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Right bundle branch block and heart failure: Can a bifocal right ventricular pacing be an alternative to biventricular pacing?

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SOUHRN

Pacienti s blokádou pravého Tawarova raménka (RBBB) a se srdečním selháním nejsou ve velkých randomizovaných klinických studiích hodnotících účinnost srdeční resynchronizační léčby (SRL) dostatečně zastoupeni, protože jsou do těchto projektů zařazováni hlavně pacienti s blokádou levého Tawarova raménka. Ve shodě s výsledky nedávno publikované metaanalýzy naše studie se 14 pacienty s RBBB a srdečním selháním léčenými klasickou SRL (biventrikulární stimulací) prokázala, že žádný z nich neodpovídá na léčbu, jde tedy o „non-respondéry".
Alternativou v případě neúspěšné biventrikulární stimulace je v současnosti bifokální stimulace, speciální metoda simultánní stimulace pomocí elektrod implantovaných do pravé komory. Na základě výsledků studie BRIGHT byla na naší kardiologické klinice provedena u 25 pacientů se srdečním selháním a s neúspěšnou biventrikulární stimulací provedena implantace bifokálního stimulátoru do pravé komory. Během 12měsíčního sledování došlo ke zlepšení funkční třídy NYHA a zvýšení ejekční frakce levé komory (dvouleté přežití 77 %). Bifokální stimulace pravé komory by u pacientů s RBBB a pokročilým srdečním selháním mohla představovat přijatelnou alternativu klasické biventrikulární stimulace, protože zajišťuje racionálnější elektrickou „resynchronizaci", i když hemodynamický a funkční přínos bifokální stimulace je teprve nutno prokázat.

Keywords:
Cardiac resynchronization therapy
Heart failure
Right bundle branch block
Right ventricular bifocal pacing

ABSTRACT

Patients with right bundle branch block (RBBB) and heart failure (HF) are not well represented in large randomized clinical trials evaluating the efficacy of cardiac resynchronization therapy (CRT), which included mainly left bundle branch block morphology. According to a recent meta-analysis, in our series we have 14 patients with RBBB and HF treated with conventional CRT (biventricular pacing), all of them turned out to be "non-responders".
Bifocal pacing, a particular modality of simultaneous pacing with two leads implanted in the right ventricle, is a current option in case of unsuccessful biventricular pacing. In accordance with the results of the BRIGHT study, 25 patients with heart failure and unsuccessful biventricular pacing underwent right ventricular bifocal pacing implantation in our Cardiology Department, with significant improvements of NYHA functional class and left ventricular ejection fraction at 12-month follow-up (survival rate 77% after 2 years).
Right ventricular bifocal pacing could be an alternative to conventional biventricular pacing in patients with RBBB and advanced HF, ensuring a more rational electric "resynchronization", even if hemodynamic and functional benefit remains to be demonstrated.

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Introduction

Cardiac resynchronization therapy (CRT) with biventricular pacing demonstrated efficacy in improving survival and quality of life in patients with advanced heart failure and wide QRS duration (> 120 ms) [1–3]. These benefits are largely documented in literature in patients with left bundle branch block (LBBB), while those with right bundle branch block (RBBB) experienced poorer outcome [4].

Moreover, CRT is sometime not applicable for several reasons (unsuccessful intubation of coronary sinus, catheter instability in left cardiac veins, high left ventricular pacing threshold, phrenic nerve stimulation) [5]. In this case, a proposed alternative technique is bifocal right ventricular pacing. Bifocal pacing is obtained with a simultaneous stimulation of the apex and of the right ventricular outflow tract, locating one catheter in apical position and one in the high inter-ventricular septum: it is easier to be performed and implies lower complication rates, not requiring coronary sinus catheterization [6].

The lack of an established strategy in case of CRT implant failure and in case of RBBB was a stimulus to analyze outcomes of patients implanted at our Center.

Methods

We prospectively collected data about all patients receiving an ICD or CRT pacemaker at our Center, compiling a database at the moment of implant and at every subsequent outpatient visit for device check. Collected data regarded demographic features, death/cause of death, complications at implant, etiology of cardiac disease, comorbidities, risk factors, pharmacological therapy, arrhythmias at follow-up, echocardiographic measures (at enrollment and at follow-up) and NYHA class. All patients gave informed consent to the collection of data. We then performed a retrospective analysis focusing on two populations:

1. Patients with RBBB receiving a conventional CRT.
2. Patients with LBBB and indication to CRT who received bifocal pacing for CRT implant failure.

Bifocal pacing was obtained with a simultaneous stimulation of the right ventricular apex (with a passive or active fixation lead) and of the high interventricular right septum in the parahisian site (with an active screw-in fixation lead).

Descriptive statistical analysis was performed with Microsoft Excel XP; Kaplan–Meier analysis of mortality, *t*-test (for normally distributed data) and Fisher exact (for distribution) were performed as appropriate with R software for Macintosh (R Foundation for Statistical Computing, 2012).

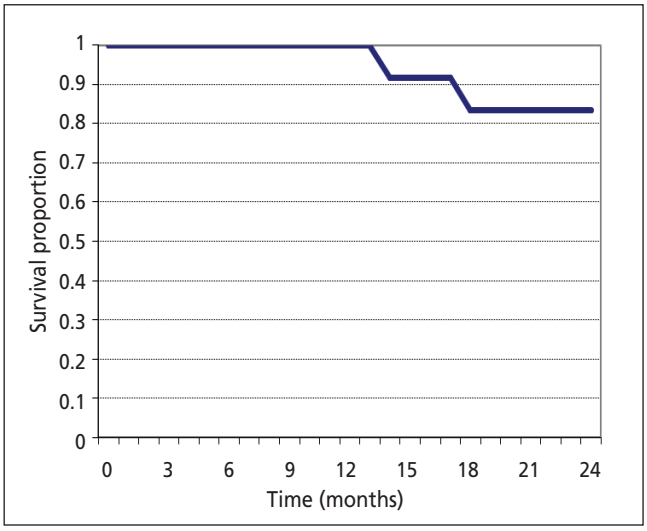

Fig. 1 – Survival curve of 14 RBBB patients implanted with biventricular pacing in our Center.

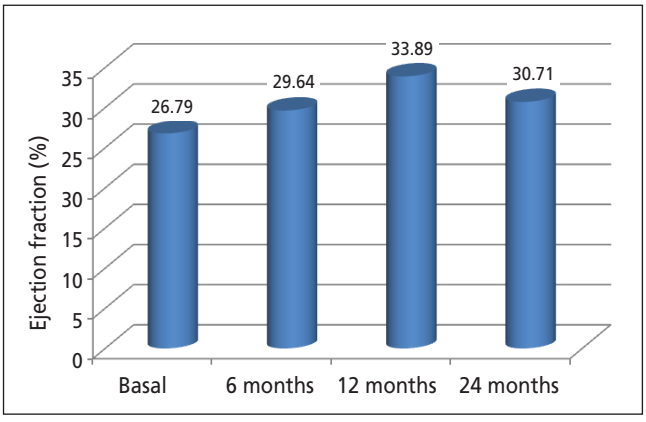

Fig. 2 – Left ventricular ejection fraction trend in 14 RBBB patients implanted with biventricular pacing in our Center.

Results

Patients with RBBB treated with CRT

From 2003 to 2012 we performed 14 biventricular pacing implants in RBBB patients (versus approximately 400 LBBB patients); all devices were CRT-D and all patients had a basal QRS > 150 ms.

At 2-year follow-up, 10 patients were alive, 2 dead (1 for refractory heart failure and 1 for extracardiac causes) and 2 lost at follow-up, with a 2-year survival of 83% (Fig. 1). Ejection fraction did not significantly improve and no improvement was obtained in New York Heart Association (NYHA) functional class (Table 1 and Fig. 2).

Table 1 – Clinical outcomes in 14 RBBB patients implanted with biventricular pacing in our Center.

	Basal	6 months	12 months	24 months
Left ventricular ejection fraction (%)	26.8 ± 6.58	29.6 ± 7.78	33.9 ± 11.9	30.7 ± 10.4
NYHA functional class	2.5 ± 0.52	2 ± 0.6	1.91 ± 0.54	2 ± 0.53

p not significant for any parameter comparison.

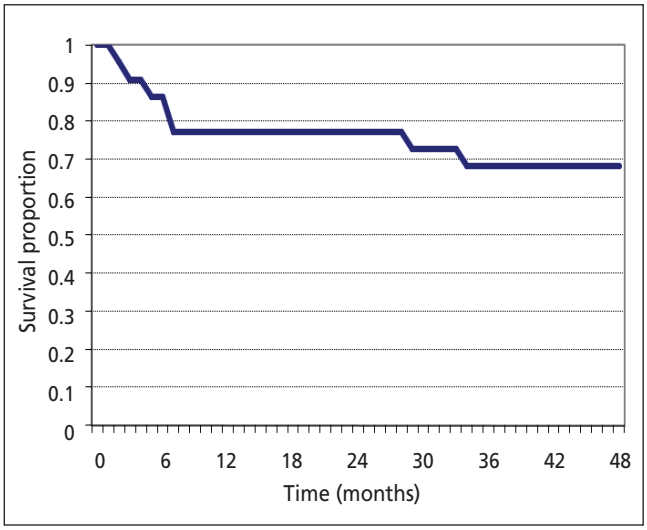

Fig. 3 – Survival curve of 25 patients implanted with bifocal right ventricular pacing in our Center.

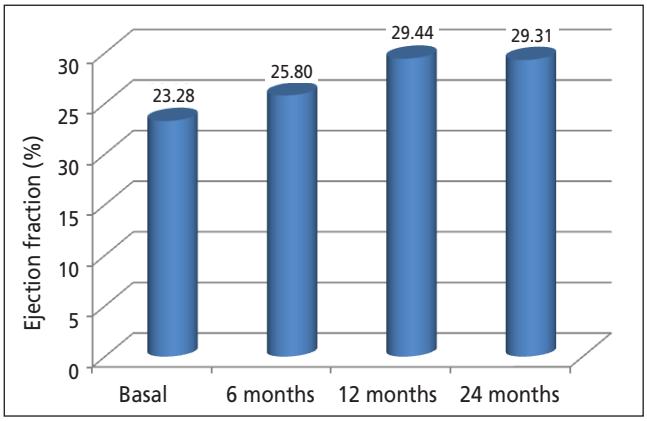

Fig. 4 – Left ventricular ejection fraction in 25 patients implanted with bifocal right ventricular pacing in our Center.

Patients with failed CRT receiving bifocal pacing

In our Center we treated with bifocal pacing 25 patients eligible to CRT (all with LBBB and QRS > 130 ms) with previous unsuccessful biventricular pacing implantation. Patients were 19 males and 6 females; mean age was 73 ± 7 years; 12 patients had ischemic, 12 idiopathic and 1 valvular dilated cardiomyopathy; 13 patients were in NYHA functional class II (52%), 11 in NYHA class III (44%) and 1 in NYHA class IV (4%); 6 patients received a biventricular pacemaker (24%), 19 patients a biventricular ICD (76%). At the pre-implant echocardiography, left ventricular telediastolic volume (mean ± st dev) was 212 ± 75 cc, telesystolic volume (mean ± st dev) was 166 ± 70 cc, and ejection fraction 23.3 ± 8.4 %.

Survival at 24-month follow-up was 77% (Fig. 3).

We observed a significant improvement of NYHA functional class both at 6-month and 12-month follow-up (respectively $p = 0.001$ and $p = 0.03$ compared with pre-implantation values), while at 24-month follow-up the improvement was not statistically significant ($p = 0.18$) (Table 2). Echocardiographic parameters showed an improvement in ejection fraction at 6-, 12- and 24-month follow-up, achieving statistical significance only at 24-month follow-up ($p = 0.08$ at 6 months; $p = 0.013$ at 12 months; $p = 0.07$ at 24 months) (Table 2 and Fig. 4).

Complication rate was extremely low in these two groups of patients (probably because of the low numbers considered): neither pneumothorax nor pericardial effusion was observed, and no procedure-related deaths were reported.

Discussion

Cardiac resynchronization therapy (CRT) with biventricular pacing demonstrated efficacy in improving survival and quality of life in patients with advanced heart failure and wide QRS duration (>120 ms).

RBBB patients are not well represented in large randomized clinical trials evaluating the efficacy of CRT that mainly included LBBB morphology. Nery et al. [4] systematically reviewed published data from randomized clinical trials of CRT considering the outcomes in subgroups of RBBB patients: MIRACLE [7], Contak CD [8], CARE-HF [2], MADIT-CRT [3] and RAFT [9]. Cumulative RBBB patients were 485, composed by 259 randomized to CRT and 226 randomized to non-CRT. Baseline demographics were not different between the two groups. MIRACLE [7] and Contak CD [8] studies did not show improvements in the two groups regarding left ventricular ejection fraction, 6-minute walk distance, VO_2 exercise consuming or norepinephrine levels. In MADIT-CRT study [3], CRT effect was neutral in all patients except for those with LBBB; even in the recent RAFT study [9] RBBB patients did not benefit from CRT. CARE-HF study [2] even highlighted how the presence of RBBB was an independent predictor of adverse outcomes, associated with doubled risk of death from any cause or cardiovascular hospitalization.

Moreover, CRT is sometime not applicable for several reasons (unsuccessful intubation of coronary sinus, catheter instability in left cardiac veins, high left ventricular pacing threshold, phrenic nerve stimulation) [5].

In such cases, other procedures may be attempted:

1. Epicardial LV stimulation, requiring cardiac surgery and thoracotomy, was usually performed at a later stage and with potential complications in frail patients [10].

Table 2 – Clinical outcomes in 25 patients implanted with bifocal right ventricular pacing in our Center.

	Basal	6 months	12 months	24 months
Left ventricular ejection fraction (%)	23.3 ± 8.41	25.8 ± 7.98	29.4 ± 7.77	29.3 ± 9.94*
NYHA functional class	2.52 ± 0.59	1.75 ± 0.44*	1.82 ± 0.73*	1.92 ± 0.76

* $p < 0.05$ compared with baseline.

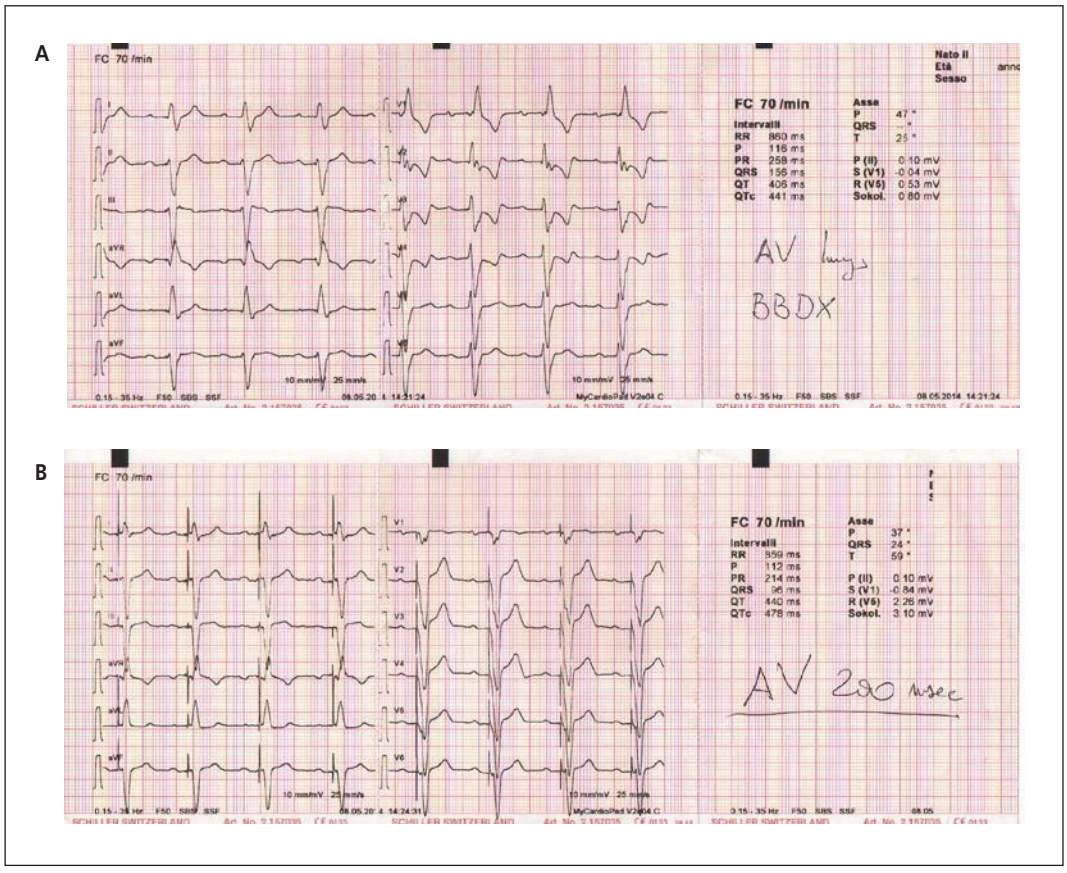

Fig. 5 – "Normalizing" of QRS complex in a patient with 1st AV block and RBBB (A): setting an optimal AV delay provides the merging between an activation front from the right ventricular apex pacing and spontaneous activation of left bundle branch (B).

2. Direct hisian stimulation, as more recently proposed, was more difficult to obtain and viable only if LBBB is due to intrahisian slow conduction [11].

An easy and immediately available alternative technique is bifocal right ventricular pacing [6].

First data in favor of this technique were obtained in 1999 by Pachón Mateos et al. [12], who described and used bifocal pacing in 39 patients with dilated cardiomyopathy (including 17 patients affected by Chagas disease), heart failure and indication to permanent pacing: they demonstrated the efficacy of bifocal pacing compared to conventional right ventricular apical stimulation, with narrowing of QRS complex, reduction in mitral regurgitation, improvements in contractility and diastolic left ventricular function, quality of life and NYHA functional class.

More recently, the BRIGHT study (Bifocal RIGHT ventricular resynchronization therapy) [13] evaluated the effects of bifocal pacing in 42 patients eligible to CRT, with a 6-month randomized crossover phase (bifocal pacing ON versus OFF). During the active phase there was a significant improvement in perceived quality of life, NYHA functional class, mean distance in 6-minute walking test, QRS duration and left ventricular ejection fraction. Mitral regurgitation grade and hospitalization admissions reduced compared with inactive phase, but these data are not statistically significant. This study also demonstrated that total procedure time is lower than biventricular pacing implantation time.

Bifocal pacing can also improve intraventricular, interventricular and global dyssynchrony (measured as sum of intra- and interventricular dyssynchrony) [14].

Based on current literature and on our data, bifocal pacing allows good improvements in cardiac function and in clinical symptoms, even if it cannot be considered as first choice technique in patients eligible to CRT, and stated the superiority of conventional biventricular pacing. Bifocal pacing could be a viable alternative method for patient where biventricular pacing has been unsuccessful [15].

Bifocal pacing in right bundle branch block patients

As already said, biventricular pacing is ineffective in RBBB patients, as reported in literature and confirmed by our experience, while no patient with RBBB and indication to CRT underwent a permanent bifocal pacing of the right ventricle. We believe that this kind of patients could benefit from this technique of pacing. There is a physiopathological rationale that can explain how patients with RBBB and heart failure with reduced ejection fraction could benefit from bifocal pacing. The activation pattern of RBBB is characterized by a delay of the right ventricle outflow tract: bifocal pacing, simultaneously stimulating the right ventricle apex and outflow tract, leads to the resynchronization of the area with the latest activation, thus allowing to obtain a narrower QRS complex.

We show the ECG recording of a patient in which a single pacing of the right ventricle, applied to an optimal site and with a custom atrio-ventricular interval, allowed to obtain a fusion with the spontaneous activation of the left bundle branch, thus leading to "normalization" of QRS complex (Fig. 5).

Crea and colleagues [16] recently confirmed this possibility in a patient with RBBB and low left ventricular ejection fraction. In RBBB patients, it is then possible to obtain an electrical resynchronization even only with right ventricular pacing.

More studies are needed in order to demonstrate if this can lead also to a clinical benefit, in terms of left ventricular ejection fraction, quality of life and functional class, especially if RBBB is associated with concomitant left ventricular systolic dysfunction [17].

Considering that heart failure patients with QRS > 130 ms and RBBB pattern are uncommon, a wide range, multicenter, randomized trial is needed to clarify these aspects, by comparing different kinds of cardiac pacing:

- Conventional CRT (biventricular)
- Bifocal right ventricular pacing
- Right ventricular pacing from optimal sites and with optimal AV interval.

Such a study will finally clarify if bifocal stimulation or right ventricular pacing from alternative sites may lead to better outcome comparing to CRT in patients with heart failure and RBBB.

Conflict of interest
No conflict of interest.

Funding body
None.

Ethical statement
I declare, on behalf of all authors, that the research was conducted according to Declaration of Helsinki.

Informed consent
I declare, on behalf of all authors, that informed consent was obtained from all patients participating in this study.

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