Left Bundle Branch Area Pacing Generates More Physiological Ventricular Activation Sequences than Right Ventricular Pacing

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Abstract

Left bundle branch area pacing (LBBAP) has been proposed as a novel physiological pacing modality to overcome ventricular dyssynchrony reported in bradycardic patients who undergo conventional right ventricular pacing (RVP). The standard non-invasive measure of depolarization synchrony is the QRS duration. However, a deeper understanding of not only the activation time but also the activation sequence is required to evaluate the effects of RVP and LBBAP in bradycardic patients. This study aimed to characterize and compare the ventricular activation sequences obtained from both pacing techniques, LBBAP and RVP, by analyzing the standard 12-lead ECGs of bradycardic patients with physiological conduction. 22 RVP and 42 LBBAP ECG recordings were collected before and after pacemaker implantation. High (HF) and low (LF) frequency-based methods for QRS complex analysis were used and the precordial activation sequence and activation delay (pAD) were estimated. Results showed more physiological activation sequences after LBBAP than after RVP, with lower pAD ($p<0.01$) after LBBAP [HF:12(-2,15) vs 29(6,56); LF:9(-25,13) vs 31(17,38)]. The proposed ECG methodology could be used in clinical practice to map more physiological pacing targets in pacemaker implantation.

1. Introduction

Right ventricular pacing (RVP) is the most common treatment for patients suffering from bradyarrhythmias. Nevertheless, it is well known that conventional RVP is associated with cardiac systolic dysfunction and increased risk of atrial fibrillation and heart failure [1]. In this context, left bundle branch area pacing (LBBAP) has recently emerged as a feasible and safe alternative to RVP generating more physiological ventricular activation [2].

QRS duration is the standard measurement for ventricular synchrony [3][4][5]. It provides information about the ventricular activation time but not about the activation sequence. The use of methods rendering additional characterization could help to better assess the effects of RVP and LBBAP in bradycardic patients with physiological ventricular conduction.

Previous studies have proposed techniques to measure ventricular synchrony and activation patterns in patients undergoing cardiac resynchronization therapy. These techniques have been applied on ultra-high-frequency (5000 Hz sampling frequency) 14-lead electrocardiograms (ECGs) using 16 different frequency bands within the 150-1000 Hz range [6]. In the present study, we propose using a lower frequency range spanning from 10 to 60 Hz, which corresponds to the frequency content of the QRS complex. Additionally, the same analysis will be conducted over frequency bands in the 150-450 Hz range. The activation times and sequences calculated with both methods in standard 12-lead ECGs of bradycardic patients undergoing either LBBAP or RVP will be evaluated and compared.

2. Methods

2.1. Study population

12-lead ECG recordings from patients with narrow baseline QRS (QRS duration $<$ 120ms) indicated for antibradycardia therapy were collected at Lozano Blesa Clinical University Hospital (Zaragoza, Spain) at baseline and after 24 hours of continuous RVP (22 patients) or LBBAP (42 patients). ECGs were acquired at a sampling frequency of 1000 Hz and amplitude resolution of 3.75 μV. Table 1 shows the baseline characteristics of the patients included in the study.

2.2. Signal processing

ECG preprocessing included removal of 50 Hz powerline noise and of baseline wander. A spike cancellation

Table 1. Baseline characteristics of the study population. AV = atrioventricular; SSS = sick sinus syndrome; AF = atrial fibrillation

Variables	RVP	LBBAP	P-value
Age, y (mean $\pm$ SD)	78 ± 9	79 ± 7	0.92
Male sex, n(%)	55	60	0.70
Hypertension, n(%)	82	64	0.14
Diabetes, n(%)	50	29	0.09
Dyslipidemia, n(%)	64	57	0.61
Pacing indications, n(%)			
Complete AV block	32	33	0.90
AV block grade II	36	26	0.39
SSS	27	21	0.60
AF + ablation	5	7	0.68
Slow AF	0	9	0.13
Cardiomyopathy, n(%)	14	17	0.75

strategy (only for those ECGs at post-implantation state) was implemented as described in [3] which is based on the detection of the start and end of the spike and subsequent linear interpolation between both.

Preprocessed ECG signals were delineated using a multi-lead wavelet-based approach [7] with updates in the derivative thresholds used to identify the onset and end of the QRS complex to better reproduce annotations by expert electrophysiologists. QRS fiducial, onset and end points were identified for each cardiac beat. QRS selection was performed to remove extrasystolic beats. To do so, the RR interval was calculated from consecutive QRS fiducial points. Beats contained in a 20-ms bin centered in the RR mode were selected and an initial median beat was calculated. Subsequently, only cardiac beats whose QRS complex showed a Pearson coefficient with the median beat above 0.95 were included.

2.3. Ventricular activation sequences and precordial activation delay

Two frequency-based analyses of the QRS complex in precordial leads V1-V6 were conducted using: (1) high-frequency (HF) bands between 150 and 450 Hz (150-250, 200-300, 250-350, 300-400 and 350-450); (2) low-frequency (LF) bands between 10 and 60 Hz (10-30, 20-40, 30-50 and 40-60).

For LF and HF frequency analyses, the ECG recording was filtered in each of the described frequency bands. Positive envelopes of the selected QRS complexes were computed using the Hilbert transform, with the QRS complex window spanning from 120 ms before the delineated QRS fiducial point to 120 ms after. In the HF analysis, an additional strategy was applied to avoid the interpolation performed after applying the spike cancellation method from disrupting the QRS analysis.

For each of the two frequency analyses and for each precordial lead, the following steps were implemented. Median amplitude envelopes were calculated for each described frequency band from final QRS complex selected. These were normalized by dividing the median amplitude envelope by its integral. The average over all frequency bands was subsequently computed and the resulting beat was normalized by the maximum amplitude. The obtained QRS complexes in each lead were denoted as HF-QRS and LF-QRS for HF and LF analysis, respectively, Figure 1D-E. A quality criterion was applied over HF-QRS and LF-QRS complexes due to noise presence. A minimum of 3 high quality leads per ECG recording were required for further analysis.

To compute the lead activation time (AT_l), the sample with the maximum amplitude in each HF-QRS and LF-QRS was located. The first samples before and after it falling above 50 % of its amplitude were used to define the interval where the center of mass was computed in each lead and defined as AT_l. Precordial activation delay (pAD) was defined as the maximal time difference over V1-V6 AT_l. pAD positive values indicated left ventricular activation delay and negative values indicated right ventricular activation delay. Shorter absolute pAD values indicated faster and more synchronized ventricular activation.

Activation sequences were constructed by drawing the line connecting AT_l values from leads V1 to V6, Figure 1F-G. To compute the median activation sequence over all patients in an analyzed group, the activation sequence of each patient was shifted so that the minimum AT_l became 0 ms. Subsequently, 25th and 75th percentiles of AT_l values for each lead were calculated. To facilitate visual group comparisons, the activation sequences were centered in V2 to make them comparable between different patients groups.

2.4. Statistics

pAD data are presented as median (25th and 75th percentiles). Comparisons between post-implantation and basal states for each pacing technique were performed using Wilcoxon signed-rank test. Statistical differences between stimulation techniques were analyzed using the Wilcoxon rank-sum (Mann–Whitney U) test. The χ^2 test was performed for comparisons of nominal data. P-values < 0.05 were considered as statistically significant. Activation sequences are displayed as median (25th and 75th percentiles).

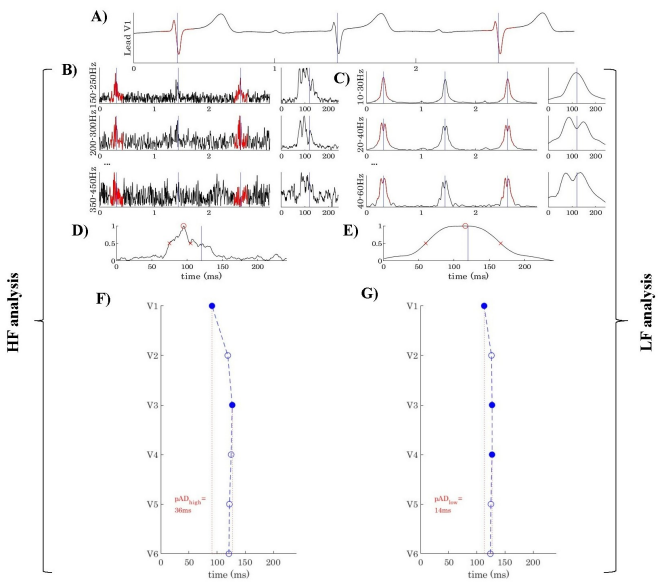

Figure 1. Activation sequence and pAD computation for a patient with narrow QRS at baseline. (A) ECG beats in lead V1. (B) HF and (C) LF analysis, with display of amplitude envelopes in different frequency bands (selected beats in red) and of the normalized median amplitude envelope. (D) HF-QRS and (E) LF-QRS complexes, with the red circle indicating maximum amplitude and red crosses, 50% of such amplitude. Blue line indicates delineated QRS fiducial point. (F) HF-QRS and (G) LF-QRS activation sequences, with first and last activated leads in full circles.

3. Results

HF-QRS and LF-QRS analyses included 41 and 63 patients, respectively, with the difference being due to the quality criteria applied . At baseline, no significant differences were observed between LBBAP and RVP patient groups. Baseline activation sequences built with the two frequency methods showed highly synchronized V1-V6 activation sequences, both for LBBAP and RVP groups. At post-implantation, significantly higher pAD values were found ($p<0.01$) for RVP than for LBBAP with both frequency analysis, as shown in Figure 2.

Patients after RVP showed left ventricular delay, and this difference was statistically significant when the LF analysis was performed [HF-QRS: 15 (4,27) ms vs 29 (6,56) ms, p=0.19; LF-QRS: 7 (-12,16) ms vs 31 (17,38) ms, p=0.001]. pAD after LBBAP showed values close to 0. No significant differences were observed in LF-QRS analysis but pAD presented significant changes in HF-QRS analysis [HF-QRS: 12(-2,15) vs -7(-18,6), p=0.004; LF-QRS: 5(-10,13) vs 9(-25,13), p=0.24].

4. Discussion

The main findings of this study are: (1) in patients with physiological conduction (QRS duration $<$ 120 ms), LBBAP preserved activation synchrony but RVP did not; (2) LF-QRS rendered similar results to HF-QRS, thus confirming the suitability of studying frequency components up to 60 Hz for ventricular activation analysis.

The two frequency methods implemented in this study indicated that RVP increased dyssynchrony in ventricular activation, in line with previous studies [8]. Significant differences in post-implantation pAD values were observed between LBBAP and RVP, with remarkably lower dyssynchrony found in patients treated with LBBAP when compared to those treated with RVP. These findings support LBBAP as a more physiological pacing modality.

The RVP activation sequences in this study were similar to those shown in previous ultra-high-frequency studies [4, 5]. When pacing at the RV apex, inflow and outflow tract, the ventricular delays reported in [5] were of the same order as here, with mean values of 34, 19 and 33 ms, respectively, in a population with 32% patients with normal conduction. When performing left ventricular septal pacing (LVSP) and non-selective LBB pacing (nsLBBp) in a population with 32% patients suffering from conduction disorders, mean delays of –24 ms and –12 ms for each of the two pacing modalities were found. Our work showed median pAD values after RVP of 29 ms and 31 ms and after LBBAP of 12 ms and -7 ms using HF-QRS and LF-QRS analyses in a population with normal conduction.

The two frequency analyses rendered consistent results and showed that LBBAP improves cardiac depolarization synchrony in a bradycardic population without conduction disorders, while RVP did not achieve the same improvement. While the LF-QRS analysis could be applied to all QRS complexes, the HF-QRS analysis was restricted to 41, as all other filtered complexes did not satisfy the noise-quality criteria. These results suggest the use of LF-QRS analysis as a more feasible technique to characterize the effects of pacing in bradycardic patients.

5. Conclusions

By performing QRS complex LF and HF analysis, this study has shown that RVP increases ventricular dyssynchrony while LBBAP preserves ventricular synchrony in patients without conduction disorders. Moreover, these results support the use of LF analysis to characterize the pacing effects, given that both frequency analyses showed similar results and LF analysis can be performed in standard ECG recordings with lower sampling frequencies. Finally, the developed method, derived from the study of 12-lead ECG recordings, could be applied to improve the identification of pacing sites for more physiological ven-

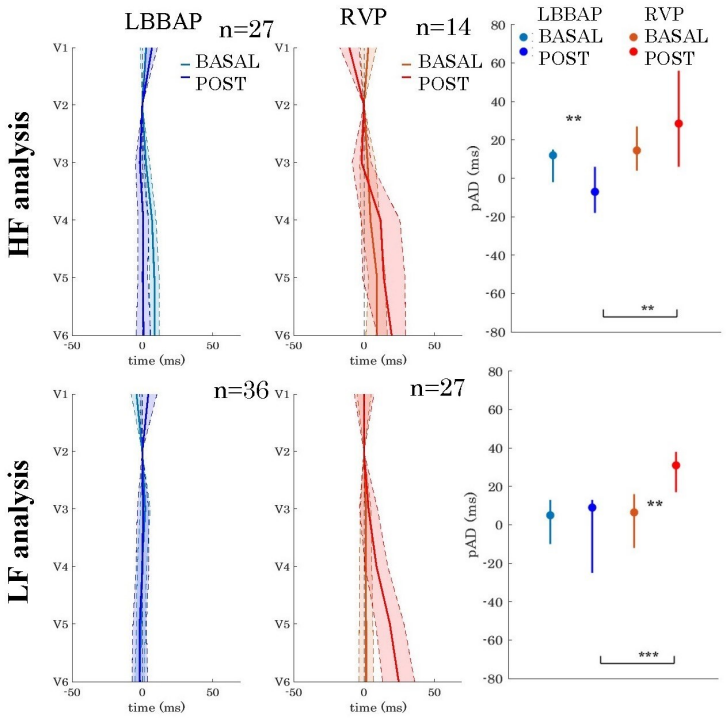

Figure 2. Median (solid line), 25th and 75th percentiles (dash lines) activation sequences and median, 25th and 75th percentiles of pAD for LBBAP and RVP groups at baseline and post-implantation states for HF-QRS and LF-QRS analyses.

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