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EDITORIAL

Left Bundle Branch (LBB) Area Pacing for Cardiac Resynchronization Therapy (CRT): Most Promising Alternative CRT Pacing Modality

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Abstract

Cardiac resynchronization therapy (CRT) via biventricular pacing (BiVP) has benefitted a large group of heart failure (HF) patients with low ($\leq$35%) left ventricular (LV) ejection fraction (LVEF) and cardiac dyssynchrony, mostly in the form of left bundle branch (LBB) block, conferring amelioration of their HF symptoms and prolongation of their survival. However, it entails a tedious procedure to place and find a stable and functional position of the LV lead in a coronary sinus tributary, which may fail in a considerable percentage of patients, while up to one third of patients, even then, may turn out to be non-responders. Over the recent years, strong new data from observational studies and meta-analyses have shown the safety and feasibility of LBB area pacing (LBBAP) in patients with bradyarrhythmias and most importantly in HF patients in need for CRT. LBBAP yields satisfactory pacing threshold and R wave sensing and low complication rates. Particularly, in patients with CRT indication, LBBAP, as an alternative approach to CRT, has shown significant improvement of functional class and LVEF during short-and mid-term follow-up. Thus, LBBAP, as a relatively novel CRT modality, demonstrates a most promising potential (equivalent or even superior) role for effective CRT for HF patients in need of a viable alternative to BiVP, and also circumvents certain limitations of His bundle pacing, which is another, albeit potentially problematic, mode of CRT. Nevertheless, we are still in dire need for confirmatory data from properly designed randomized controlled trials to further establish the role and value of this alternative CRT pacing modality. ***Rhythmos 2022;17(4): 71-74***.

Key Words: cardiac pacing; cardiac resynchronization therapy; left bundle branch area pacing; heart failure; conduction system pacing

Abbreviations: BiVP = biventricular pacing; CRT = cardiac resynchronization therapy; CSP = conduction system pacing; ECG = electrocardiogram; HBP = His bundle pacing; HF = heart failure; LBBB = left bundle branch block; LBBAP = left bundle branch area pacing; LV = left ventric-le(ular); LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; RBB = right bundle branch; RBBB = right bundle branch block; RCT = randomized controlled trial

Introduction

His bundle pacing (HBP) produces a narrow QRS reflective of effective electrical and mechanical cardiac synchronization and has been suggested as equivalent or even superior to biventricular pacing.[1, 2] Although HBP has been successfully utilized for both bradyarrhythmia indications and for cardiac resynchronization therapy (CRT) in patients with heart failure (HF), there are certain limitations of HBP which include implant complexity and rising pacing thresholds over time.[1, 3] On the other hand, selective left bundle branch (LBB) pacing predominantly yields a wide QRS as a result of delayed right bundle branch synchronization, whereas non-selective left bundle branch area pacing (LBBAP) results in shorter QRS duration because of recruitment of the basal right ventricular (RV) septum [4] and appears to confer similar physiological benefits with shorter duration of the implant procedure and more stable pacing thresholds in patients with HF and left bundle branch block (LBBB).[3] More recently, hybrid systems utilizing HBP or LBBAP in combination with left ventricular (LV) leads have been used to treat heart failure (HF) patients, and may be useful in multilevel or mixed conduction blocks. Thus, there is growing interest in conduction system pacing (CSP) for both bradycardia and HF indications; however, there is still lack of robust data direly needed from randomized controlled trials (RCTs) to help guide optimal pacing options with beneficial and durable effects in both of these patient populations, i.e. patients with bradyarrhythmias where chronic conventional pacing at the RV apex may be deleterious [5, 6] and patients with HF in need for CRT.[7]

Studies on LBB Pacing

Recent studies indicate that LBBP is feasible with a high success implantation rate and effective to correct LBBB and improve LV structure and function with a low and stable pacing threshold in both young and old patients.[8, 9] Some studies have suggested that CSP in patients with LV ejection fraction (LVEF) ≤45% and atrioventricular block improves the LVEF and induces a response similar to that of biventricular (BiV) CRT leading to significantly improved mitral regurgitation and New York Heart Association (NYHA) functional class, rendering it an alternative to BiV CRT in these patients. [10] Other studies have indicated greater LVEF improvement with LBBP-CRT than BiVP-CRT in HF patients with nonischemic cardiomyopathy and LBBB.[11]

An RCT compared the efficacy of LBBP-CRT with BiVP-CRT in 40 patients with HF due to nonischemic cardiomyopathy and reduced LVEF (20 males, mean age 63.7 years, LVEF 29.7% ± 5.6%).[11] Crossovers occurred in 10% of LBBP-CRT and 20% of BiVP-CRT. Intention-to-treat analysis showed significantly higher LVEF improvement at 6 months after LBBP-CRT than BiVP-CRT (mean difference: 5.6%; P=0.039). LBBP-CRT also appeared to have greater reductions in LV end-systolic volume (-24.97 mL) and NT-proBNP (-1,071.80 pg/mL), and comparable changes in NYHA functional class, 6-minute walk distance, QRS duration, and rates of CRT response compared with BiVP-CRT.

An observational study included 477 consecutive patients (mean age 72 ± 12 years; 32% women) with LVEF ≤35% (mean LVEF 26% ± 6%) and class I or II indications for CRT who underwent successful BiVP or CSP.[12] Patients underwent BiVP 219; CSP 258 (HBP 87, LBBAP 171). Comorbidities included hypertension 70%, diabetes mellitus 45%, and coronary artery disease 52%. Paced QRS duration in CSP was significantly narrower than BiVP (133±21 ms vs 153±24 ms; P<0.001). LVEF improved in both groups during follow-up of 27±12 months and was greater after CSP compared to BiVP (39.7±13% vs 33.1±12%; P<0.001). Primary outcome of death or HF hospitalization was significantly lower with CSP vs BiVP (28.3% vs 38.4%; hazard ratio 1.52; P = 0.013). The authors concluded that CSP improved clinical outcomes compared to BVP in this large cohort of patients with indications for CRT.

In patients with RV pacing who have developed RV pacing induced cardiomyopathy, upgrading to LBB pacing has been shown to be feasible and safe to effect CRT in these patients, demonstrated to effect significant electrical resynchronization and favorable improvement in LV function and NYHA functional class at short-term follow-up.[13] LBBAP has also been shown to be a viable alternative to CRT in patients who failed conventional BiVP due to coronary sinus lead failure or who are nonresponders.[14]

A prospective multicenter observational study (N=100) indicated that the feasibility and efficacy of LBBP-CRT (n=49) led to better electromechanical resynchronization and higher clinical and echocardiographic response, especially higher super-response than BiVP-CRT (n=49) at 6 (53% vs 37%, P=0.016) and 12 months (61% vs 39%, P<0.001) in HF patients with LBBB.[15] The pacing threshold was lower in LBBP-CRT at implant and at 1-year (both P<0.001). Procedure-related complications and adverse clinical outcomes including HF hospitalization and mortality were similar in the two groups.

Finally, LBBAP has been suggested even for patients with LBBB and LVEF >35% as this mode of pacing can significantly shorten the QRS duration and improve cardiac function in LBBB patients with either LVEF >35 or ≤35%.[16] Thus, LBBAP may be an effective therapy for preventing the deterioration of LV function in early-stage HF patients with LBBB and LVEF >35%.

Meta-analyses. A meta-analysis of 18 studies (N=1517) comparing the clinical outcomes associated with CSP vs BiVP in patients with HF reported that after a follow-up period of 9.3±5.4 months, CSP was found to have shorter QRS duration in the CRT population compared to that in the BiVP (SMD, -1.17; *P*<0.00001; I^2=74%). [17] No statistical difference was found in QRS duration (SMD, 0.04; *P* = 0.82; I^2=84%) between the two modes of pacing. In the comparison of CSP and BiVP, the LBBP subgroup showed improved LVEF (SMD, 0.67;

$P<0.00001$; $I^2=0\%$), shorter LVEDD (SMD, 0.59; $P=0.0005$; $I^2=0\%$), and higher NYHA class (SMD, -0.65; $P<0.00001$; $I^2 = 45\%$). Also, in a comparison of clinical outcomes of HBP and LBBP, LBBP had a lower pacing threshold (SMD, 1.25; $P<0.00001$; $I^2=47\%$) and higher R-wave amplitude (MD, -7.88; $P<0.00001$; $I^2=8\%$) compared to HBP. The authors concluded that CSP had a lower pacing threshold and higher R-wave amplitude and produced higher LVEF, shorter QRS duration, and higher NYHA class in the CRT population than the BiVP.

Another meta-analysis of 6 studies involving 389 patients indicated that after a mean of 8.03 ± 3.15 months, LBBAP resulted in a greater improvement in LVEF (MD=7.17), followed by HBP (MD=4.06) compared with BiVP.[18] HBP resulted in a narrower QRS duration (MD=31.58 ms), followed by LBBAP (MD=27.40 ms) compared with BiVP. No significant differences of changes in LVEF improvement and QRS narrowing were observed between LBBAP and HBP. The pacing threshold of LBBAP was lower than those of BiVP and HBP.

A meta-analysis of 8 nonrandomized studies with a total of 527 patients who underwent LBBAP as CRT indicated that patients with LBBAP had a greater reduction in paced QRS (mean difference -MD 27.91 ms), and a greater improvement in NYHA class (MD 0.59) and LVEF (MD 6.77%) compared with those having BiVP.[19] Patients with underlying LBBB appeared to benefit the most from LBBAP vs patients without LBBB. The authors concluded that LBBAP is a reasonable option for patients who meet indications for CRT, particularly in those who have limited anatomy or do not benefit from CRT.

A meta-analysis of 6 studies reported a success rate of LBBP at 93.2%. [20] Compared with baseline, LBBP could shorten QRS duration (QRSd) (MD = 61.23, P<0.01). Echocardiographic parameters including LVEF and LV end-diastolic diameter (LVEDD) significantly improved (both with P<0.01). Clinical outcomes including NYHA classification and BNP improved significantly (both with P<0.01). Compared with BiVP, LBBP could further improve QRSd, LVEF, LVEDD, and NYHA classification (all with P<0.01). However, the pacing threshold at follow-up was 0.06 V higher than that at baseline (P<0.01), and the incidence of complications was 2.4%.

ECG Features

LBBAP results in narrower-paced QRS duration than RV apical pacing with most common ECG features of a qR or Qr pattern in lead V1. [21] Patients with right bundle branch block (RBBB) at baseline show lesser paced QRS shortening compared to patients with baseline LBBB.

Durability of LBB Pacing

Long-term data on the safety and performance of LBBAP 1 year post-device implantation were reported by a retrospective study in 65 patients (aged 75.7±10.1 years, LVEF 59.8±10.4%, 49% females) who received LBBAP for bradycardia indications using the SelectSecure 3830 lead (Medtronic).[22] Indications for pacing were atrioventricular block 55%, sinus node dysfunction 19%, tachy-brady syndrome 15%, atrioventricular node ablation 8%, and bail out CRT 3%. Mean baseline QRS measured 120 ± 38 ms, paced QRS duration was 138 ± 22ms. Paced QRS narrowed by 24 ms in those with pre-existing LBBB, increased by 1 ms in those with pre-existing RBBB, and increased by 42 ms in those with no BBB. LBBAP threshold at implant was 0.521 ± 0.153 V at 0.4 ms, and increased to 0.654 ± 0.186 V at 3 months (+26%), 0.707 ± 0.186 V at 6 months (+36%), and 0.772 ± 0.220 V at 12 months (+48%). Patients with LBBB showed the maximum benefit with QRS narrowing 24 ms. Pacing impedance remained unchanged with no procedure-related complications. The authors concluded that LBBAP is a durable form of CSP with pacing thresholds remaining relatively stable over 1 year post device implantation. Patients with LBBB display the narrowest paced QRS.

A study compared the long-term clinical outcomes between LBBAP (n=21) and BiVP (n=20) in 41 patients with HF and complete LBBB. [23] Over 23.71 ± 4.44 months, LBBAP produced lower pacing thresholds, shorter procedure time and fluoroscopy duration compared to BiVP. The QRS duration was significantly narrower after LBBAP than BiVP (129.29±31.46 vs 156.85 ± 26.37 ms, P=0.005). Importantly, both LBBAP and BiVP significantly improved LVEF, LVEDD, NYHA class, and BNP compared with baseline. However, LBBAP significantly lowered BNP compared with BiVP (416.69 ± 411.39 vs 96.07 ± 788.71 pg/ml, P=0.007) from baseline to 24-month follow-up. Also, patients who received LBBAP exhibited lower number of hospitalizations than those in the BiVP group (P=0.019). Interestingly, patients with moderately prolonged LV activation time and QRS notching in limb leads at baseline ECG respond better to LBBAP for LBBB correction.

Conclusion

Robust data from large observational studies and meta-analyses show the safety and feasibility of LBBAP in patients with bradyarrhythmias and most importantly in HF patients in need for CRT. LBBAP yields excellent pacing electrical parameters (pacing threshold and R wave sensing) and low complication rates including lead revision <1%.[24] Particularly, in patients with CRT indication, LBBAP has shown significant improvement of NYHA class and LVEF during short-and mid-term follow-up. Thus, LBBAP is a relatively novel CSP modality demonstrating excellent results for patients with conventional bradycardia pacing indications and a most promising potential (equivalent or even superior) role for effective CRT for patients in need of a viable alternative to BiVP, including patients who failed conventional BiVP due to coronary sinus lead failure or who are nonresponders to this mode of CRT, and also circumventing certain limitations of HBP. Nevertheless, confirmatory data are still needed from properly designed RCTs to further establish the role and utility of this alternative CRT modality.

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