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ORIGINAL ARTICLE

Learning Curve for Left Bundle Branch Area Pacing – the Experience of a Romanian Academic Center

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ABSTRACT

Introduction: There is an increasing interest in the past decade for more physiological pacing strategies due to detrimental long-term right ventricular pacing. His bundle pacing is the most physiological one, but it has some drawbacks, mainly an increased pacing threshold. Left bundle branch area pacing (LBBAP) emerged in the recent years as the next step in conduction system pacing. We present our initial experience and learning curve with this latter procedure.

Material and methods: During January 2019 and February 2021, 20 patients with pacing indications that failed initial permanent His bundle pacing underwent successful LBBAP.

Results: The mean age was 65.9 ± 12.7 years. The indications for cardiac pacing were AV block in 14 patients (70%) and cardiac resynchronization therapy in 6 patients (30%). At baseline, normal QRS complex was noted in 9 patients, a left bundle branch block pattern in 10 patients and a right bundle branch block in one patient. A total of 18 dual-chamber and one single chamber pacemakers were implanted and a cardiac resynchronization therapy defibrillator (CRT-D) device. The acute pacing threshold was 0.56±0.2 V at 0.4ms, the sensing threshold was 10.3±3.9 mV and the impedance was 684.9±112.2 Ω. The overall QRS duration decreased after LBBAP from 128.5 ± 27ms to 103.6 ± 17.4ms (p= 0.001). In patients with baseline wide QRS complex there was a highly significant decrease from 148.2 ± 11.6 ms to 104.7 ± 19.4 ms (p<0.001). The fluoroscopy time, including the time spent for His bundle location, was 13.8 ± 8.5 minutes. The pacing thresholds remained constant after three-months (0.6 ± 0.2 V vs. 0.56 ± 0.2 V at 0.4 ms). We had two intraprocedural septal perforations without any consequences and three micro dislodgements at follow-up with pure left septal capture.

Conclusion: Left bundle branch area pacing is a feasible physiological pacing technique with a high success rate and the potential to overcome the limits of permanent His bundle pacing. It can be successfully performed virtually in all types of pacing indications, including cardiac resynchronization therapy as provides a rapid and synchronous activation of the left ventricle.

Keywords: left bundle branch area, cardiac pacing, learning curve.

REZUMAT

Introducere: În ultima decadă s-a înregistrat un interes crescut pentru noi strategii de stimulare cardiacă fiziologică, pentru a evita efectele detrimentale ale stimulării pe termen lung a ventriculului drept. Stimularea permanentă a fasciculului His este cea mai fiziologică, dar are anumite dezavantaje, cum ar fi un prag de pacing crescut. Prin urmare, stimularea ariei ramului stâng a apărut ca următorul pas logic în stimularea sistemului de conducere. Prezentăm în această lucrare experiența noastră inițială și curba de învățare cu stimularea ariei ramului stâng.

Material și metodă: În perioada ianuarie 2019 și februarie 2021, 20 de pacienți cu indicație de cardiostimulare permanentă și tentativă eșuată de stimulare a fascicului His au fost supuși cu succes stimulării permanente a ariei ramului stâng.

Rezultate: Vârsta medie a pacienților a fost 65,9 ± 12,7 ani. Indicațiile de cardiostimulare permanentă au fost bloc atrioventricular la 14 pacienți (70%) și resincronizare cardiacă la 6 pacienți (30%). Un total de 18 stimulatoare bicamerale, un stimulator monocameral și un defibrilator tricameral au fost implantate. Un complex QRS normal a fost observat la 9 pacienți, un aspect de bloc de ramură stângă a fost observat la 10 pacienți și un aspect de bloc de ramură dreaptă la un singur pacient. Pragul de stimulare a fost 0,56±0,2 V la 0,4 ms, detecția a fost 10,3±3,9 mV și impedanța a fost 684,9±112,2 Ω. Per total, durata complexului QRS a scăzut de la 128,5 ± 27 ms la 103,6 ± 17,4 ms (p= 0,001). La pacienții cu complex QRS bazal larg s-a înregistrat o reducere înalt semnificativă de la 148,2 ± 11,6 ms la 104,7 ± 19,4 ms (p<0,001). Timpul de fluoroscopie, incluzând și timpul folosit pentru căutarea fasciculului His, a fost de 13,8 ± 8,5 minute. Pragul de pacing a rămas constant la controlul de trei luni (0,6 ± 0,2 V vs. 0,56 ± 0,2 V la 0,4 ms). S-au înregistrat două perforări intraprocedurale ale septului interventricular fără consecințe clinice

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și trei microdepoziționări în evoluție soldate cu pierderea capturii sistemului de conducere și stimulare pur septală.
Concluzie: Stimularea ariei ramului stâng este o tehnică de stimulare fiziologică fezabilă, cu un succes procedural ridicat și cu potențialul de a depăși obstacolele apărute la stimularea fasciculului His. Poate fi efectuată practic la toți pacienții, inclusiv la cei cu indicație de resincronizare cardiacă, deoarece produce o activare rapidă și sincronă a ventriculului stâng.
Cuvinte cheie: aria ramului stâng, stimulare cardiacă, curba de învățare.

INTRODUCTION

It is widely accepted nowadays that long-term right ventricular pacing is detrimental for left ventricular function. Therefore, an increasing interest has emerged in the past years for more physiological pacing strategies. Out of these, His bundle pacing is undoubtedly the most physiological, but global acceptance of this procedure amongst practitioners has been limited due to concerns regarding high chronic pacing thresholds and low success rates in more distal conduction diseases. A new procedure that aims to pace transseptally the left bundle branch area has recently been proposed to overcome these concerns. This retrospective observational study presents our initial experience with left bundle branch area pacing (LBBAP).

MATERIAL AND METHODS

Between January 2019 and February 2021, 20 patients with pacing indications that failed initial permanent His bundle pacing underwent successful LBBAP. The procedural technique used was the one described by Huang in 2017[1]. In brief, a lead delivery system consisting of a C315 His sheath and a 3830 Select Secure lead (Medtronic, Minneapolis) was initially placed at the septal AV junction, where we searched for a His bundle signal. If we could not find the His bundle signal or if the His pacing threshold was higher than 3V/1 ms, we moved on to LBBAP. The His bundle location was stored as a fluoroscopic reference and the C315 sheath was moved to the basal ventricular septum, 1.5-2 cm towards the right ventricular apex. The "ideal", but not necessarily the only one, site to start screwing the lead was the one where pacing the RV septum resulted in a "W" pattern in V1 and a polarity discordance in DII and DIII (R wave in DII taller than R wave in DIII) and aVL and aVR (positive in aVL and negative in aVR) (Figure 1). At this site, in the LAO projection, a counterclockwise torque was kept on the sheath to maintain perpendicularity on the septum and the lead was rapidly screwed manually, while checking the fluoroscopy for advancement deep into the septum. After several turns, the paced QRS morphology and impedance was again analyzed. As the lead penetrates the septum, the impedance gradually increases and when it reaches the left side of the septum slightly decreases. Lead advancement was stopped when a qR or RBBB pattern was observed in lead V1 (Figure 2).

Successful left bundle branch pacing (as opposed to left ventricular septal pacing) requires several criteria to be met, as was previously described in the literature[2]: 1) a change in paced QRS morphology from LBBB pattern to RBBB; 2) Presence of a LBB potential; 3) The left ventricular activation time (LVAT) suddenly shortens with increasing pacing amplitudes or remains short (<90 ms) at high and low amplitudes; and 4) demonstration of selective and/or nonselective LBB capture (Figure 3). We considered that the left bundle branch was captured if two of the above criteria were met.

To verify deep septal penetration during the procedure, we injected contrast through the sheath, which delineates the right side of the septum and gives a decent estimate of the length of penetration (Figure 4).

After the lead position was accepted, the sheath was slit and the lead was fixed to the pectoral muscle. The rest of the procedure (other leads and generator placement) continued as usually.

After the procedure, in all patients, the depth of penetration was also assessed with echocardiography (Figure 5).

Patient and procedural characteristics were evaluated during the procedure and at three months follow-up to assess feasibility and success of the procedure.

Continuous variables were reported as means ± standard deviation and categorical variables were reported as counts and percentages. Differences between groups were calculated with the *Student's t*-test or 2-tailed Fisher exact test for continuous and categorical variables, respectively. A p value < 0.05 was considered statistically significant.

RESULTS

The patient and procedural characteristics are presented in Table 1.

The mean age was 65.9 ± 12.7 years with a preponderance of male sex (60%). The indications for cardiac

Figure 1. The „ideal" site to start penetrating the septum is where pacing results in a „W" pattern in V1 and polarity discordance in DII vs. DIII and aVL vs. aVR. (His d channel records the electrograms from the pacing lead tip).

pacing were AV block in 14 patients (70%) and cardiac resynchronization therapy in 6 patients (30%). One patient with AV block was in permanent atrial fibrillation. At baseline, normal QRS complex was noted in 9 patients, a left bundle branch block pattern in 10 patients and a right bundle branch block in one patient. A total of 18 dual-chamber and one single chamber pacemakers were implanted and a CRT-D device.

The baseline mean ejection fraction of the patients was 44±16 %. The acute pacing threshold was 0.56±0.2 V at 0.4 ms, the sensing threshold was 10.3±3.9 mV and the impedance was 684.9±112.2 Ω.

Figure 2. A Qr pattern in V1 indicates that the lead tip has reached the left side of the septum and the screwing should stop (His d channel records the electrograms from the pacing lead tip).

Figure 3. The lead is placed deep into the septum where a left bundle potential is recorded (black arrow). Pacing at this site results in a narrow QRS complex with a RBBB morphology and a short LVAT, similar to the one in sinus rhythm (His d channel records the electrograms from the pacing lead tip).

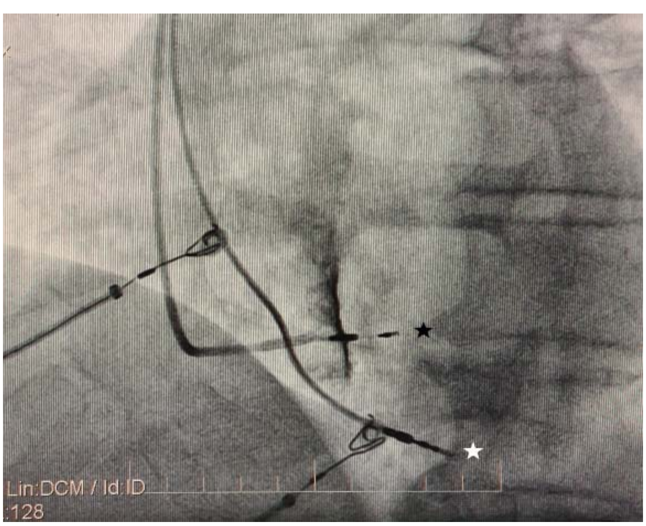

Figure 4. Left anterior oblique (LAO) fluoroscopy image. Contrast injected through the sheath delineates the right side of the septum and gives an estimate of the depth of penetration of the pacing lead (black star). Another pacing lead was placed for back-up pacing at the RV apex (white star).

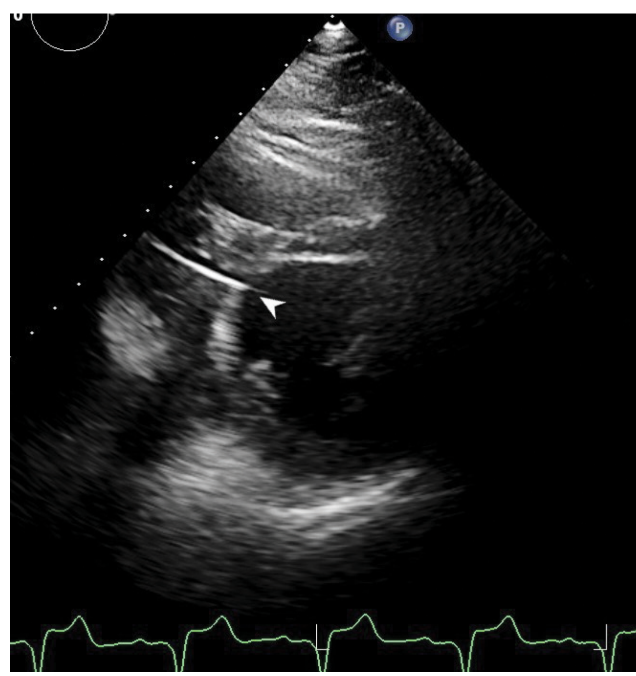

Figure 5. Parasternal short axis echocardiographic view showing the lead tip (white arrow) reaching the LV endocardium.

The overall QRS duration decreased with LBBAP from 128.5 ± 27 ms to 103.6 ± 17.4 ms (p=0.001). There was no difference between preprocedural and postprocedural QRS duration in patients with normal baseline QRS, but in patients with baseline wide QRS complex there was a highly significant decrease from 148.2 ± 11.6 ms to 104.7 ± 19.4 ms (p<0.001) (Figure 6).

The fluoroscopy time, including the time spent for His bundle location, was 13.8 ± 8.5 minutes and the

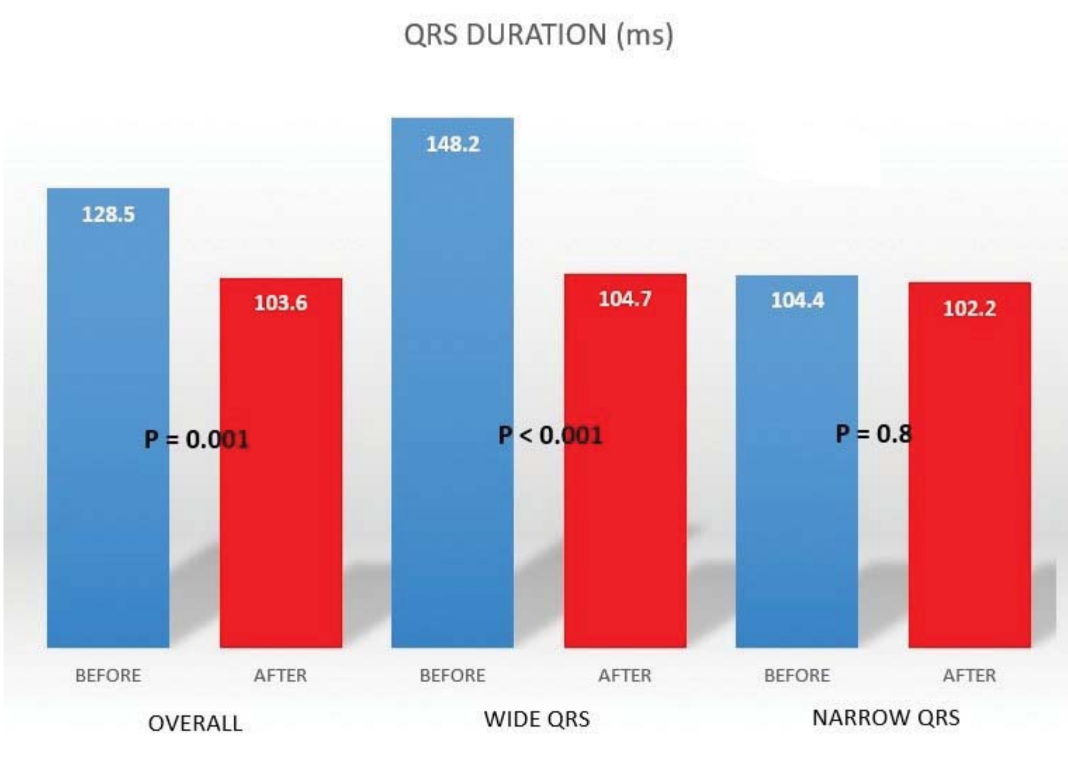

Figure 6. QRS duration before and after the procedure.

Table 1. Patient and procedural characteristics

Patient characteristics	Nr. (%)
Age	65.9 ± 12.7 years
Male sex	12 (60)
Mean Ejection Fraction (%)	44±16
Pacing indications	
AV block in sinus rhythm	14 (65)
Cardiac resynchronization therapy	6 (30)
Slow conducting atrial fibrillation	1 (5)
QRS aspect	
Normal	9 (45)
Left bundle branch block (LBBB)	10 (50)
Right bundle branch block (RBBB)	1 (5)
Procedural characteristics	**Nr. (%)**
Device implanted	
Dual chamber pacemaker	18 (90)
Single chamber pacemaker	1 (5)
CRT-D device	1 (5)
Procedural parameters	
Pacing threshold (V/0.4 msec)	0.56±0.2
Detection (mV)	10.3±3.9
Impedance (Ohm)	684.9±112.2
Fluoroscopy time (min)	13.8±8.5

total procedural time was 135± 37 minutes. The fluoroscopy time spent during the first 10 cases was significantly longer than the time during the last 10 cases (17.70 ± 10.3 vs. 9.9 ± 3.7 minutes, $p = 0.037$) (Figure 7). Also, the total procedural time improved during the last 10 cases (155 ± 41 vs. 115 ± 16 minutes, $p = 0.015$).

The QRS morphology and the pacing thresholds remained constant at the three-month follow-up (0.6 ± 0.2 V vs. 0.56 ± 0.2 V at 0.4 ms).

Regarding lead related complications, we had two intraprocedural septal perforations, evident on left anterior oblique fluoroscopy as free lead advancement in the left ventricle past the septum, managed with lead and sheath retraction and fixation at another site without any consequences.

There were also three micro dislodgements at follow-up, which resulted in loss of conduction system capture and pure LV septal pacing (the above-mentioned criteria for LBBAP was no longer met).

DISCUSSION

Right ventricular pacing causes significant electrical dyssynchrony, which may lead to a decrease in left ventricular ejection fraction[3]. The so-called pacing in-

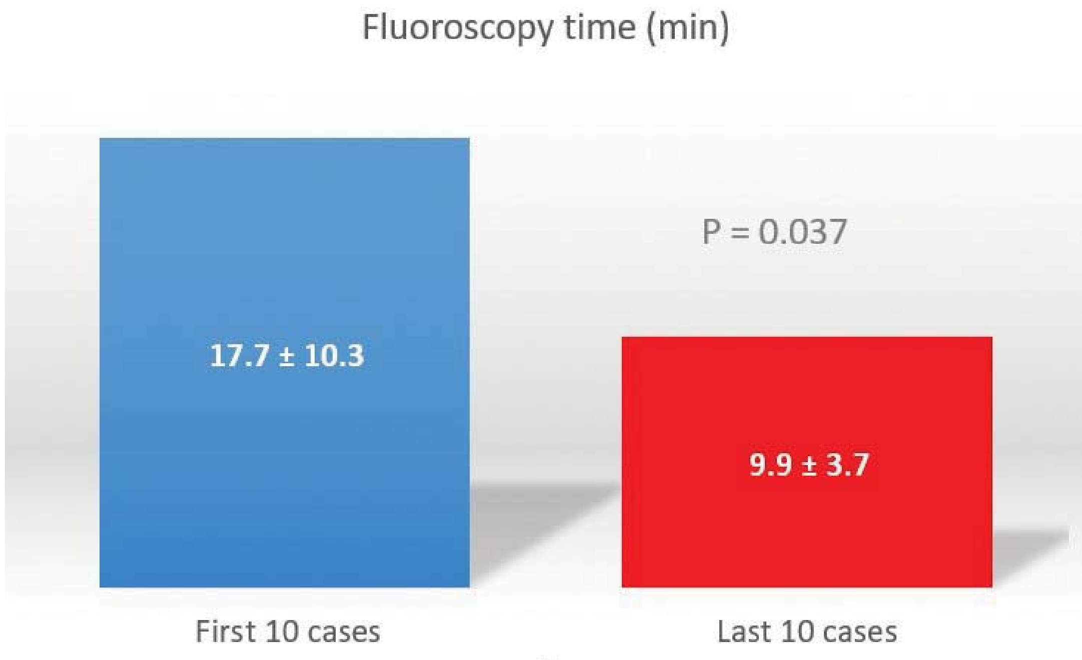

Figure 7. Comparison of the fluoroscopy time between the first and the second half of the procedures.

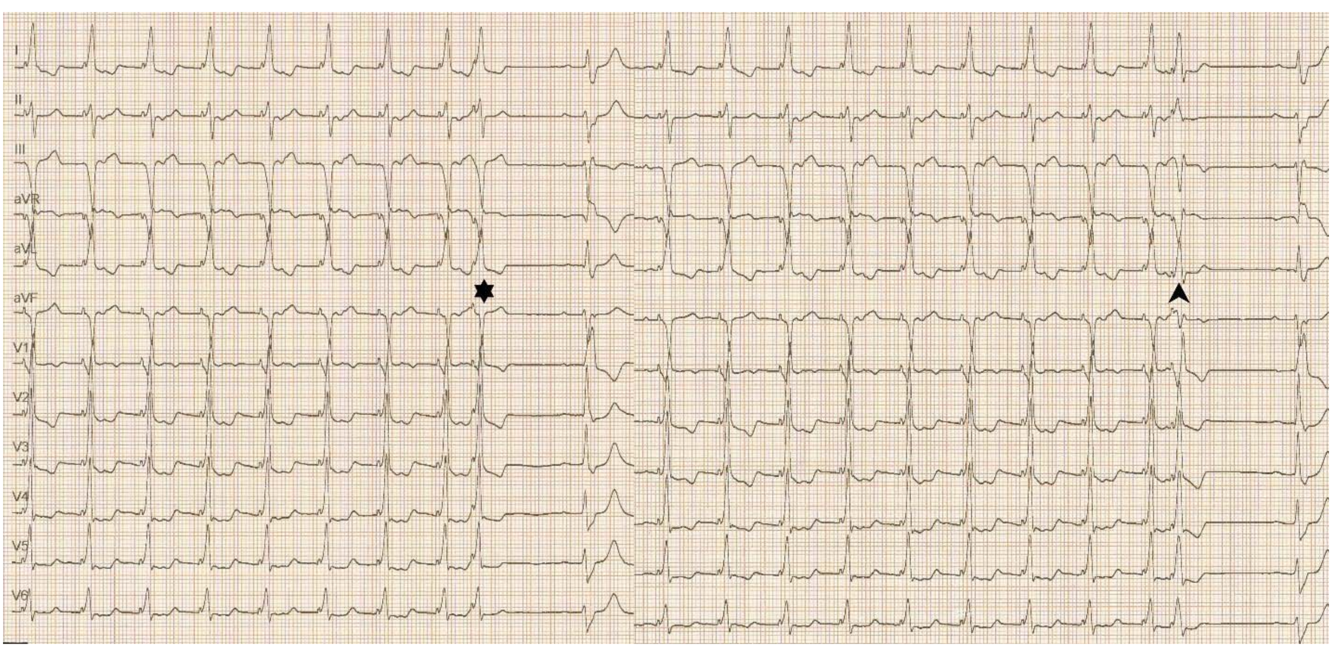

Figure 8. Differential extrastimulus pacing to demonstrate nonselective left bundle branch capture. After a drive train of 8 beats at 600 ms, an early extrastimulus (black star) results in a similar morphology to the one in the driving train. An even earlier extrastimulus (black arrow) results in a different morphology (more obvious in DII, DIII and V1) as the refractory period of one structure is encountered (see text for details).

duced cardiomyopathy was observed in up to 20% of the chronically paced patients and it is dependent on the burden of ventricular pacing as well as other parameters like baseline ejection fraction and paced QRS duration[4].

Permanent His bundle pacing achieves the almost perfect ventricular electrical synchronization because it uses both intrinsic bundle branches for concomitant biventricular activation. However, the most encountered problem with this type of pacing is a higher procedural pacing threshold and a risk for further increase during follow-up, which may lead to premature device battery depletion[5]. In addition, the success rate is much lower in cases of distal His-Purkinje disease, like infrahisian AV block and bundle branch block[6]. For these reasons, with the concept of conduction system pacing in mind, left bundle branch pacing seems the next logical pacing site that may overcome the above listed problems.

The advantage of LBBAP is that it uses the same tools needed for His bundle pacing, so if one procedure fails one can move to the other in the same setting. Furthermore, due to proximal extensive branching of the left bundle, the area available for capture is significantly larger than in the case of the His bundle or the right bundle branch[7].

In all of our patients we have attempted first His bundle pacing and then, if unsuccessful, we moved on to LBBAP.

As mentioned before, in order to correctly label a procedure as LBBAP, several criteria have to be met. During our first cases we evaluated the QRS pattern in V1, the QRS duration and the QRS complex morphology at both high and low pacing amplitudes. As we gained more experience and newer definitions emerged in the literature, we started looking for left bundle branch potentials as well as, measuring the LVAT and we performed differential pacing in all patients. This last method, elegantly described by Jastrzębski et al.[8], is based on the difference in refractoriness between the conduction system and working myocardium and uses the extrastimulus technique. If there is nonselective LBB pacing, the earlier an extrastimulus is introduced, the higher the chance to encounter the refractoriness in one of the structure, so the resulting QRS morphology is different from the driving train (Figure 8).

Studies comparing left ventricular electrical activation showed that LBBAP achieves similar patterns to His bundle pacing and far better than right ventricular pacing[9].

In our patients we achieved QRS duration comparable with His bundle pacing and significantly shorter than conventional right ventricular apical pacing. However, the pacing and sensing thresholds were far better when compared to His bundle pacing, leading to an important impact on battery longevity.

In patients with baseline wide QRS complex, there was a significant reduction after LBBAP, consistent with published literature. Our study was designed to look at the feasibility and success of the procedure, so we didn`t incorporate the LV function at follow-up in the analyses, but there is already significant data showing improvement in LV function with LBBAP. This is another argument for the important role of conduction system pacing in cardiac resynchronization therapy[10].

The major advantage of this procedure is that it can be performed successfully in virtually all patients regardless of the baseline rhythm or pacing indication. Feasibility studies have shown a success rate of more than 90%[11]. There are occasionally situations in which the lead would not penetrate the septum (fibrosis or lead entanglement) but usually choosing another site, more apically, solves the problem.

Similar to any other procedure, one must go through a learning curve, but, as we found out, it is not very difficult, so after understanding the theory behind it and performing a few cases, there is an improvement in all procedural aspects.

The most common lead related complications are micro dislodgement of the lead resulting in septal capture, macro dislodgement of the lead and septal perforation[12].

In our series we encountered two intraprocedural septal perforations, which were managed with lead and sheath retraction and fixation at another site without any consequences.

We had no macro dislodgements, but we had three micro dislodgements at follow-up with pure septal capture. Because these patients had normal LV function and the myocardial pacing threshold was low (similar to the intraprocedural ones), lead revision was not necessary.

Nevertheless, the technique is young and there is no long term experience yet. There are justifiable questions about lead extraction and the potential to create a septal defect in that area and about the thromboembolic risk if a part of the helix is protruding in the left ventricle[13].

So far, the technique appears to be safe and efficient, but a longer follow-up period is required to conclude its long-term benefits and pitfalls.

CONCLUSION

Left bundle branch area pacing is a feasible physiological pacing technique with a high success rate and the potential to overcome the limits of permanent His bundle pacing. It can be successfully performed virtually in all types of pacing indications, including cardiac resynchronization therapy, as provides a rapid and synchronous activation of the left ventricle. Future randomized studies are further required to establish this technique as a standard of practice.

Compliance with ethics requirements:

The authors declare no confl ict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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