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Mini Review

Pacing-Induced Cardiomyopathy: Long-Term Retrospective Study of Superficial Right Ventricular Mid-Septal Pacing

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ABSTRACT

Pacing Induced Cardiomyopathy (PICM) can be a significant problem with long term right ventricular pacing, especially from the apex. It is unclear if PICM may be minimized by standard pacing of the Right Ventricle (RV) at sites other than the RVA. The purpose of our recent study was to compare the relative frequency of PICM in a population of patients paced at either the superficial RV Mid Septum (RVMS) or RV Apex (RVA) and other outcomes that may differ between these sites.

A retrospective evaluation was performed on all patients undergoing pacemaker implantation between 2011 and 2022. Potential study patients were those with Medtronic 3830 superficial RVMS leads placed with a septal specific guidance catheter and any with RVA leads. Patients were included if they had >20% RV pacing, available baseline and follow-up measurements of Left Ventricular Ejection Fraction (LVEF) at least 6 months post implantation and a baseline LVEF>50%. PICM was defined as a decline in the LVEF of at least 10%, resulting in LVEF<50%. Patients were excluded for biventricular devices and for alternative causes of cardiomyopathy.

The study criteria were met in 220 RVMS and 104 RVA paced patients. PICM occurred in 4.5% of RVMS patients and 22.1% of RVA patients (p<0.001). Additionally, the paced QRS duration was significantly shorter in the RVMS group (144+15.5 msec in RVMS, 166+19.4 msec in RVA; p<0.001) and the QRS axis was more normal (2.3+64.9 in RVMS, -65.2+49.5 in RVA; p<0.001).

Patients with normal LVEF experienced significantly less PICM with superficial RVMS pacing performed *via* septal specific guidance catheters than similar counterparts with RVA pacing. Narrower paced QRS duration and less left axis deviation was also demonstrated.

Keywords: Pacing induced cardiomyopathy; Right ventricular mid septal pacing; Right ventricular apical pacing; Cardiomyopathy

INTRODUCTION

Pacing Induced Cardiomyopathy (PICM) limits the benefit of chronic Right Ventricular (RV) pacing in a significant number of patients [1]. Almost two decades ago attempts at selective site RV pacing were undertaken, but failed to show clear benefits [2-5]. Recent efforts to limit this complication have centered on conduction system pacing [6]. However, these approaches can be complex and require a higher level of expertise, time and equipment. Routine His bundle pacing has now been abandoned by many electrophysiologists due to multiple issues. Left Bundle Branch Area Pacing (LBBAP) has become the new area of intense interest and utilization, but the Multicentre European Left Bundle Branch Area Pacing Outcomes Study (MELOS) registry has documented an ongoing 8.3% complication rate specific to LBBAP [7]. Concerns also continue

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to exist for new and possibly increased long term negative consequences, especially lead durability [8].

In the mid to late 2000s I was an investigator for the Optimize RV selective site pacing trial (Optimize RV), which targeted the RV Mid Septum (RVMS) [9]. Unfortunately, the study was prematurely closed by the sponsor due to low enrollment. The author continued utilizing the RVMS technique as the preferred approach for RV pacing in my large clinical pacing practice, utilizing a lumen-less active fixation lead (Medtronic 3830). The initial deflectable sheath was quickly replaced with a septal specific guidance catheter. However, multiple episodes of limited availability of the 3830 lead resulted in frequent reversion to traditional RVA pacing over the same time period. The author experience with superficial RVMS pacing suggested significant mitigation of PICM was being achieved compared to the published incidences and anecdotal reports of results from other centers. A long-term retrospective investigation of a large population of patients with normal left ventricular function was undertaken to explore this potential reduction of PICM with superficial RVMS *vs.* RVA pacing, which we have recently published [10]. We add the term superficial to differentiate this technique from LBBAP, which drives the pacing lead tip deep into the septum. This investigation concluded that patients with normal left ventricular function experienced significantly less PICM with superficial RVMS pacing than similar counterparts with RVA pacing (Figure 1). Narrower paced QRS duration and less left axis deviation was also demonstrated.

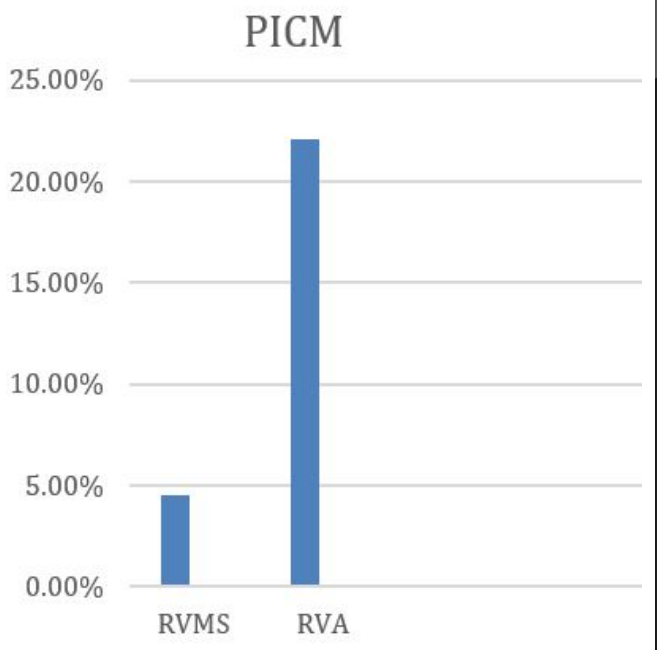

Figure 1: Prevalence of pacing induced cardiomyopathy in the two pacing populations, p<0.001.

LITERATURE REVIEW

Left ventricular dysfunction with chronic RV pacing was identified in the 1990s [11]. Early attempts to manage the problem included new programming options to minimize ventricular pacing, which remain an important standard today [12]. While this removed the issue of pacing induced left ventricular dysfunction from patients with isolated sinus node disease and low levels of atrioventricular conduction disease, it remains an issue for those requiring significant RV pacing.

Attempts to prevent or minimize left ventricular dysfunction then shifted to alternative site RV pacing, primarily septal pacing. In the mid to late 2000s, three large prospective randomized trials were designed and initiated to answer this issue: Optimize RV Selective Site Pacing Trial (Optimize RV), right ventricular apical and high septal pacing to preserve left ventricular function (Protect Pace) and Right Ventricular Apical *versus* Septal Pacing (RASP) [9]. Unfortunately, only the Protect Pace study was ever completed and reported no protective effect of RV High Septal pacing on left ventricular function over two years [13]. However, the study was limited by difficulty in accurate septal lead placement and with significant patient data drop out. Additionally, it did not target the RV Mid Septum (RVMS). Multiple other studies (most quite small) have been reported targeting the RV septum and other nonapical sites. Some have shown possible mild improvement in some parameters or limited end points and in selected populations, but systematic reviews have not concluded any clear advantage [2-5]. Additionally, none of these studies have examined the specific incidence of PICM in these differently paced populations. They generally compared differences in the group mean LVEF as the primary end point.

PICM was described and quantitated after most of these studies were initiated. Multiple different definitions for PICM were utilized in multiple reports and thus a wide range in the frequency was reported [1]. The definition of PICM that became the accepted norm was a reduction in Left Ventricular Ejection Fraction (LVEF) of at least 10%, with a resulting LVEF of <50% [6]. We have applied this definition for our study and limited our study population to those with significant RV pacing burdens, as these are the highest risk group. We chose PICM as the major endpoint for our study, believing that the patient level diagnosis of PICM was the most important end point which needs to be addressed by improved pacing techniques.

Additional approaches to minimize PICM were undertaken, including formal biventricular pacing [14]. Currently many centers are promoting newer approaches to provide more physiologic cardiac pacing for patients requiring substantial RV pacing, such as His bundle pacing and Left Bundle Branch Area Pacing (LBBAP). These approaches have now been recognized and formalized as a class 2b recommendation for patients with normal baseline left ventricular function "who are expected to require substantial RV pacing" [6]. However, these approaches can be complex and require a higher level of expertise, time and equipment. Additionally, there are no universally accepted criteria for what constitutes true LBBAP. Concerns also continue to exist for new and possibly increased long term

negative consequences from these new approaches compared to classical RV pacing [6,8]. Finally, Recent data from leadless pacing systems, which specifically target the RV septum (and generally the mid septal region), have shown low prevalences of PICM [15,16]. One of these studies has shown that a mid to high septal location for pacing, as opposed to apex or apical septum, is associated with a lower prevalence of PICM [16].

DISCUSSION

Our recently published results demonstrate a significant reduction in the prevalence of PICM in our RVMS cohort compared to RVA pacing and is the first report to clearly document this. Why do we believe our new data has plausible validity, when multiple prior studies of standard selective site pacing have failed? First and foremost, we believe that our success in septal placement was paramount. This is not due to special skills, but to the use of a septal specific delivery catheter (the Medtronic C315His). Prior studies have either not utilized such a catheter, or utilized it partially as one of several approaches, not as the dedicated method. Specific septal placement has historically been quite difficult and has clearly limited prior studies [13,17]. However, a recent study has indicated significantly better success with true septal placement using this same guide catheter [18]. Without a high percentage of actual septal placement, the benefits of true septal pacing cannot be demonstrated. In addition to our radiographic evidence of septal placement, which has known limitations, our mean paced QRS duration of 144 msec is further indication of successful septal placement, allowing recruitment of the native conduction system. This QRS duration is quite similar to that reported by the MELOS study for LBBAP (137+19 msec with narrow baseline QRS, 145+22 msec for baseline bundle branch blocks or conduction abnormalities) [7]. Also, the above mentioned leadless data add further credibility to septal pacing as a valid way to minimize PICM.

Additionally, we believe that the patient level diagnosis of PICM is a more appropriate endpoint to evaluate for improved outcomes with different pacing techniques. Prior studies have all evaluated differences in group level left ventricular function. We instead chose the relative incidence of PICM, believing it is the most important end point which needs to be addressed by improved pacing techniques. While our group level LV function measures only trended towards improvement in the RVMS group, the difference in PICM was quite clear. It is after all, the diagnosis of PICM in the individual patient that indicates the need for any new therapy or intervention (CRT). Finally, we have also reported the largest number of paced patients and have longer duration of follow up than most studies.

Clearly our study is not prospective, nor randomized. However, it is an extremely large patient experience of excellent outcomes for greater that 10 years. While not randomized, physician driven bias was minimized due to the manner of selection of the patients to be paced *via* the RVA. The preferred lead during this entire time frame was the 3830 and it was placed at the superficial RVMS. Unfortunately, this lead faced recurring production and availability limitations. These issues were clearly out of the physicians' hands, but provided an unusual and unexpected randomness to the lead and the site chosen for patients requiring RV pacing over that time.

Finally, why not just accept LBBAP as the new answer to the issue of PICM in all RV paced patients? The answer is both the problem of complications and the reports of some continuing incidence of PICM with LBBAP [7,19,20]. While select group reports indicate low incidence of complications, the very large multicenter MELOS study indicates something very different. Along with limited success at implantation, they also report a high incidence of 8.3% acute complications directly related to LBBAP [7]. We experienced low incidences of lead dislodgement and few chronic pacing threshold elevations. We avoided any known coronary or intracardiac vascular complications. The concern of long term lead durability and potential extractability also remain to be clarified, but early issues are being reported [8]. As yet, there are also no prospective randomized trials of LBBAP demonstrating better long term outcomes.

CONCLUSION

The study shown that in patients with normal left ventricular function, superficial RVMS pacing performed with a septal specific guidance catheter experienced significantly less PICM than those with RVA pacing. There was an almost 5 fold reduction in PICM with this approach. If confirmed by further studies, we believe that superficial RVMS pacing, utilizing septal specific lead delivery catheters, should be reconsidered as a preferred initial pacing strategy for patients with normal LV function. This approach uses available standard leads and delivery systems, has excellent long term lead function and has resulted in extremely good clinical outcomes over greater than 15 years. While LBBAP is rapidly being adopted, serious questions remain. Superficial RVMS pacing can provide an extremely low incidence of PICM, potentially obviating the need for highly specialized LBBAP in the general pacing patient or population.

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