9 (n = 26)
DFT (ms)		NA		
	349 ± 95 (n = 27)		357 ± 133 (n = 27)	
	346 ± 99 (n = 24)			405 ± 143 (n = 24)
LVEF (%) radionuclides		NA		
			NA	
	26.7 ± 6.9 (n = 19)			30.4 ± 7.8 (n = 19)
CT ratio	0.61 ± 0.07 (n = 36)	0.60 ± 0.07 (n = 36)		
	0.61 ± 0.07 (n = 26)		0.60 ± 0.06 (n = 26)	
	0.61 ± 0.07 (n = 27)			0.60 ± 0.07 (n = 27)

CT = cardiothoracic; DFT = diastolic filling time; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end systolic diameter; MR = mitral regurgitation; M6 = six months; M9 = nine months; M12 = 12 months; NA = not applicable.

the study was planned. The predominant cause of HF in the MUSTIC trial was dilated cardiomyopathy, contrasting with what has been reported in the drug trials but in agreement with other studies on BiV pacing (5,8,15). The mean Minnesota quality-of-life scores were 51 ± 20 and 46 ± 22 in the SR and AF groups, respectively, corresponding with what can be expected in NYHA class III patients (16).

Table 4. Hospitalizations for Heart Failure

	SR Group		AF Group	
Pacing Mode	**VVI40**	**BiV**	**RV-VVIR 70**	**BiV**
Hospitalization (no.)	22	11	28	9
Total time spent in pacing mode (no. of months)	156	475	198	218
Hospitalization per month	0.14	0.02	0.14	0.04

No statistical analysis performed.
AF = atrial fibrillation; BiV = biventricular; RV = right ventricle; SR = sinus rhythm; VVI40 = ventricular inhibited pacing at a rate of 40 bpm; VVIR = rate adapted ventricular inhibited pacing.

Effect of therapy delivery on electrical and mechanical remodeling. As evidence that pacing therapy had been delivered and was partly successful in reducing the intraventricular conduction delay, the QRS duration during BiV pacing decreased significantly in both groups of patients. However, in concordance with previous observations, no signs of a progressive decrease in the spontaneous QRS duration were seen, indicating a lack of electrical remodeling by BiV pacing (17). By contrast, the LV ejection fraction increased in both patient groups; mitral regurgitation de-

creased, and in the SR group, LV dimensions were reduced, indicating a potential mechanical reverse remodeling by BiV pacing. Gras et al. (15) previously reported a 5% to 10% increase in ejection fraction as measured by echocardiographic technique in an uncontrolled study. Reduction in LV dimensions by BiV pacing was recently reported by Lau et al. (18) in a small patient material. This is the first study to show improvements in LV global ejection fraction by BiV pacing using a reliable technique. One might speculate that an increased systolic function could be hazardous because studies of drugs with inotropic effect have been linked to a worse survival (19). An increased contractility could be explained by an increase in sympathetic nerve activity. However, in this study of an electromechanical intervention, the significant decrease in HR as by the normal sinus node during BiV pacing could be interpreted as an indirect sign of a lesser activation of the sympathetic nervous system. Our study results yield indices suggesting that BiV pacing improves contractility without increasing sympathetic nerve activity.

Long-term clinical improvements. The magnitude of improvements in exercise tolerance and quality of life by BiV pacing in addition to ACE inhibitors in the present study was greater than what has previously been observed in drug trials with similar patients studied over a similar duration (16,20). Importantly, these benefits were maintained over a 12-month follow-up and reinforced in the AF group. In general, however, the results for patients with AF were less impressive. Overall, the magnitude of improvements agree with the one-year results from a similar study (21). Moreover, the recently reported Multicentre InSync Randomized Clinical Evaluation trial—a six-month parallel study comparing BiV pacing with conventional drug treatment (22)—reported improvements of similar degree in similar patients, however, with a QRS width criterion less strict than ours.

Hospitalizations and mortality. Costs for hospital care have been found to constitute the major cost for society in HF management (23). A pilot study has indicated a lesser need for hospital care after the implantation of BiV pacing (24). This observation was confirmed in the present study in which we found seven times less need for hospital care for HF in the SR group and four times less in the AF group compared with the crossover phase in inactive or RV-VVIR pacing. The overall one-year survival rate was 85%, corresponding to what has recently been reported in drug trials for similar patients (3). The present study was, however, not designed as a mortality study, and the question of whether BiV pacing favorably affects morbidity and mortality remains to be answered by larger ongoing studies such as the Controlled Resynchronization in Heart Failure study and the Comparison of Medical Therapy Pacing and Defibrillation in Chronic Heart Failure trials (25).

Study limitations. The calculation of sample size was made for the crossover phase and not for the long-term follow-up of the study. Although the echocardiography results thus have to be interpreted with caution, they all indicate a long-term benefit of BiV pacing. Ongoing studies, adequately powered to detect long-term differences, will add the final proof of long-term benefits by this treatment modality.

Conclusions. This is the first study to report favorable one-year results of BiV pacing in patients with severe HF and major intraventricular conduction disturbances in either SR or AF. We found a significant sustained benefit in exercise tolerance quality of life from BiV over a 12-month follow-up period. A reduction in mitral regurgitation and an improvement in ejection fraction were also observed. Hospitalizations for HF were fewer during BiV pacing. Whether these favorable results translate into an improved survival remains to be established.

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