Review Article

Alternative Endocardial Sites for Artificial Cardiac Stimulation

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Abstract

The conventional right ventricular stimulation can be associated with deleterious effects on cardiac function. The need for a more physiological artificial cardiac stimulation is undoubtedly one of the most important points in the area of cardiac electrotherapy. The programming algorithms for the maintenance of adequate atrioventricular conduction, the stimulation of alternative endocardial sites and the cardiac resynchronization therapy are used with the objective of attaining these goals. The stimulation of the bundle of His and the septal stimulation have been studied as alternative endocardial sites for the positioning of the electrode on the right ventricle. The septal stimulation represents a simple and practical alternative, with no additional costs involved and with potential benefits in decreasing the deleterious effects of the right ventricular stimulation.

However, this alternative site involves a heterogeneous group of patients and presents conflicting results regarding its long-term clinical benefit.

This article reviews the scientific evidence on the alternative sites for right ventricular stimulation, with emphasis on the safety of the procedure, the measurement of the electrophysiological parameters, assessment of the left ventricular function and the clinical follow-up of patients.

Introduction

At the age of cardiac resynchronization, the anti-bradycardia therapy, through the implant of conventional pacemaker, still represents the largest number of procedures carried out in the area of artificial cardiac stimulation[1]. Since the beginning of the endocardial cardiac stimulation in 1958[2] and for more than 4 decades, the prolonging of life by implanting an electrode in the right ventricle apex, due to its accessibility and lower risk of complications, has represented the therapeutic scope.

Since the 1980s, there has been evidence of the deleterious effects of the long-term apical stimulation of the right ventricle (RV)[3-6]. In the last 12 years, several studies have been carried out with the objective of finding alternative sites for the implant of electrodes in RV endocardial stimulation. The region of the bundle of His[7-12], the right ventricular outflow tract (RVOT)[13-23] and the mid-septal region[24-26] have been assessed.

Most studies involved a small sample size, without randomization, and the criteria used to define the stimulation site might have led to the assessment of heterogeneous groups. Likewise, different methods have been used to evaluate the functional outcome of cardiac stimulation.

Therefore, in spite of the demonstration of the deleterious effects of the RV apical stimulation and potential benefits of the alternative sites, conflicting results have been reported and the site of choice for the implant of the right ventricular electrode is yet to be defined.

The objective of this study is to analyze the alternative sites for artificial cardiac stimulation in the context of evidence-based cardiology.

Historical aspects of artificial cardiac stimulation

The heart-stimulating complex results from a process of cell specialization and reflects the efforts of millions of years in phylogenetic evolution for the maintenance of life.

Naturally, the substitution of components of this conduction system, with the maintenance of its properties, has always constituted a huge challenge in the field of cardiac electrotherapy.

Ever since the first experimental studies, the differences between the artificial stimulation and the physiological activation have not gone unnoticed[27,28]. In 1924, Wiggers demonstrated that the artificial stimulation results in a decreased pumping function, in an experimental dog model[28].

The age of cardiac endocardial stimulation started in August 1958, when Seymour Furman described the transvenous pacemaker implant technique[2]. In October of the same year, in Sweden, the first definitive endocardial pacemaker implant was performed[29].

The transvenous access started to substitute the epicardial access in pacemaker implants, allowing the procedures to be carried out without thoracotomy and general anesthesia. The positioning of the electrode started to be carried out under radioscopic guidance, with the help of the radiological anatomy.

For more than 4 decades, the apex of the right ventricle (RV) was used worldwide as the preferential site for the positioning of the ventricular electrode[30] (Figure 1). This fact was due mainly to safety reasons. Due to the incipient technology used in the manufacturing of the electrodes, there was a higher risk

Keywords

Pacemaker, artificial; septal stimulation; ventricular function, left.

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Manuscript received October 21, 2009; revised manuscript received October 26, 2009; accepted November 30, 2009.

of dislocation, cardiac perforation, threshold increase and consequent loss of command. The electrodes, then affixed passively, were well-anchored in the apex, with a favorable curvature and decreased risk of dislocation.

After the 1980s, the first experimental evidence on the deleterious effects of the apex stimulation of the RV appeared[3-6]. Subsequently, in the 1990s, the first clinical studies comparing the conventional position with alternative sites of stimulation were published and the site of choice for RV stimulation in the conventional pacemakers has yet to be defined[31].

Scientific evidence of the deleterious effects of the unifocal right ventricular stimulation

The narrow QRS complex is crucial for the cardiac function and its enlargement causes significant damage to the left ventricular function[32-35]. In general, the narrower the QRS complex, the better the left ventricular function[36].

In spite of the safety of positioning the ventricular electrode in the apex of the RV for the correction of bradyarrhythmias, observed along the decades, the studies on the functional outcome and clinical follow-up started to demonstrate the deleterious effects of this positioning and indicated the need to reassess the preferential site for endocardial stimulation[37-54]. The technological development applied to the manufacturing of the electrodes represented a vital ally in the search for alternative positions, bringing safety to the process of change.

The stimulation of the apex of the right ventricle promotes an inversion of the natural sequence of cardiac electrical activation, generates an artificial left bundle branch block (LBBB), with an enlarged QRS complex, which is a predictor of heart failure in individuals with definitive pacemakers[55-57]. These alterations promote adverse effects on the ventricular structure and function (Chart 1) and can cause or aggravate mitral regurgitation[38,39], increase the risk of atrial fibrillation (AF), heart failure (HF) and increase mortality[41-47] in patients with systolic dysfunction.

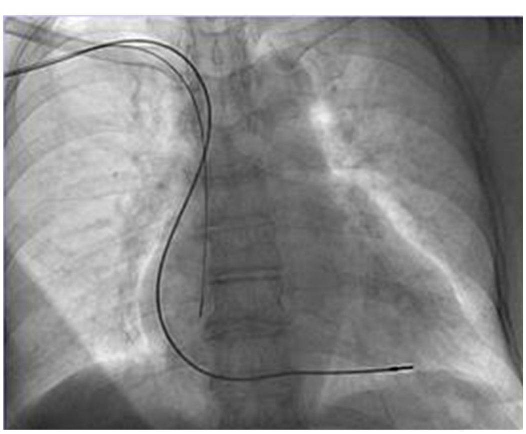

Figure 1 - Radioscopic image in the posteroanterior (PA) view of the electrode positioning at the apex of the right ventricle, during definitive pacemaker implantation.

In a retrospective analysis of the MOST (Mode Selection Trial) study, it was demonstrated that the risk of hospitalization due to HF and AF is directly associated with the cumulative percentage of stimulation in the RV apex[44].

The DAVID (The Dual Chamber and VVI Implantable Defibrillator) trial was unexpectedly discontinued due to the increase in HF and mortality in the group with a predominance of ventricular stimulation (DDDR mode at 70 bpm). In the control group, the ventricular stimulation was maximal, as the pacemaker was programmed at VVI, with a frequency of 40 ppm. Thus, the deleterious effect of the unifocal ventricular stimulation was demonstrated[41,47]. The analysis of the MADIT II study showed a correlation between the level of stimulation of the RV and HF, ventricular arrhythmias and mortality[49].

Zhang et al[58] demonstrated that the RV apex stimulation was associated with the development of HF in 26% of the patients submitted to pacemaker implant due to acquired AV block, after a mean follow-up of 7.9 years.

The structurally normal heart, without systolic dysfunction, can even be capable of compensating these deleterious effects[51]. A study of 268 patients with normal systolic function (EF > 55%) and apical stimulation of the RV due to total AV block, showed low rates of ventricular remodeling (5.3%), during a follow-up period of 80.2 months[58]. In patients with systolic dysfunction and heart failure, symptoms can appear, as well as heart failure decompensation, with the apical stimulation of the right ventricle[51].

With the objective of attaining a more physiological stimulation, the strategies for the maintenance of adequate atrioventricular (AV) conduction, when possible, as well as the alternative sites for stimulation, have been studied[54,59,60].

Chart 1 - Deleterious effects of unifocal cardiac stimulation at the right ventricular apex

Histological alterations in the cardiomyocytes	Alterations in cardiac function
Disarray of the LV myofibrils	Increased iatrogenic intraventricular conduction delay
Myofibril hypertrophy	Electrical and mechanical left ventricular dyssynchrony
Intracellular vacuolization	Left ventricular remodeling
Degeneration with fibrosis	Systolic and diastolic left ventricular dysfunction
Fat deposits	Congestive heart failure
Alterations in the size of mitochondria	Myocardial perfusion defects and segmental mobility alterations
Dystrophic calcification	Functional mitral regurgitation
	Increased atrial fibrillation risk
	Left atrial dilatation
	Ventricular arrhythmias
	Activation of the sympathetic nervous system

Source: Occhetta et al[12].

Alternative sites for endocardial cardiac stimulation

In Latin America, the importance of the Chagasic etiology, associated with the implant of pacemakers has led to the necessity to find an alternative site for the positioning of the ventricular electrode, considering some characteristics of the disease. The right ventricular apex in Chagasic patients can present an endocardial thinning in 20-30% of the patients, in addition to the presence of intracavitary thrombus in a significant number of cases[61].

Due to these characteristics, Kormann and Jatene[62] described the subtricuspid position (vertebral-costal-diaphragmatic triangle) (Figure 2) to reduce the risks of cardiac perforation and thromboembolic phenomena triggered by the ventricular electrode. This study represented a landmark for a change in conduct by several surgeons in Latin America, who started to use the position of the RV inflow tract as a preferential site for the implant of the RV electrode in Chagasic patients[62-64]. Among the patients followed at the Pacemaker Laboratory of Hospital de Clinicas of the Federal University of Minas Gerais, in 2006, 77.8% of them had ventricular electrodes fixed in the subtricuspid region[63]. However, there is no scientific evidence of the functional outcome of this site of stimulation and there have been no comparative studies with other sites for right ventricular electrode implant.

The scientific evidence at the age of cardiac resynchronization, from 1990 on, led to the introduction of selective stimulation. The basic principle of this technique is to try to reproduce the natural sequence of cardiac depolarization, through the positioning of the electrode in the areas that are closest to the conduction system, using the complex natural electrical distribution network[54]. In this sense, the stimulation of the bundle of His or para-His[7-12] and the stimulation of the RV endocardial region closest to the conduction system, along the middle and upper portions of the interventricular septum have been assessed[13-26].

In clinical practice, during the implants of definitive pacemakers, the anatomical location of the bundle of His is difficult to reproduce. In spite of these technical questions, there have been reports on the superiority of the stimulation of the bundle of His in relation to the degree of narrowing of the stimulated QRS complex and the systolic function, when compared to the RV apex[9,11]

On the other hand, the positioning of the right ventricular electrode in the middle and upper regions of the interventricular septum, with the help of the radiological anatomy and the assessment of the electrocardiographic tracing, is simple and easy to reproduce (Figures 3 and 4). This site of stimulation has been assessed as a very interesting alternative for the implant of the ventricular electrode, as it generates narrower QRS complexes, with a more physiological activation axis[24] (Figures 5 and 6) and because it is feasible at any Service that routinely performs conventional pacemaker implants[25-27].

The criteria to obtain the septal position were standardized and described in 2004 by Lieberman et al[65]. The validation of the septal position depends mainly on the radioscopic incidence at the left anterior oblique (LAO) view, in which the ventricular electrode is turned to the column, in an opposite direction to the free wall of the right ventricle.

There are other radiological parameters used to define the middle and upper[32] septal positions (Figures 3 and 4).

In addition to the radiological criteria, some caution must be exercised when using the septal position[15,66]:

- Mapping of the septum, exhaustively seeking the narrowest QRS complex (always < 150 ms);
- Obtaining QRS complexes that present an electrical axis with a variation < 30º from the patient's basal electrical axis.
- Threshold < 1 volt, to guarantee the stimulation of the septum's muscular portion.

In spite of the radiological and electrocardiographic criteria to obtain the septal position, there is always the possibility of stimulating the RV free wall, considered one of the main limitations of the technique[67]. There is also the difficulty to define the upper, middle and lower portions of the septum. Such characteristics contribute to transform the septal position into a heterogeneous group that encompasses

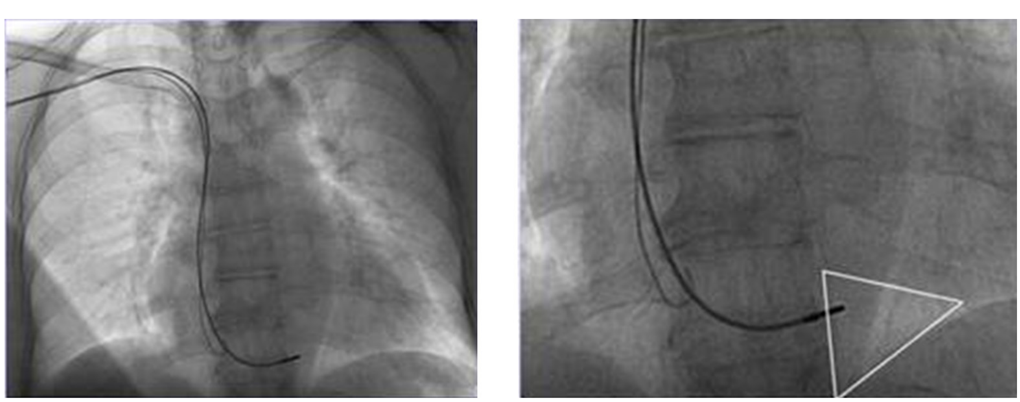

Figure 2 - Radioscopic image in posteroanterior (PA) view, showing the right ventricular electrode in the subtricuspid position. The image on the right shows the delimitation of the vertebral-costal-diaphragmatic triangle or the Kormann's triangle, at a higher magnification, at the RV inflow tract.

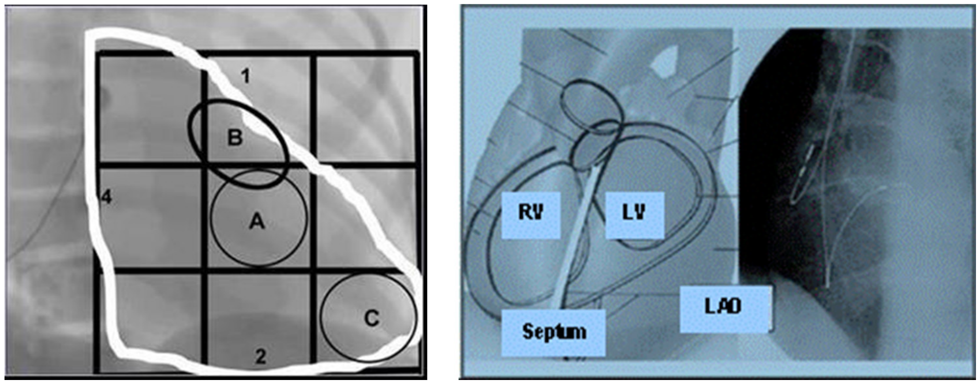

Figure 3 - Radioscopic image in right anterior oblique (RAO) view at 10º in the image on the left. A division is represented through a 3x3 grid used to define the different sites of stimulation in the septal position. The borders are delimited by the vertebral bodies and the cardiac silhouette. Circle A represents the mid-septal position and circle B represents the high septal position. Circle C represents the RV apex. The image on the right shows the radioscopic RAO view of the interventricular septum and the positioning of the electrode in the septal portion of the RVOT (validation of the septal position). Source: Kaye et al[32]; Lieberman et al[65].

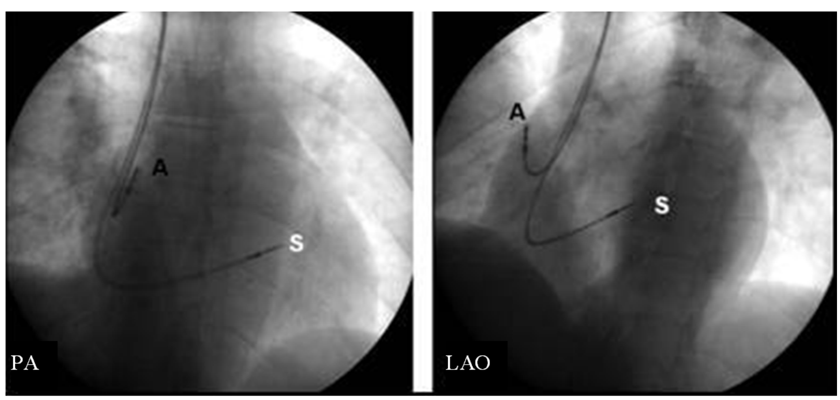

Figure 4 - Radioscopic view in PA and LAO views (30º), demonstrating the final position of the electrodes implanted in the right atrium (A) and mid-septum (S). The septal electrode in LAO is totally directed to the column, in opposite direction to the RV free wall (septal electrode implant technique).

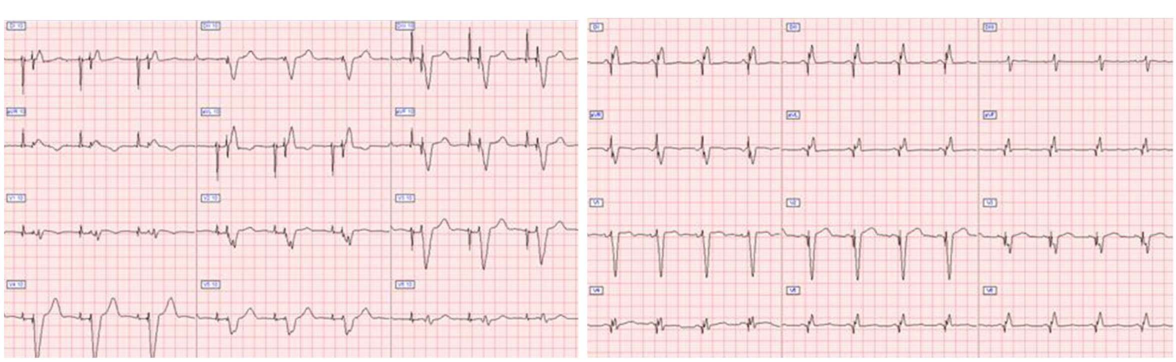

Figure 5 - Basal 12-lead electrocardiogram (ECG) 12 in patient with definitive pacemaker, with electrode in the RV apex in the image on the left (duration of the QRS complex of 200 ms and electrical axis - SÂQRS: -75º). The ECG on the right, resulting from mid-septal stimulation, shows a narrower QRS complex (116 ms) and a more physiological activation axis (SÂQRS: 45º), in comparison with the conventional stimulation.

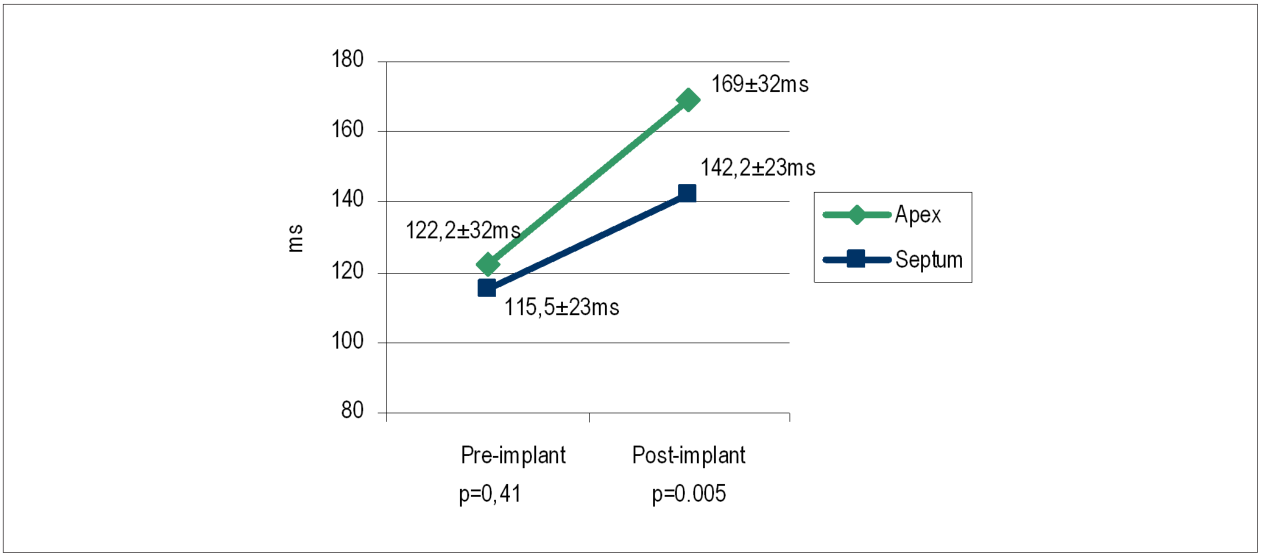

Figure 6 - Comparison of the QRS complex duration resulting from the septal position with the right ventricular apex stimulation (ms). The septal stimulation generates significantly narrower QRS complexes (p = 0.0005). Source: Pachón et al[37].

different sites for RV stimulation and translates the need to standardize the method[68,69].

Functional outcome assessment of the alternative sites for RV stimulation (Chart 2)

The first clinical trials comparing the different sites for RV stimulation appeared in the 1990s[13,70]. Blanc et al[70] evaluated the acute hemodynamic effects in 27 individuals with congestive heart failure (CHF). No differences were observed between the stimulation of the RVOT and the apical stimulation through the analysis of the pulmonary capillary pressure and systolic pressure.

Another study of 14 patients in the acute phase of dual-chamber pacemaker implant due to total AV block was carried out by Schwaab et al[66]. The septum was carefully mapped and the electrode was positioned at the site that generated the narrowest QRS complex. The QRS duration decrease was correlated with the homogenization of the left ventricular contraction and improvement in the systolic function. Similar results were obtained by Mera et al[15] in 12 patients submitted to a single-chamber pacemaker implant, after ablation of the AV junction. This second study showed left ventricular ejection fraction (LVEF) values at rest that were higher at the septal stimulation, when compared to the RV apical stimulation.

A significant improvement in LVEF was reported by Deshmukh et al[8] in 12 patients submitted to a pacemaker implant with the stimulation of the bundle of His. These patients presented narrow QRS complexes, chronic atrial fibrillation (AF) and decreased LVEF (<40%).

Tse et al[71] demonstrated that the stimulation of the RVOT region does result in the the same deleterious effects of LVEF decrease or the perfusion defects, in comparison with the stimulation of RV apex.

Victor et al[72] published a prospective, randomized study with a crossover every three months, to evaluate the quality of life and the systolic function in 103 patients submitted to definitive pacemaker implant. These patients presented CHF, LV systolic dysfunction (LVEF ≤ 40%) and chronic AF. Three types of stimulation were compared: apical, RVOT and bifocal RV stimulation. The conclusion was that the stimulation of the RVOT and the bifocal RV stimulation promoted a narrowing of the QRS interval, but did not consistently improve the quality of life scores or other clinical outcomes after three months of evolution, when compared to the apical stimulation.

Cai et al[73] demonstrated that the stimulation of the RVOT and the bundle of His, in addition to yielding narrower QRS complexes, showed better indices of mechanical synchronization, evaluated by the echocardiogram, when compared to the apical stimulation.

In 2008, Erdoğan et al[22] demonstrated that the stimulation of the RVOT is safe and presents electrophysiological parameters comparable to those obtained with the long-term conventional RV apex stimulation.

Vanerio et al[20] retrospectively evaluated 150 patients, with a mean age of 72 ± 7 years, submitted to definitive pacemaker implant. The patients were divided in two groups: apex stimulation (95) and RVOT stimulation (55). The mean follow-up of the patients was 3.4 ± 2 years, between 1999 and 2004. The multivariate analysis showed that the stimulation of the RVOT and the LVEF were independently correlated with survival (p = 0.006 and p = 0.003, respectively). The mortality with the RVOT stimulation was 37.3% lower (long-rank = 0.02). The authors emphasized the need to carry out randomized prospective studies with a larger sample size, to confirm these findings[20].

On the other hand, Ten Cate et al[21] demonstrated that both the apex and the RVOT stimulation acutely presented mechanical dyssynchrony at the echocardiogram (echo) in patients with normal systolic function. Similarly, alterations in the echocardiographic parameters were observed, indicating mechanical dyssynchrony in all sites of unifocal stimulation evaluated (apex, RVOT and middle septal region) in a study presented at the meeting of the Heart Rhythm[74].

Kypta et al[75] carried out a prospective and randomized study to compare the effects of the RV septal and apex stimulation on cardiac function. A total of 98 patients were assessed, with a follow-up of 18 months, through clinical evaluation, brain natriuretic peptide (BNP) levels, functional capacity and LVEF assessment. No significant differences were observed between the two groups regarding the evaluated parameters. The conclusion of the study was that the septal stimulation is not superior to the apical stimulation in individuals with atrioventricular block submitted to definitive pacemaker implant among a non-selected population[75].

Ng et al[69] carried out a longitudinal prospective study to evaluate the benefits of long-term septal stimulation. A total of 55 patients were studied and the mean follow-up period was 436 days for the septal position and 2,398 days for the electrode positioned at the RV apex. The echocardiographic parameters of the dimensions of the left chambers and the LVEF were evaluated, as well as the measurements of ventricular dyssynchrony and the QRS duration. The mean QRS duration was shorter in the patients with an electrode positioned at the RV apex ($p < 0.001$). It was observed that the electrocardiographic and radiological criteria used for the septal implant resulted in a heterogeneous group, with different sites of stimulation. The study concluded that the septal stimulation was associated with a poorer systolic function and a higher degree of dyssynchrony in relation to the RV apex stimulation[69].

The four most recent reports[21,69,74,75], associated with the description by Victor et al[72], suggest that, in spite of the closeness of the artificial electrical stimulation in relation to the bundle of His, the unifocal stimulation is not capable of fully substituting the natural activation through multiple ramifications of the specialized Purkinje fibers. Another interesting aspect is that they represent conflicting evidence regarding the real benefit of the septal position demonstrated in other studies (Chart 2).

Considering the large number of patients that have been successfully followed in the correction of bradyarrhythmias, some centers remain faithful to the RV apex and the subtricuspid region, mainly in patients without structural cardiopathy, with normal systolic function and in cases where it is possible to minimize the stimulation in the ventricular channel[76]. In this sense, some ongoing studies are using the implant in the RV apex for all patients[77,78]. This question shows the need to prove the real benefit of septal stimulation in the context of evidence-based Medicine.

Another aspect to considered is that the studies carried out to evaluate alternative sites for RV stimulation encompassed all etiologies related to pacemaker implant and there have been few reports on the septal stimulation in individuals with Chagas disease[27,79].

Finally, in an attempt to provide a definitive answer to the question of the superiority of the septal position when compared to the RV apex, three multicenter, prospective, randomized and blind clinical trials are being carried out (OPTIMIZE RV, PROTECT and RASP)[32]. In total, 58 centers are involved in the study, with an estimated sample size of 800 patients. The primary outcome is the assessment of the ejection fraction through the echocardiography and radioisotope ventriculography. The secondary objectives include clinical events, 6-minute walking test, BNP measurement and echocardiographic measurements of the left chamber. The time of follow-up of the patients is up to 36 months.

Discussion

During approximately 40 years, since the start of the artificial cardiac stimulation, the RV apex was considered the preferential site for the implant of the ventricular electrode in conventional pacemakers. The concerns regarding the assessment of the damages caused by the iatrogenic left bundle-branch block produced by the stimulation of the RV apex in conventional cardiac pacemakers are relatively recent.

In spite of the data obtained with the experimental and clinical studies, the deleterious effects associated with the apical stimulation of the RV depend on the interaction between specific factors of each patient (basal atrial rhythm, inherent atrioventricular and intraventricular conduction, LVEF and underlying cardiomyopathy). Additionally, there are conditions related to the artificial stimulation, such as programming mode, duration of the stimulated QRS complex, percentage and duration of the artificial stimulation in the ventricular channel.

Since 1997, alternative sites to the RV apex have been studied, based on the rational search for a more physiological depolarization, caused by the artificial unifocal stimulation[57].

However, due to the small number of assessed patients, the lack of randomization in some studies, difficulty to standardize the criteria to define the alternative sites and different methods for the assessment of the outcome on cardiac function, there are important limitations in the performed studies.

The stimulation of the bundle of His presents technical difficulties that prevent its practical use[68]. The electrocardiographic and radiological criteria used for the septal implant are not so accurate and result in a heterogeneous group of different stimulation sites[69]. To make the question even more complex, the narrowing of the QRS complex in the septal position, when compared to the RV apex stimulation, did not correspond to the improvement in clinical, functional and echocardiographic parameters during the follow-up of the patients in some studies[75].

Another aspect to be defined is whether patients with systolic dysfunction should not be treated with cardiac resynchronization, considering the limitations of the RV unifocal stimulation[75].

In spite of all the advancements in cardiac electrotherapy in the last 50 years, the RV artificial stimulation is still not capable of fully substituting the natural activation through the specialized fibers of the His-Purkinje system. This limitation can be deleterious to the cardiac function, mainly in patients with systolic dysfunction, and justifies the intensive search for strategies to minimize these deleterious effects.

Conclusions

There have been reports on the safety and potential benefits of alternative sites for right ventricular stimulation

Chart 2 - **Summary of some studies on the functional assessment of alternative sites for right ventricular endocardial stimulation**

Authors	Study profile	N	Methods of assessment	Results
Blanc and cols., 1997	Observational	27	Systemic arterial and pulmonary capillary pressure	RVOT and apical present similar results regarding hemodynamic parameters*
Giudici and cols., 1997	Observational	89	Cardiac output (ECHO)	RVOT results in increased CO in comparison with apical stimulation
de Cock and cols., 1998	Experimental	17	Cardiac output (ECHO)	RVOT results in higher cardiac index in comparison with apical stimulation
Mera and cols., 1999	Pilot study	12	ECG and ECHO	SS results in narrower QRS complexes and preserves systolic function †
Schwaab and cols., 1999	Observational	14	ECG and ECHO	SS results in narrower QRS complexes and acutely increases systolic function
Kolletis and cols., 2000	Observational	20	ECHO	RVOT presents better diastolic function parameters in comparison with SS
Bourke and cols., 2002	Prospective	20	Radioisotopic ventriculography	RVOT and apical present no differences regarding the duration of the QRS complex and regarding systolic function
Tse and cols., 2002	Prospective	24	Myocardial scintigraphy and radioisotopic ventriculography	RVOT stimulation prevents the long-term deleterious effects on myocardial perfusion and LV systolic function
Molina and cols., 2005	Observational	60	Evaluation of cardiac output by thermodilution	SS was associated with increased CO when compared to apical stimulation
Mazzoca and cols., 2005	Prospective	24	ECG, electrophysiological parameters	SS is viable and safe
Victor and cols., 2006	Pilot study	28	functional class, ECG, ECHO, ET	RVOT results in narrower QRS complexes, but does not improve quality of life after three months of evolution
Pachón and cols., 2006	Prospective	104	Electrophysiological parameters	RVOT and apical stimulation present no differences regarding the electrophysiological parameters
Burri and cols., 2007	Retrospective	362	Electrophysiological parameters and time of fluoroscopy	SS and apical stimulation present no differences regarding the electrophysiological parameters
Penteado and cols.,2007	Retrospective	21	Electrophysiological parameters	SS and apical stimulation are similar regarding technical difficulties and electrical results
Silva Jr. and cols., 2007	Prospective	102	Electrophysiological parameters	SS presents excellent electrophysiological parameters in the acute and chronic phases ‡
Alhous and cols., 2008	Experimental	16	Tissue Doppler	Apex, SS and RVOT presented mechanical dyssynchrony
Erdoğan and cols., 2008	Prospective	32	Electrophysiological parameters	RVOT stimulation is safe in the long term
Cai and cols., 2008	Observational	20	ECG and ECHO	Apex and RVOT presented similar CI and CO. RVOT and para-His bundle preserved the mechanical synchronism
Ten Cate and cols., 2008	Prospective	14	Tissue Doppler	Apex stimulation and RVOT presented signs of mechanical dyssynchrony §
Kypta and cols., 2009	Prospective	98	ECHO, BNP, functional assessment and clinical follow-up	SS is not superior to apical stimulation
Ng and cols., 2009	Retrospective	55	ECG, ECHO and tissue Doppler	SS resulted in the long-term worsening of the systolic function and a higher degree of dyssynchrony when compared to apical stimulation
OPTMIZE study	Prospective	400	ECHO, BNP, functional assessment and clinical follow-up	Ongoing
RASP study	Prospective	160	ECHO, BNP, functional assessment and clinical follow-up	Ongoing
PROTECT RV study	Prospective	238	ECHO, BNP, functional assessment and clinical follow-up	Ongoing

RVOT - stimulation of the right ventricular outflow tract; ECHO - echocardiogram; CO - cardiac output; CI - cardiac index; ECG - electrocardiogram; SS - septal stimulation of the right ventricle; Apex - apical stimulation of the right ventricle; Electrophysiological parameters - command, sensitivity and impedance threshold; ET - ergometric test; BNP - brain natriuretic peptide measurement. (*) Patients with congestive heart failure; (†) After ablation of the AV junction due to chronic atrial fibrillation in patients with mild to moderate systolic dysfunction; (‡) Study involving Chagasic patients only; (§) Patients with normal systolic function. Source: adapted from Manolis[55].

on the cardiac function. However, the most frequently studied endocardial site, the septal position, encompasses a heterogeneous group of different stimulation sites and there is only a slight agreement regarding the criteria for obtaining it. Therefore, it is still necessary to wait for the results of prospective studies, involving a significant number of patients, including all the etiologies associated to the implant of cardiac pacemaker and with a long-term follow-up, to define the selective site of choice for the unifocal stimulation of the right ventricle.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This article is part of the thesis of doctoral submitted by Otaviano da Silva Júnior, from Universidade Federal do Triângulo Mineiro.

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