Pacing-induced mitral regurgitation treated by cardiac resynchronisation therapy. Evaluation by exercise echocardiography

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MADARIC J, VANDERHEYDEN M, GOETHALS M, MALACKY T, BARTUNEK J. **Pacing-induced mitral regurgitation treated by cardiac resynchronisation therapy. Evaluation by exercise echocardiography.** Cardiol 2006;15(2):113–116

In patients with functional mitral regurgitation and left ventricular dysfunction, exercise-induced mitral regurgitation can identify patients at high risk of poor clinical outcome. Cardiac resynchronisation therapy is associated with improvement in mitral regurgitation, exercise tolerance and left ventricular function, leading to improved survival in patients with congestive heart failure and cardiac dyssynchrony. However, the effects of cardiac resynchronisation therapy on dynamic mitral regurgitation in relation to resynchronisation and left ventricular remodelling are not known.

The authors refer to the case of a 63 year-old woman with mitral regurgitation induced by right ventricular apical pacing, successfully treated by cardiac resynchronisation therapy. Described are the effects of cardiac resynchronisation therapy on left ventricular synchrony and dynamic mitral regurgitation assessed by exercise echocardiography including tissue Doppler imaging, three days and one year after cardiac resynchronisation therapy.

The cardiac resynchronisation therapy was associated with acute improvement in right ventricular apical pacing induced mitral regurgitation at rest, but did not attenuate exercise-induced mitral regurgitation soon after cardiac resynchronisation therapy. In contrast, the long-term effect of cardiac resynchronisation therapy resulted in the left ventricular reverse remodelling preventing both the recurrence of left ventricular dyssynchrony during exercise, as well as exercise-induced mitral regurgitation. Reduction of dynamic mitral regurgitation could represent a mechanism contributing to beneficial effects of cardiac resynchronisation therapy on clinical outcomes of patients with congestive heart failure.

Key words: Cardiac resynchronisation therapy – Right ventricular apical pacing – Congestive heart failure – Mitral regurgitation – Echocardiography – Remodelling

MAĎARIČ J, VANDERHEYDEN M, GOETHALS M, MALACKÝ T, BARTÚNEK J. **Pravokomorovou stimuláciou indukovaná mitrálna regurgitácia liečená resynchronizáciou srdca. Hodnotenie záťažovou echokardiografiou.** Cardiol 2006;15(2):113–116

U pacientov s funkčnou mitrálnou regurgitáciou a dysfunkciou ľavej komory je záťažou indukovaná mitrálna regurgitácia nepriaznivým prognostickým znakom. Kardiálna resynchronizačná liečba sa spája so zlepšením mitrálnej regurgitácie, záťažovej tolerancie a funkcie ľavej komory, ktoré zlepšujú dĺžku prežívania pacientov s chronickým srdcovým zlyhávaním a kardiálnou dyssynchróniou. Napriek tomu efekt kardiálnej resynchronizačnej liečby na dynamickú mitrálnu regurgitáciu vo vzťahu k resynchronizácii a remodelácii ľavej komory nie je objasnený.

Autori opisujú prípad 63-ročnej ženy s mitrálnu regurgitáciou indukovanou pravokomorovou apikálnou stimuláciou, úspešne liečenú kardiálnou resynchronizačnou liečbou. Opisujú efekt tejto liečby na synchróniu ľavej komory a dynamickú mitrálnu regurgitáciu, stanovený záťažovou echokardiografiou spolu s tkanivovým dopplerovským vyšetrením, tri dni po a jeden rok po implantácii biventrikulárneho stimulátora.

Kardiálna resynchronizačná liečba sa spájala s akútnym zlepšením mitrálnej regurgitácie v pokoji, avšak nie počas záťaže, v skorom období po kardiálnej resynchronizačnej liečbe. Dlhodobejší efekt kardiálnej resynchronizačnej liečby viedol k reverznej remodelácii ľavej komory, ktorá bránila indukcii opätovnej dyssynchrónie počas záťaže, takisto ako záťažou indukovanej mitrálnej regurgitácie. Redukcia dynamickej mitrálnej regurgitácie môže predstavovať jeden z mechanizmov, ktorý prispieva k pozitívnemu efektu kardiálnej resynchronizačnej liečby na klinické zlepšenie pacientov s chronickým srdcovým zlyhávaním.

Kľúčové slová: kardiálna resynchronizačná liečba – pravokomorová stimulácia – srdcové zlyhávanie – mitrálna regurgitácia – echokardiografia – remodelácia

Conventional right ventricle (RV) apical pacing may have adverse long-term effects on cardiac electromechanical dyssynchrony, left ventricular (LV) remodelling, LV function, and mitral valve regurgitation (MR) (1). In addition, in patients (pts) with functional MR and LV dysfunction, exercise-induced MR can identify pts at high risk for poor clinical outcome (2). Correcting electrical activation with biventricular (BiV) pacing has potential to improve cardiac function and extent of MR in pts with RV apical pacing and congestive heart failure (CHF) (3 – 5). However, the effect of cardiac resynchronisation therapy (CRT) on dynamic MR is not completely understood.

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Case Report

We describe the case of a 63 year-old woman referred to our centre due to progression of CHF. She had a history of permanent idiopathic atrial fibrillation with fast

ventricular rate resistant to medicaments. She was treated in 1986 by radiofrequency ablation of the atrioventricular conduction system, and a RV apical pacemaker implantation programmed in VVI-R mode. There was no LV dysfunction or mitral valve regurgitation, or any known structural heart disease present at the time of ablation procedure. At current admission, clinical examination revealed 3/6 systolic murmur, discreet bilateral lung rarels; the chest X-ray revealing the signs of discreet lung congestion. No oedemas of lower extremities were present. Systemic blood pressure was 100/70 mmHg.

A two-dimensional transthoracic and transoesophageal echocardiogram showed LV end-diastolic diameter of 49 mm and end-systolic diameter of 39 mm in parallel with decreased LV systolic function [ejection fraction (EF) 39%, Simpson biplane]. Left atrium (LA) was dilated up to 48 mm. Mitral valve was morphologically normal with leaflets malcoaptation due to moderately dilated mitral annulus. At rest, the slightly eccentric regurgitant jet was visualised, graded as moderate MR [effective regurgitant orifice (ERO) 0.19 cm^2, regurgitant volume (Reg Vol) 35ml]. Right-sided study confirmed tricuspid regurgitation (TR) grade 1+ with right ventricular pressure (RVP) 35 mmHg at rest (**Figure 1, 2**). The symptom-limited exercise echocardiography using the semi-supine bicycle exercise (initial workload of 25 Watts for 2 minutes followed by 10-Watts increment each minute) demonstrated an increase in MR with an increase in ERO to 0.25 cm^2 and Reg Vol 39 ml associated with an increase in TR up to grade 2+ and RVP of 50 mmHg. Duration of exercise was 5 min, maximal achieved workload 55 Watts. Pulsed-wave tissue Doppler imaging (TDI) was used to assess LV dyssynchrony at rest and, at peak exercise, from measurements of regional electromechanical coupling times in basal segments of the left ventricle as described previously (6). The TDI showed borderline significant LV dyssynchrony at rest with LV intraventricular delay of 46 ms, with worsening during exercise to 68 ms. There was no significant coronary artery stenosis detected by angiography. Based on clinical presentation and results of rest and exercise Doppler echocardiography study, patients underwent cardiac resynchronisation therapy (CRT) with upgrading of RV pacing to BiV pacemaker instead of alternatively considered surgical mitral valve reconstruction.

Three days after CRT, the patient underwent control echocardiography study. At rest, LV EF increased up to 45%, intraventricular dyssynchrony disappeared and only a mild MR was noted (**Figure 3, 4**). However, during exercise, dynamic MR was induced with ERO of 0.20 cm^2, Reg Vol 36 ml, along with induction of exercise-induced

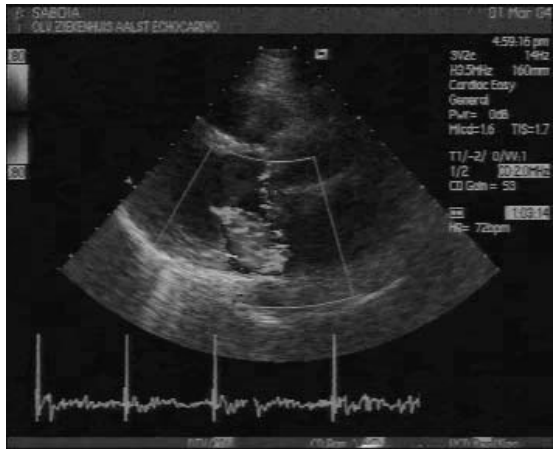

Figure 1 Mitral regurgitation at rest before cardiac resynchronisation therapy, parasternal long axis view

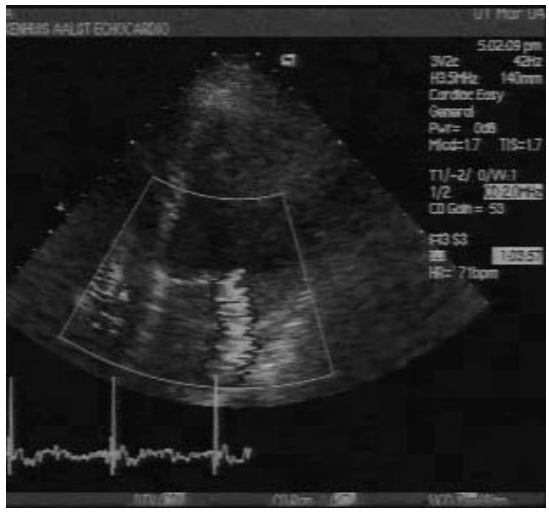

Figure 2 Mitral regurgitation at rest before cardiac resynchronisation therapy, apical four-chamber view

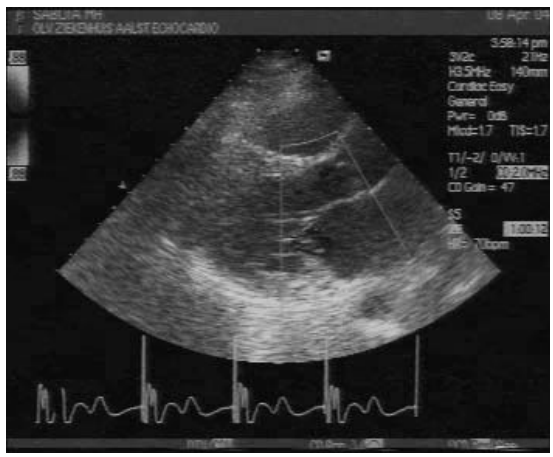

Figure 3 Mitral regurgitation at rest soon after cardiac resynchronisation therapy, parasternal long axis view

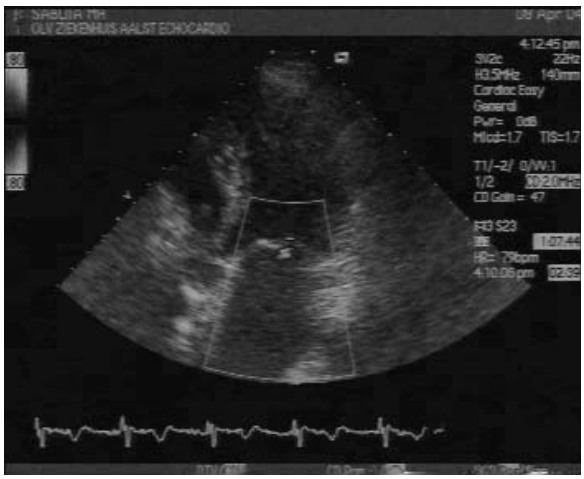

Figure 4 Mitral regurgitation at rest son after cardiac resynchronisation therapy, apical four-chamber view

LV dyssynchrony (LV delay 50 msec). No changes in LV morphology were noted. The patient was discharged on 5th day after implantation on standard unchanged therapy including diuretics, beta-blockers, and angiotensin-converting enzyme inhibitor.

At one-year follow-up, the patient presented with major improvement and remained in NYHA class I. Rest echocardiography study documented further improvement in LV function with EF 50% with only discrete MR and no dyssynchrony. Notably, exercise study failed to induce an increase in MR (ERO during exercise 0.07 cm^2, Reg Vol 12 ml) or exercise-induced LV dyssynchrony (LV delay 20 msec). Duration of exercise prolonged to 8 min with maximal achieved workload 85 Watts. Improvement in cardiac function and dynamic MR was paralleled by signs of reversed LV remodelling as evidenced by reduction in LVEDD to 41 mm and LA to 39 mm (**Table 1**).

Discussion

Cardiac resynchronisation therapy (CRT) is associated with improvement in MR (7 – 11), exercise tolerance and LV function (7, 8), leading to improved survival in pts with congestive heart failure (CHF) in NYHA class III, IV, and prolonged QRS duration (9, 10).

Following radiofrequency ablation of the AV conduction system, LV function occasionally deteriorates and MR can worsen (12). The RV apical pacing could negatively affect mitral valve closure as well as LV contractility, due to induction of electrical and mechanical LV dyssynchrony and long-term remodelling of global ventricular shape. Comparison between BiV pacing and RV pacing has been assessed only in a few studies (13, 14). Cazeau et al. showed BiV pacing as superior to RV pacing, resulting in a higher cardiac output and a decrease in pulmonary capillary wedge pressure (13). In the study of Hamdan et al. (14) BiV pacing resulted in improved hemodynamics and a decrease in sympathetic activity compared with RV pacing.

Our case underscores the importance of exercise study in patients with underlying or RV-induced dyssynchrony for evaluation of dynamic MR and eventual consideration of CRT. We would like to emphasize the presence of significant exercise-induced LV dyssynchrony before BiV pacing, which could have importantly contributed to long-term deterioration of LV systolic function. Moreover, increase in MR as a result of dynamic LV dyssynchrony may progressively increase myocardial stiffness and accelerate LV remodelling and LV dysfunction (15).

The case corroborates the previously described beneficial effect of CRT on MR and global LV function at rest. In addition, it illustrates the effect of CRT on exercise-induced MR, early and late after BiV pacemaker implantation. The exercise-induced MR appears to be associated with persistence of exercise-induced LV dyssynchrony early after CRT. In contrast, in the late period the presence of LV reversed remodelling prevented both exercise-induced MR, as well as exercise-induced LV dyssynchrony.

Conclusion

The CRT is a clinically indicated option for patients with symptomatic heart failure and electromechanical

Table 1 Echocardiography and exercise parameters before, soon after, and late after CRT

	Before CRT		**Early CRT** (3 days)		**Late CRT** (1 year)	
	Rest	Exercise	Rest	Exercise	Rest	Exercise
LV EF (%)	39	43	50	52	55	60
LV dys (ms)	46	68	3	50	7	20
ERO (cm_2)	0.19	0.25	discreet	0.20	discreet	0.07
LVESV (ml)	47	44	44	46	28	24
Max. workload (Watts)	–	55	–	55	–	85

CRT – Cardiac resynchronisation therapy, ERO – Effective regurgitant orifice, LV dys – Left ventricular dyssynchrony, LVESV – Left ventricular end-systolic volume

dyssynchrony potentially induced by chronic RV pacing. These patients should be considered for upgrade from one lead pacing to biventricular system.

Importantly, reduction of dynamic MR could represent a mechanism contributing to beneficial effects of CRT on clinical outcomes of patients with congestive heart failure.

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