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Comparison of electrophysiological parameters of septal and apical endocardial cardiac stimulation

Comparação de parâmetros eletrofisiológicos das estimulações cardíacas endocárdicas septal e apical

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Abstract

Background: **The conventional right ventricle (RV) endocardial pacing leads QRS widening and myocardial desynchronization compromising ventricular function. With the need for less deleterious stimulation, RV septal pacing has been used more. Eventually have been reported higher thresholds and smaller R waves in the septal stimulation.**

Objective: **To compare the parameters of the septal and apical stimulation, intra-patient, if there are any differences that may affect the choice of the point of stimulation.**

Methods: **A prospective controlled study. We included 25 patients, 67.2±9 years, 10 (40%) women with indications for pacemaker for bradyarrhythmias. Etiologies were degenerative in nine (36%), Coronary disease in eight (32%), Chagas disease in seven (28%), and valve disease in one (4%) patient. Electrodes were active fixation and assessed the thresholds of command, impedance and R wave in uni- and bipolar implant and after six months.**

Results: **The average acute threshold command, R wave and impedance unipolar / bipolar septais x apicais were respectively 0.73 x 0.73V and 0,74V x 0,78V; 10 x 9,9mV and 12,3 x 12,4mV; 579 x 621Ω and 611 x 629Ω. Comparisons between parameters with septal and apical two-tailed paired t-test showed a *P* > 0.1. After six months, the mean control thresholds, R wave impedances and unipolar/bipolar septais x apicais were respectively 0.5V x 0 72V and 0.71V x 0,87V; 11.4 x 9,5mV and 12x11,2mV; 423x426 Ω and 578x550 Ω, with *P* > 0.05, except compared to unipolar pacing threshold septal apical unipolar *P* 0.02.**

Conclusion: **Using intra-patient comparisons, no significant differences between electrophysiological parameters septal and apical pacing and there are no restrictions for choosing the right ventricular septal pacing.**

Descriptors: **Pacemaker, artificial. Bradycardia. Cardiac resynchronization therapy.**

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Abbreviations, acronyms & symbols	
AV block	Atrioventricular block
Complete AV block	Complete atrioventricular block
DECA	Departamento de Estimulação Cardíaca Artificial [Artificial Heart Stimulation Department]
SND	Sinus Node dysfunction
AF	Atrial Fibrillation
EF	Ejection Fraction
CAD	Coronary Artery Disease
NYHA	New York Heart Association
RV	Right Ventricle
SOBRAC	Sociedade Brasileira de Arritmias Cardíacas [Brazilian Society of Cardiac Arrhythmias]
LV	Left Ventricle

Resumo

Fundamento: **A estimulação endocárdica convencional do ventrículo direito (VD) ocasiona alargamento do QRS e dessincronização do miocárdio, comprometendo a função ventricular. Com a necessidade de estimulação menos deletéria, a estimulação septal do VD tem sido mais utilizada. Eventualmente têm sido relatados limiares mais altos e ondas R menores na estimulação septal.**

Objetivo: **Comparar os parâmetros das estimulações apical e septal, intrapaciente, para verificar se existem diferenças que possam interferir na escolha do ponto de estimulação.**

Métodos: **Estudo prospectivo controlado. Foram incluídos 25 pacientes, com 67,2 ± 9 anos, 10 (40%) mulheres, com indicações de marca-passo por bradiarritmias. Etiologias foram degenerativa em nove (36%), coronariopatia em oito (32%), doença de Chagas em sete (28%), e valvopatia em um (4%) pacientes. Foram utilizados eletrodos de fixação ativa e avaliados os limiares de comando, impedância e onda R uni e bipolares no implante e após seis meses.**

Resultados: **A média aguda dos limiares de comando, ondas R e impedâncias unipolares/bipolares septais x apicais foram, respectivamente, 0,73x0,74V e 0,73x0,78V; 10x9,9 mV e 12,3x12,4 mV; 579x621 Ω e 611x629 Ω. Comparações entre parâmetros septais e apicais com teste t-pareado bicaudal demonstraram um *P* > 0,1. Após seis meses, a média dos limiares de comando, ondas R e Impedâncias unipolares/bipolares septais x apicais foram, respectivamente, 0,5 x 0,72 V e 0,71 x 0,87 V; 11,4x9,5 mV e 12x11,2 mV; 423x426Ω e 578x550Ω, com *P* > 0,05, exceto comparando-se limiar de estimulação unipolar septal com apical unipolar p de 0,02.**

Conclusão: **Utilizando comparações intrapaciente, não existem diferenças expressivas entre parâmetros eletrofisiológicos de estimulação septal e apical sendo que não há restrições para a escolha da estimulação septal em ventrículo direito.**

Descritores: **Marca-Passo artificial. Bradicardia. Terapia de ressincronização cardíaca.**

INTRODUCTION

The normal QRS duration is < 120 ms owing to the very rapid ventricular activation mediated by the His-Purkinje system and by the subendocardial branches of Purkinje. This organized activation also determines the location of the normal QRS axis to the left (between -30 and +90 degrees) and backwards, pointing to the left ventricle (LV) due to its electrical predominance. Apart from speed and synchronism, the normal course of the cardiac conduction favors the optimum maintenance of the intramyocardial tensions. These benefits are lost when the QRS widens, which results in significant damage of the cardiac function [1-3]. The wide QRS (mainly with morphology of left bundle branch block-LBBB) promotes ventricular desynchronization. Thus, while part of the cells is contracting the other part is still relaxing, blunting the increase in intraventricular pressure which creates a high preload in lately activated cells. Eventually, the desynchronized activation of the papillary muscles worsens or even provokes mitral regurgitation. These abnormalities result in significant loss of ventricular effectiveness, especially in cases with cardiomyopathy.

The conventional cardiac pacemaker with the implanted lead in the right ventricle (RV) apex promotes an important widening of the QRS which is similar in morphology and mechanical dyssynchrony to the one caused by LBBB [4-6]. This phenomenon is an important factor which promotes an unwanted ventricular remodeling [7-9]. Great progress has been achieved to prevent, correct or reduce the ventricular desynchronization, such as biventricular (BiV) pacing [10,11] or the bifocal right ventricular pacing [12,13] which depend on placement of one more ventricular lead. Septal pacing has been widely used in the search for a less deleterious right ventricular pacing, but preliminary data have possibly shown isolated cases with higher thresholds and shorter R waves.

Primary Endpoint

To compare apical and septal pacing during acute and chronic phases in the same patient. It aims to identify any significant differences in threshold, R wave and impedance which may reject or recommend any pacing point.

Secondary Endpoints

1. To compare the QRS durations originated by septal and apical pacing;

2. To check if the QRS axis is more or less physiological

(between -30 degrees and +90 degrees) in septal pacing in relation to apical pacing;

3. To evaluate the stability of the septal lead and the risk of displacement.

METHODS

The features of the patients of this trial are summarized in Table 1.

The pacemakers indications were determined according to SOBRAC-DECA and American Heart Association [14] guidelines.

Implantation Technique

In each patient two leads were intravenously implanted, one in the RV apex, in the classical position of the conventional endocardial pacing, and another in high portions of the intraventricular septum next to His Bundle, called septal in this trial, searching for the best command and sensitivity parameters. The lead was placed in high, mid-septal or para-Hisian region, and that of narrower QRS was chosen. The endocardial injury current in endocavitary electrogram was registered and evaluated in both septal and apical implantations, searching for a good myocardial viability and for the best placement of the lead.

In order to access the high septum, it was used a manual modeling of a steel guide in two planes, so that it could be directed to the high portions with its tip turned backwards. This position was confirmed by radioscopy in left anterior oblique position (Figure 1), aiming to prevent unintended and unwanted implantation into the RV free wall.

It was used endocardial leads from three manufacturers with the following features: active fixation by screw-in, narrow diameter, short distance between the poles and similar impedances. Biotronik DR Philos II and Entovis were used because they were the only pacemakers allowing programming to a DVIR mode with an very short AV interval of 15 ms. These resources are indispensable for the RV bifocal pacing, since it allows virtually simultaneous activation of the two points being the high septum 15 ms prior to the RV apex. Additionally this mode of pacing enables a noninvasive and independent programming of the two points, at any stage of the follow-up.

Unipolar and bipolar parameters - threshold, R wave and impedance - in both positions were evaluated by Biotronik ICS-300 system during the implantation and six months later by telemetry.

The12-lead electrocardiograms (EKG) were recorded by the TEB ECG PC computerized electrocardiograph.

Table 1. Basic patients features.

Feature	N or Mean	%	Interval
Male	15	60	-
Female	10	40	__
Age	67,2 ± 8,8	-	44 to 81
Etiology		-	
Chagas Disease	7	28	__
SND	9	36	__
CAD	8	32	__
Valvar pathology	1	4	__
Pacemaker Indication			
AF + High Degree AV block	21	84	__
AF + complete AV block	4	16	__
EF (%)	36 ± 6	-	21 to 48
Functional class (NYHA)	2,8 ± 0,4	-	II to IV
II	4	16	__
III	20	80	__
IV	1	4	__
Paced QRS duration (ms)	134 ± 19	-	90 to 160
Paced QRS axis (degrees)	45 ± 73,8	-	-150 to +135
Pacemaker Philos II DR	20	80	__
Pacemaker Entovis DR	5	20	__

NYHA = New York Heart Association, AV block = atrioventricular block, complete AV block = complete atrioventricular block; CAD = coronary artery disease; AF = atrial fibrillation; EF = ejection fraction; SND = sinus node dysfuntion

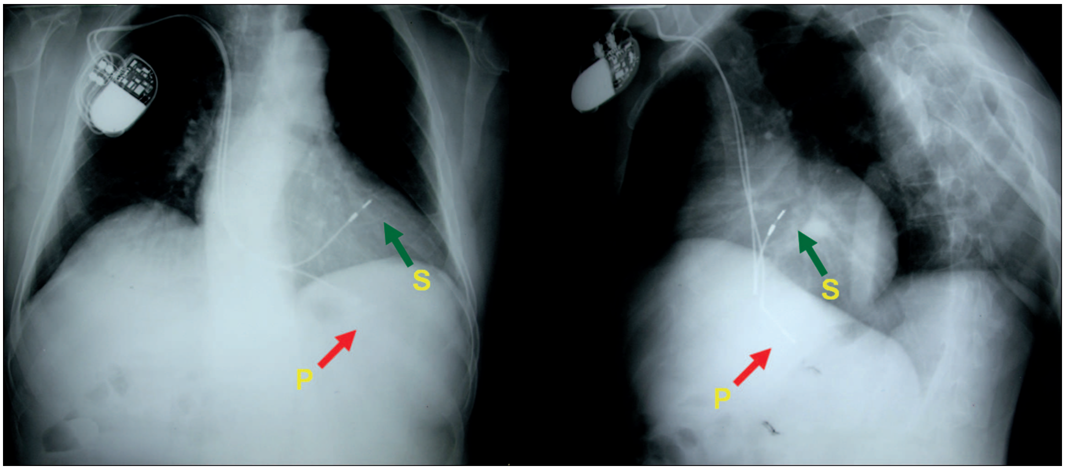

Fig. 1 – Chest X-ray (CXR) in PA and in left anterior oblique (LAO) position, showing the final position of the implanted leads into the RV apex (A) and into RV septal region (S). It is observed that in LAO position the septal lead is fully geared to the vertebral column, opposite to the RV free wall of

Table 2. Means of the measures of the thresholds, R wave and impedances, unipolar and bipolar in acute phase (implantation) and chronic phase (six months later) with two-tailed p-value *t*-test.

	Acute						Chronic					
	Threshold		R		Impedance		Threshold		R		Impedance	
	Uni	Bi	Uni	Bi	Uni	Bi	Uni	Bi	Uni	Bi	Uni	Bi
Septal	0.73	0.73	10.0	12.3	579	611	0.5	0.71	11.4	11.2	423	578
Apical	0.74	0.78	9.9	12.4	621	629	0.72	0.87	9.5	12.0	426	550
P	0.17	0.39	0.8	0.93	0.09	0.34	0.02	0.12	0.09	0.5	0.8	0.24

During the follow-up all the patients were kept with RV bifocal pacing as this stimulation was the one with the narrower paced QRS.

The patients were observed for 60 days to check possible complications associated with the implantation.

Statistical Analysis and Informed Consent

Data were inserted on Excel-2010 spreadsheet and means, standard deviation, maximum and minimum values, confidence intervals as well as median were established. The continuous variables were evaluated by two-tailed paired t test. The differences with *P* value < 0.05 were considered significant. Informed consent was obtained from all patients for pacemaker and lead implantation and for all the measurements during the follow-up.

Table 3. Comparison of the QRS duration under apical and septal RV pacing. Even though it is not the aim of this study, QRS duration of bifocal pacing was also compared, since it provided the narrower paced QRS and was chosen as the background pacing method in these patients.

	Mean ±SD (ms)	Interval (ms)		*P*
Apical QRS	192.5 ± 18.9	160 to 227		< 0.01
Septal QRS	164 ± 13.3	140 to 187	< 0.01	< 0.01
Bifocal QRS	152.7 ± 16.9	107 to 177		

RESULTS

The pacing thresholds, R wave and impedances unipolar and bipolar, acute and chronic at the sixth month of follow-up are shown in Table 2.

The means of septal and apical values unipolar and bipolar were very similar without significant statistical difference ($P \geq 0.09$) except when comparing unipolar thresholds in chronic phase, in which the mean of unipolar ones was slightly lower in septal pacing than in apical pacing, 0.5Vx 0.72V, (P=0.02).

Table 3 shows the comparisons of QRS duration obtained from the 12-lead ECG in the chronic phase, in apical and septal pacing. The mean of QRS duration obtained by septal pacing was clearly lower than the mean of QRS duration of apical pacing with highly significant difference (P<0.01).

Incidentally, were observed that the mean of QRS duration obtained by RV bifocal pacing (being septum 15 ms before apex) was even lower.

In terms of the QRS axis there was a clear tendency of keeping the axis inside the normal limits under septal pacing, while the apical pacing caused complete non-physiological QRS axis, (Table 4). This difference was statistically very significant.

Table 4. Comparison with the QRS axis obtained in chronic phase with apical and septal pacing in right ventricle. Although it have been not the aim of this study, QRS axis of bifocal pacing was also compared, considering that it was the final stimulation mode since as it showed the narrowest QRS.

	Mean±SD (degrees)	Interval (degrees)	*P*	
Apical QRS axis	-68.4 ± 20.3	-120 to -30		< 0.01
Septal QRS axis	79.8 ± 43.4	-60 to 135	< 0.01	< 0.01
Bifocal QRS axis	44.2 ± 87.2	165 to 150		

Although being not the objective of the study, bifocal QRS axis were measured to determine the best method to stimulate the enrolled patients.

Complications

There was one lead displacement from the septal position and one hematoma caused by the oral anticoagulant use as these patients presented permanent atrial fibrillation. The lead was replaced with one with longer screw-in system and the hematoma was easily solved with surgical repair before the hospital discharge.

DISCUSSION

Many patients who suffer from heart failure (HF) due to dilated cardiomyopathy (DCM) show bradyarrhythmia with cardiac pacemaker indication. However, classical ventricular pacing of the RV apex with wide QRS causes systolic and diastolic function impairment, besides mitral regurgitation [7]. Consequently, although the bradyarrhythmia be solved, the classical (apical) pacing worsens or even triggers HF. The functional impairment is even greater in patients with cardiomyopathy who are long-term pacemaker dependent and usually show widen QRS such as LBBB, reaching even more than 250 ms. The same unwanted hemodynamic phenomenon is observed in spontaneous complete left branch block.

Actually, the classical pacing is deleterious for the myocardium and it is even used in hypertrophic obstructive cardiomyopathy, situation in which the functional impairment reflects on the desired reduction of the intraventricular gradient.

Problems of RV Apical Pacing

Ventricular endocardial pacing in the RV apex (apical) is broadly used worldwide since the Sixties' and is the most widespread method of artificial cardiac pacing. However, although it has been revolutionary, safe and efficient to correct bradyarrhythmias, it induces a functional left branch block and promotes a serious desynchrony of the LV walls [15]. This undesirable "side effect" may cause or even worsen the HF, whose symptoms may not be completely taken into account since they are blunted by the increase in the cardiac output obtained by the bradyarrhythmia correction. However, if sustained , this condition promotes an undesirable myocardial remodeling which predisposes the patient to the appearance or worsening the HF, reduces the quality of life and leads to an increase in mortality, even in normal functioning AV sequential pacemakers [16].

In addition, several multi-center randomized trials have shown valuable information of the RV apical pacing damage, although they have been intended for another objective. MOST [17], DAVID [18] and MADIT-II [18] trials showed that the longer the time of RV apical pacing, the higher the HF, hospitalization, atrial fibrillation (AF), ventricular arrhythmias and mortality incidence.

These considerations make us to conclude that regardless these problems the RV endocardial pacing is the most frequently used treatment for bradyarrhythmias, although it causes several and unwanted consequences such as:

- Structural and histological remodeling of the myocardium
- Favors the AF
- Promotes or increases mitral regurgitation
- Promotes myocardial dysfunction
- Favors the HF progression
- Reduces quality of life
- Increases mortality

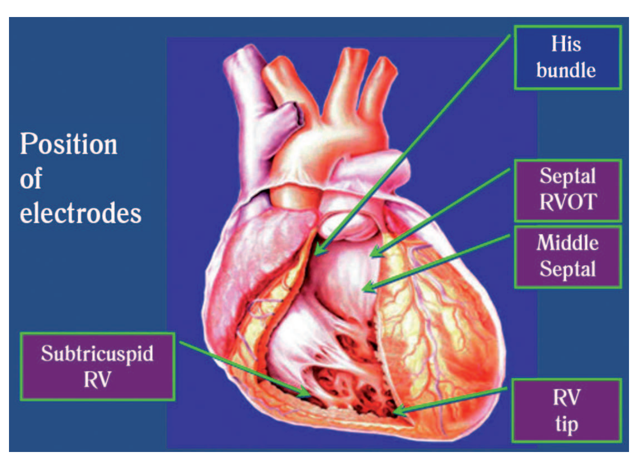

Fig. 2- Schemashowing several alternative positions for RV pacing. His Bundle pacing would be the ideal method in all the cases with previous narrow QRS. However, some limitations prevent it from being currently used

Alternative Pacing of the RV with one lead

Several areas of the RV may be safely stimulated by using modern active fixation leads (Figure 2).

In an experimental trial comparing the hemodynamic result of different points of pacing in the RV [19], His Bundle pacing showed the best result as expected. However, the most important observation is that the worst outcomes were obtained from the RV apical pacing, namely conventional stimulation.

Although the stimulation of the His Bundle is more physiological and enables the maximum resynchronization with normal QRS which prevents the impairment of systolic and diastolic functions and mitral regurgitation, there are practical limitations which have been hindering its common use, such as: it is technically more difficult; it has higher thresholds; it needs special leads and introducers; it is susceptible to oversensing of atrial far-field and it may not be recommended in cases of previous His-Purkinje system lesions.

Considering the problems of apical pacing and to the limitations of currently using the His Bundle pacing it makes sense to pay greater attention to the septal pacing. lead, Modern active-fixation electrodes have low profile and are highly flexible which makes it relatively easy to lead the implantation by using the pre-shaped guide-wire to the mid-septal or para-Hisian region. The electrocardiographic benefit is usually the first consequence observed during the pacemaker implant: the narrower QRS and the QRS axis closer to normal condition (positive or isodiphasic QRS in D1 and positive in D2, D3 and aVF). In addition, there is a significant echocardiographic improvement followed by clinical benefit that is usually reflected bythe reduction of the quality of life score.. These findings are strengthened by the experimental study of Karpawich et al. [20] who obtained great histological benefit from septal pacing in relation to apical pacing. They showed a very significant and udesirable histological remodeling by RV apical pacing that was prevented by the RV septal pacing (Figure 3).

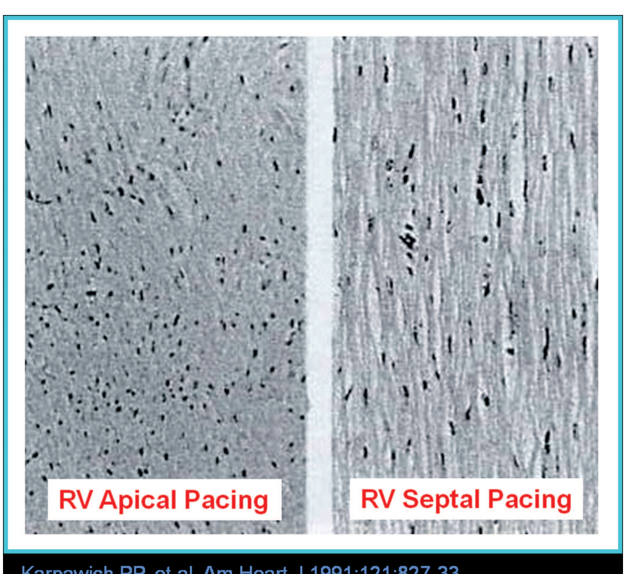

Fig.. 3- Prevention of the histological remodeling of the myocardium of the LV by means of the septal pacing of the RV (Karpawich e al. [20])

Implantation Technique and Complications

Although it depends on a more accurate surgical procedure, no significant difficulty with the septal implantation or to para-Hisian implantation was observed since the technique and the radiological confirmation are taken into account during the lead placement. In general, the implantation was fast which did not increase the risk of infection and of radiological exposure.

One case of generator pocket hematoma caused by the chronic use of oral anticoagulants was observed. It was completely solved by surgical drainage before the hospital discharge. The sole complication directly associated with the septal implantation was an acute dislodgement which was corrected by lead repositioning during the same hospitalization. This fact deserves additional comments since they were associated with the use of an endocardial active fixation lead with a short screw. After this observation, this kind of lead was changed and only a model with longer fixation screw started to be used.

Threshold

The means of the unipolar and bipolar septal thresholds were 6.8% lower than the means of the unipolar and bipolar apical thresholds in the acute phase, but there was no statistically significant difference (P = 0.17 and 0.39 [two-tailed paired t test] respectively) (Table 2). In the chronic phase (six months later), the means of the unipolar and bipolar septal thresholds were 44.4% (P =0.02) and 22.5% (P = 0.12) lower than the means of the unipolar and bipolar apical thresholds (Table2). In this case, although the means are quite similar, the chronic unipolar septal threshold was statistically lower (two-tailed paired t test). In relation to the pacing threshold, these results suggest that the septal pacing can be used or even preferred with no additional risk.

R Wave

Septal and apical R waves of 21 patients with bifocal implantation in RV were compared. Four patients were completely dependent on the artificial pacing, which made it impossible to measure R wave. The results are shown in Table 2. It was observed that the unipolar and bipolar septal R waves are on average 1.1% and 0.8% higher and lower than the unipolar and bipolar apical R waves, respectively. However, these differences were not statistically significant, *P* = 0.80 and 0.93 (two-tailed paired t test).

These findings suggest that despite the septal position shows a slightly lower R wave, the means obtained with this cohort demonstrated excellent values: unipolar and bipolar 10.0 and 12.3 mV, respectively.

In the chronic phase, the means of the unipolar and bipolar septal R waves were 20% and 7.1% higher than the means of the unipolar and bipolar apical R waves, respectively, not showing statistically significant difference *P* = 0.09 and 0.50 (two-tailed paired t test) (Table 2). Accordingly, the amplitude of the R wave does not impose a limitation on septal implantation.

Impedances

Impedances were compared among 25 patients and it was observed that unipolar and bipolar septal impedances were on average 13.2% and 2.8% lower than the unipolar and bipolar apical impedances, respectively. However, these differences were not statistically significant, *P* = 0.09 and 0.34 (two-tailed paired t test). In the chronic phase, the means of the unipolar and bipolar septal impedances were respectively 0.6% and 5.1% lower and higher than the mean of unipolar and bipolar apical impedances, not showing statistically significant difference *P* = 0.8 and 0.24 (two-tailed paired t test) (Table 2). These results demonstrate that in relation to the impedance, the septal pacing and the apical pacing are indifferent.

QRS Duration (QRSd)

Notwithstanding being a secondary endpoint of this study, an extremely relevant finding is that the QRS obtained with septal pacing was significantly narrower than the QRS resulted from the apical pacing ($P < 0.01$) (Table 3). Several studies demonstrate that in patients with cardiomyopathy, the longer the QRSd, the higher the mortality [21]. Furthermore, a number of evidences indicate that the myocardial desynchronization is proportional to the QRSd. In addition, recent observations corroborate less desynchrony of the LV with septal pacing [22].

Since these facts are now confirmed, we have definitely changed the ventricular pacing from conventional to septal pacing, starting from the 1990s when the advances in technology enabled the use of more suitable active-fixation leads [23].

In all the cases, the RV bifocal paced QRS was the narrowest, so that all the patients of the study could remain with this type of stimulation.

QRS AXIS

As secondary endpoint, electrical axis of paced QRS from septum and apex of the 25 bifocal implantations in the RV were also compared. The outcomes are shown in Table 4.

It was observed that the electrical axis of the septal paced QRS was positive and closer to the normal axis. The same situation was observed in relation to the QRS axis of bifocal pacing. Conversely, the mean axis of the QRS resulting from the apical pacing showed great difference in relation to the normal QRS axis. These differences were statistically significant, *P* = 0.0004 (two-tailed paired t test, measured between septal and apical positions); P1 = 0.0013 (two-tailed paired t test, measured between bifocal and apical positions); P2= 0.001(two-tailed paired t test, measured between bifocal and septal positions). These findings suggest that the electrical axis is more physiological when the QRS results from the septal in relation to the apical pacing. Hence, considering the electrical axis of the paced QRS, the septal pacing should be preferred in relation to the classical pacing, since the physiological progression of the myocardial activation reduces the histological remodeling of the wall of the LV [20], besides improving its hemodynamic performance [24].

CONCLUSION

The data yielded for this study demonstrate that the septal thresholds were slightly lower than the apical ones in an intrapatient comparison. This difference was not statistically significant. The electrical axis obtained in septal position was closer to the normal axis in relation to the apical position with important statistical significance.

The measurements of R waves and impedances in septal and apical positions did not show statistically significant differences. The QRS of the septal pacing was significantly narrower than the one produced by apical pacing.

These data show that the septal pacing may be regularly used with no electrophysiological objection.

Thus, according to the electrophysiological parameters studied here, besides there having no restrictions, there are even advantages in septal pacing, and it must be considered whenever as possible in cases with sole RV lead implantation.

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