Right Ventricular vs Left Bundle Branch Pacing-Induced Changes in ECG Depolarization and Repolarization

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Abstract

Patients suffering from bradycardia are indicated for pacemaker implantation. Right ventricular pacing (RVP) has been conventionally used for this purpose, but it can increase the risk of atrial fibrillation and heart failure. Left bundle branch area pacing (LBBAP) has been proposed as a new physiological pacing technique. The aim of this study was to compare changes induced by RVP and LBBAP in the ECG. 10-minute 12-lead ECG recordings were acquired at baseline and after pacemaker implantation from 83 patients (31 RVP, 52 LBBAP). Median beats were calculated for each patient at baseline and post-implantation states. ECG markers including QRS duration (dQRS) and area (aQRS) and heart rate-corrected QT (QTc) and Tpeak-to-Tend (Tpec) intervals were measured. dQRS and aQRS decreased significantly at post-implantation with respect to baseline, both being significantly lower for LBBAP than RVP after pacemaker implantation. QTc was significantly reduced at post-implantation for both pacing techniques with no differences between them. Tpec did not change either between states or techniques. In conclusion, LBBAP led to more synchronized ventricular depolarization, supporting potentially improved clinical outcomes with LBBAP as compared to RVP for anti-bradycardia therapy.

1. Introduction

Patients with bradycardia present slower heart rate than usual, commonly below 60 beats per minute, which may lead to an insufficient supply of blood pumped by the heart, thus depriving all organs of oxygen. The prevalence of bradycardia and conduction disorders increases with age due to heart rate slowdown and intercellular conduction changes [1]. Abnormalities in the sinus node, atrioventricular node and cardiac conduction system can contribute to bradycardia and irregular ventricular excitation.

In some patients with bradycardia, pacemaker implantation is indicated to receive external stimulation aimed at increasing heart rate and improving cardiac pumping efficiency. The right ventricular apex is the most common site chosen for pacemaker pacing, known as conventional right ventricular pacing (RVP). Nevertheless, different studies have reported that RVP can lead to intra- and inter-ventricular electrical dyssynchrony and, in the long-term, it can result in atrial fibrillation and heart failure [2]. Recently, left bundle branch area pacing (LBBAP) has been proposed as a new physiological pacing form that specifically activates the cardiac conduction system. Different studies have demonstrated LBBAP's feasibility and safety and have suggested that LBBAP leads to improved electrical and mechanical ventricular synchrony compared to RVP [3], [4].

The purpose of this study was to analyze and compare changes induced by RVP and LBBAP in the standard 12-lead ECG after 24 hours of continuous pacing.

2. Methods and Materials

2.1. Population

Standard 12-lead ECG recordings from 83 patients (31 RVP, 52 LBBAP) indicated for anti-bradycardia therapy were collected at Lozano Blesa Clinical University Hospital (Zaragoza, Spain) before pacemaker implantation (baseline: 10-minute ECG) and after 24 hours of RVP or LBBAP (post-implantation: 1-hour ECG). 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 preprocessing

ECG signal preprocessing included removal of 50 Hz power-line noise and baseline wander, a spike cancellation strategy (only for those ECGs recorded during pacemaker

activity) and low-pass filtering at 50 Hz. The spike cancellation strategy was based on the identification of each spike start and end. We first calculated the absolute value of the ECG derivative in each lead and we took the first sample in each beat that exceeded a threshold of 200 mV/s for each individual lead. We considered this sample as a potential spike onset mark. If more than 3 spike onset marks calculated from all leads were found within a distance of 50 samples, a spike was considered to exist and the earliest mark was identified as the onset. The duration of the spike was set to 20 samples and, thus, the spike end was identified 20 samples after the spike onset. In addition, to confirm the existence of a spike, an ECG sample in the spike interval with a value below -100 mV was required in each of the 12 leads. Finally, linear interpolation was applied to replace the spike.

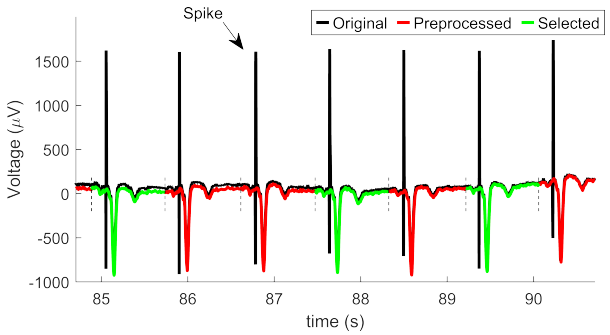

Figure 1. Raw (black) and preprocessed (red) post-implantation ECG recording of a patient. In green, beats selected to compute the median beat in lead V1 are shown.

2.3. Median beat calculation

The preprocessed ECG signals were delineated using a multi-lead wavelet-based approach [5], with updates in the derivative thresholds used to identify the onset and end of the QRS complex. For each cardiac beat, the following delineation marks were identified: QRS onset, QRS end, QRS fiducial point, T peak and T end. The RR interval was calculated from consecutive QRS fiducial points. For computation of a representative median beat, an RR histogram was built and the beats in a 20-ms RR bin containing the RR mode were selected. A preliminary median beat was calculated based on the selected beats. Subsequently, only those beats whose QRS complex showed a Pearson correlation coefficient with the QRS complex of the preliminary median beat greater than 0.95 were selected, and the final median beat was computed as the median of all of them. Figure 1 shows the post-implantation raw ECG signal, the preprocessed ECG signal without spikes and the beats selected to compute the median beat in lead V1 for one of the patients in the population.

2.4. ECG markers

ECG markers describing QRS and T wave characteristics measured in this work included: QRS duration (dQRS), QRS area (aQRS) and heart-rate corrected QT (QTc) and Tpeak-to-Tend (Tpec) intervals. dQRS was measured from QRS onset to QRS end in the computed median beat. aQRS was calculated as described in [6]. In brief, the 12-lead median beat was transformed into a 3-orthogonal-lead beat, with the Kors conversion matrix used to compute the vectorcardiographic leads X, Y and Z [7]. The area under the QRS complex was computed in each X, Y and Z lead and aQRS was defined as $\sqrt{X_{area}^2 + Y_{area}^2 + Z_{area}^2}$. The QT interval was defined as the interval between the QRS onset and T wave end and the Tpe interval as the interval between the T wave peak and T wave end. These intervals were measured from all selected beats and were heart-rate corrected by the Fridericia formula. The mean over beats was computed to provide QTc and Tpec intervals for each ECG recording.

The change between the basal and post-implantation states was calculated for each patient and each ECG marker. The following notation was used for the changes in the analyzed markers: ΔdQRS, ΔaQRS, ΔQTc and ΔTpec.

Table 1. Baseline characteristics of the study population. AV = atrioventricular; SSS = sick sinus syndrome; AF = atrial fibrillation; LBBB = left bundle branch block; RBBB = right bundle branch block; LHB = left hemiblock; IH = isolated hemiblock

Variables	LBBAP (n=52)	RVP (n=31)	P-value
Age, y (mean $\pm$ SD)	80 $\pm$ 9	75 $\pm$ 11	0.04
Male sex, n(%)	48	69	0.06
Hypertension, n(%)	87	75	0.18
Diabetes, n(%)	35	37	0.92
Dyslipidemia, n(%)	48	46	0.84
Pacing indications, n(%)			
Complete AV block	52	42	0.41
AV block grade II	23	31	0.42
SSS	22	17	0.55
AF	3	4	0.88
Syncope	0	4	0.26
Basal QRS, n(%)			
<120 ms	26	23	0.78
RBBB	13	23	0.26
RBBB+LHB	35	35	0.93
LBBB	23	15	0.41
IH	3	4	0.88
Cardiomyopathy, n(%)	84	85	0.93

2.5. Statistical analysis

Data is presented as mean ± standard deviation. Comparisons between post-implantation and basal states for each pacing technique were performed using Wilcoxon statistic test. Mann–Whitney U test was used to assess differences between stimulation techniques. χ^2 test was performed for comparisons in nominal data. P-values $<$ 0.05 were considered as statistically significant.

3. Results

3.1. Depolarization was more synchronized after LBBAP than after RVP

Significant differences (p<0.01) were observed in ΔdQRS and ΔaQRS between the two pacing techniques, as shown in Table 2. RVP led to a significant increase in dQRS with respect to the basal state (ΔdQRS: 13 ± 34, p=0.04) while LBBAP caused a significant reduction (ΔdQRS: -14 ± 27, p<0.01). Similarly, RVP increased aQRS (ΔaQRS: 51 ± 58, p<0.01) while LBBAP reduced it (ΔaQRS: -18 ± 49, p=0.03). Figure 2 shows the QRS complexes recorded before and after pacemaker implantation for a LBBAP and RVP patient with AV block with LBBB.

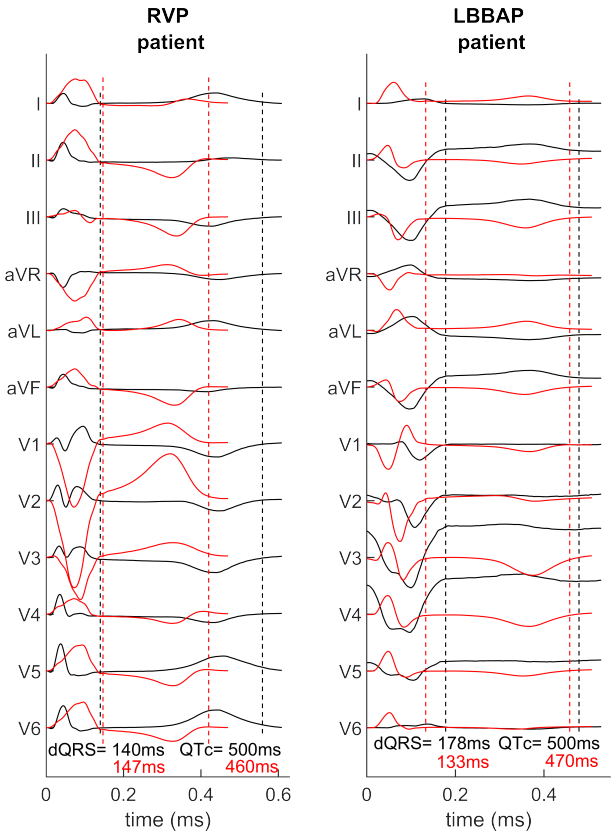

Figure 2. Calculated median beats before (black line) and after (red line) 24 hours of RVP and LBBAP.

3.2. RVP and LBBAP reduced QTc but not Tpec

Regarding repolarization characteristics, no significant differences were found when comparing ΔQTc (p=0.34) or ΔTpec (p=0.76) between the two pacing techniques. After pacemaker implantation, QTc decreased significantly in both the RVP (-22 ± 46, p=0.01) and the LBBAP (-27 ± 52, p<0.01) groups. Tpec did not significantly change for any of the two pacing techniques (ΔTpec in RVP: 7 ± 26, p=0.12,ΔTpec in LBBAP: 4 ± 26, p=0.09). Figure 2 illustrates the changes in the QTc intervals.

4. Discussion

This study shows that LBBAP, which paces the left bundle branch, improves cardiac synchrony by significantly reducing dQRS and aQRS with respect to basal state. On the contrary, conventional pacing via RVP is associated with increases in both depolarization markers. A wider QRS complex and/or with larger area reflects increased dispersion in the activation times of different ventricular regions. Therefore, a reduction in dQRS and aQRS after pacemaker implantation accounts for a more synchronized depolarization of the ventricles. By specifically stimulating the specialized cardiac conduction system with faster conduction velocity than the cardiac muscle, LBBAP leads to a more synchronous activation than RVP, which stimulates the ventricular muscle and is thus associated with slower propagation. These results are in accordance with [8] and with previous studies that have associated reduced dQRS and aQRS with better clinical outcomes [9], [10].

Regarding the effects of the two investigated pacing techniques on ventricular repolarization, we show that both are associated with moderate QTc shortening, with no significant differences between them. On the basis of previous studies showing an association between longer QTc interval and increased arrhythmic risk [11], our results could possibly point to both pacing techniques leading to beneficial effects. The Tpec interval did not significantly change after pacing with either LBBAP or RVP techniques, showing similar values both at baseline and at post-implantation in the two groups. Although the interpretation of Tpec is controversial, it has been related to ventricular repolarization dispersion, not necessarily restricted to transmural heterogeneities but more generally including other heterogeneities like apico-basal or inter-ventricular ones. While an increase in Tpec has been associated with higher arrhythmic risk [12], we could not find significant effects

Table 2. ECG markers at baseline (B) and after RVP or LBBAP (P) and associated changes. P-value* refers to baseline vs after pacing, P-value$^+$ refers to LBBAP vs RVP.

ECG markers (mean $\pm$ SD)	LBBAP (n=52)	RVP (n=31)	P-value$^+$
RR B, ms	1056 ± 350	1091 ± 299	0.62
RR P, ms	792 ± 131	826 ± 133	0.24
P-value*	$4{\times}10^{-7}$	$3{\times}10^{-5}$	-
ΔRR, ms	-264 ± 323	-264 ± 252	0.83
dQRS B, ms	142 ± 29	133 ± 26	0.15
dQRS P, ms	128 ± 17	147 ± 25	$3{\times}10^{-5}$
P-value*	$9{\times}10^{-4}$	0.04	-
ΔdQRS, ms	-14 ± 27	13 ± 34	$5{\times}10^{-4}$
aQRS B, μVs	75 ± 45	66 ± 39	0.61
aQRS P, μVs	57 ± 26	117 ± 66	$6{\times}10^{-6}$
P-value*	0.03	$8{\times}10^{-5}$	-
ΔaQRS, μVs	-17 ± 49	51 ± 58	$2{\times}10^{-6}$
QTc B, ms	476 ± 54	478 ± 51	0.70
QTc P, ms	449 ± 26	456 ± 28	0.29
P-value*	$2{\times}10^{-4}$	0.01	-
ΔQTc, ms	-27 ± 52	-22 ± 46	0.34
Tpec B, ms	100 ± 24	103 ± 21	0.51
Tpec P, ms	103 ± 11	109 ± 18	0.3
P-value*	0.09	0.11	-
ΔTpec, ms	4 ± 26	7 ± 26	0.76

induced by LBBAP or RVP. In a previous study, LBBAP and RVP were shown to lead to a slight reduction in Tpe [8], not corrected for the effect of heart rate as here, but, as in our study, with no differences in the induced effects between techniques.

5. Conclusion

By analyzing the width and area of the QRS complex of the ECG, we have shown that physiological pacing by LBBAP induces a faster and more synchronized ventricular activation than conventional RVP. We have not found any significant differences between the two pacing techniques in terms of repolarization characteristics, either analyzed by heart rate-corrected QT or Tpe intervals.

Acknowledgments

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