

# Electromechanical Resynchronization with High Energy Septal Pacing

## *Resincronización electromecánica con estimulación septal de alta energía*

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### ABSTRACT

**Background:** Standard cardiac pacing in the right ventricular apex alters electrical synchrony generating left bundle branch block that in some cases causes mechanical dyssynchrony. Pacing taking into account the anatomy (septal pacing) and with enough energy to narrow the QRS complex could have a beneficial effect, improving electrical and mechanical synchrony, and consequently myocardial function.

**Objective:** The aim of this study was to evaluate acute electrical, mechanical and hemodynamic behavior in patients with severe intraventricular conduction disorders treated with high-energy septal pacing, and compare it with other pacing sites in the right ventricle (apex and outflow tract).

**Methods:** Thirty patients whose average age was 65 years were continuously analyzed. They were divided into: Group I (n=15) with severe conduction disorders, complete left bundle branch block or complete right bundle branch block associated with left anterior hemiblock, all with dilated cardiomyopathy and ejection fraction (EF) <35%, and Group II (n=15) without conduction disorders and preserved EF.

All patients underwent an electrophysiological study where the following parameters were evaluated in the acute phase: QRS duration in ms, time between the onset of surface QRS or spike and the most distal sites of the basal left ventricular (LV) wall, measured in the coronary sinus (R-LV), isovolumic contraction time (ICT) and ejection fraction measured by tissue Doppler echocardiography (performed off-line by an echocardiography specialist) and LV dp/dtmax assessed with an intracardiac Millar catheter (only in 18 cases). All these variables were evaluated at baseline (without pacing), with high energy septal pacing (7.5 V and 1 ms pulse width), and with right ventricular apical and outflow tract pacing. High energy pacing was used to evaluate the thresholds for QRS "narrowing".

**Results:** In Group I, QRS, R-LV and isovolumic contraction times improved with high energy septal pacing, but not with pacing in other sites, even with improved EF. Conversely, in Group II without conduction disorders, high energy septal pacing did not prolong QRS, R-LV or isovolumic contraction times, nor improved EF, but these parameters increased with pacing in other sites.

Left ventricular dp/dtmax showed an average increase of 14% in 16 of the 18 patients evaluated in the acute phase.

**Conclusions:** In patients with severe conduction disorders and low ejection fraction (EF), septal pacing allows electromechanical resynchronization with improved EF and dp/dtmax. In patients without conduction disturbances, this septal pacing does not modify electrical synchrony while pacing in other sites such as the right ventricular apex and outflow tract impairs it.

**Key words:** High-energy Septal Pacing - Synchrony - Severe Conduction Disturbances - Resynchronization

### RESUMEN

**Introducción:** La estimulación cardíaca estándar en el ápex del ventrículo derecho altera la sincronía eléctrica por la generación de un bloqueo de rama izquierda, provocando en algunos casos disincronía mecánica. Una estimulación que respete la anatomía (estimulación septal) y tenga la energía suficiente para generar un angostamiento del QRS podría tener un efecto beneficioso, que se evidencia por la mejoría de la sincronía eléctrica y mecánica con mejoramiento de la función miocárdica.

**Objetivo:** Evaluar el comportamiento eléctrico, mecánico y hemodinámico agudo en pacientes con trastornos graves de la conducción intraventricular ante la estimulación de alta energía a nivel septal, comparándola con otros sitios de estimulación en el ventrículo derecho (ápex y tracto de salida).

**Material y métodos:** Se analizaron en forma continua 30 pacientes con edad promedio de 65 años, divididos en: Grupo I (n = 15), con trastornos graves de la conducción, bloqueo completo de rama izquierda o bloqueo completo de rama derecha asociado con hemibloqueo anterior izquierdo, todos con miocardiopatía dilatada con fracción de eyección (FEy) < 35%; y Grupo II (n = 15), sin trastornos de la conducción con FEy conservada. A todos se les realizó un estudio electrofisiológico en el que se constataron parámetros en agudo de duración del QRS en mseg, distancia entre el inicio del QRS de superficie o espiga y las porciones más distales de la pared basal del ventrículo izquierdo (VI) a través del seno coronario (R-LV), el tiempo de contracción isovolumétrica (TIV) por ecocardiografía tisular, la FEy por eco-Doppler (mediciones realizadas off-line por un especialista en imágenes ecocardiográficas) y la evaluación de la dp/dtmax del VI por catéter Millar intracavitario (solo 18 casos). Estas variables se evaluaron en estado basal (sin estimulación), con estimulación septal de alta energía (7,5 V y 1mseg de ancho de pulso), con estimulación en el ápex del ventrículo derecho y estimulación en el tracto de salida del ventrículo derecho. En la estimulación con alta energía se evaluaron umbrales de "angostamiento" del QRS.

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**Resultados:** El tiempo del QRS, del R-LV y de contracción isovolumétrica mejoraron en el Grupo I con estimulación septal de alta energía, no así en otros sitios, incluso con mejoría de la FEy, mientras que en el Grupo II sin trastornos de la conducción la estimulación septal de alta energía no prolonga el QRS, el R-LV o el TIV ni mejoran la FEy, como sí lo hacen otros sitios de estimulación. La  $dP/dT_{\text{máx}}$  del VI presentó un incremento promedio del 14% en 16 de los 18 pacientes evaluados en agudo.

**Conclusiones:** En pacientes con trastornos graves de la conducción con deterioro de la FEy, la estimulación septal de alta energía permite la resincronización electromecánica y la mejoría de la FEy y la  $dP/dT_{\text{máx}}$ . En pacientes sin trastornos de la conducción, esta estimulación septal no altera la sincronía eléctrica, mientras que en otros sitios de estimulación como el ápex y el tracto de salida la deteriora.

**Palabras clave:** Estimulación septal de alta energía -Sincronía - Trastornos de conducción - Resincronización

## Abbreviations

<b>AV</b>	Atrioventricular	<b>LBBB</b>	Left bundle branch block
<b>dP/dt<sub>max</sub></b>	Maximum time derivative of pressure	<b>RBBB</b>	Right bundle branch block
<b>EF</b>	Ejection fraction	<b>R-LV</b>	Coronary sinus
<b>HESP</b>	High energy septal pacing	<b>RV</b>	Right ventricular
<b>ICD</b>	Implantable cardioverter defibrillator	<b>RVAP</b>	Right ventricular apical pacing
<b>ICT</b>	Isovolumic contraction time	<b>RVOTP</b>	Right ventricular outflow tract pacing
<b>LAHB</b>	Left anterior hemiblock		

## INTRODUCTION

In the early days of cardiac pacing, its main objective was to maintain adequate heart rate, not taking into account some aspects of cardiac function. Consequently, standard right ventricular (RV) apical pacing has achieved high reliability in heart stability, proper control of heart rate and a very easy implementation. (1)

It was evidenced over the years that this "safe" RV apical pacing causes deleterious effects in many aspects, altering electrical synchrony and generating left bundle branch block that, in some cases, causes mechanical dyssynchrony. Numerous studies have revealed asymmetrical ventricular hypertrophy, ventricular dilatation, abnormal fiber arrangement, increased myocardial catecholamine concentration and impaired myocardial perfusion. (2,3)

This worsens patients' clinical outcome, with increased morbidity and mortality, prompting, several years ago, the search for alternative pacing sites in order to improve electrical and hemodynamic parameters of permanent pacing.

Normal conduction through the His-Purkinje system allows a rapid synchronous sequential depolarization of the myocardial fibers, generating an efficient ventricular contraction. The trunk of the bundle of His would therefore be an ideal pacing site to prevent ventricular dyssynchrony maintaining the normal activation pattern.

The first description of septal pacing in humans was conducted by Narula et al. (4) However, due to the technical difficulties in its implementation and the lack of adequate catheters to ensure a correct stability, some decades passed prior to the application of this technique as a method of permanent pacing.

During the last decade, our group studied acute electrical and mechanical pacing at different RV sites and showed that the pacing site with least delay from the left ventricular (LV) free-wall is undoubtedly septal para-Hisian pacing, to achieve a QRS complex with similar baseline characteristics. (5-7)

Therefore, pacing that respects the anatomy (septal pacing) and has enough energy to generate QRS narrowing could have a beneficial effect as evidenced by the improvement in electrical and mechanical synchrony with the consequent improvement of myocardial function (13-16) and no worsening of standard electromechanical pacing conditions.

Moreover, the idea of also implementing resynchronizers emerged in the nineties, adding to standard pacing a catheter in the left ventricle through the coronary sinus. With this therapy, the rate of non-responders ranges from 30% to 50%, due to the difficulty of coronary sinus catheter placement in a suitable location, (8, 9) incorrect thresholds, large areas of necrosis, no assessment of effectively delayed and dyssynchronous areas, and inadequate and difficult programming of devices, among other causes.

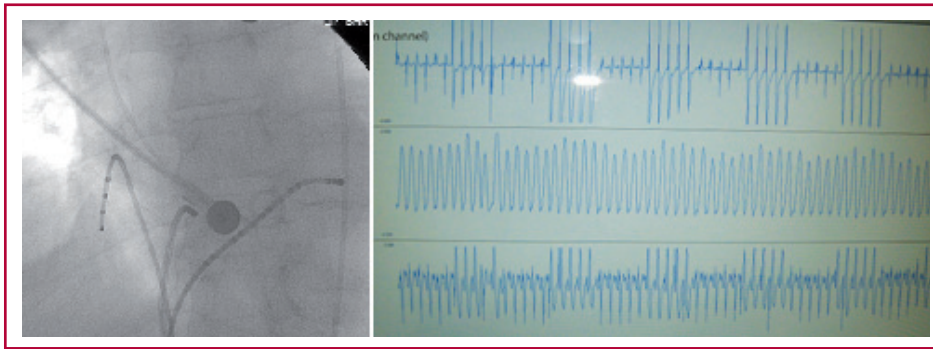
The possibility of achieving resynchronization in these patients with a single catheter seems encouraging as it simplifies the implantation technique and significantly reduces the complexity of the system.

In patients without conduction disorders there is consensus that septal pacing, by following the natural atrioventricular (AV) conduction pathways, turns it into a more physiological pacing than the current one, mainly in those with moderately impaired left ventricular function, since it would avoid dyssynchrony due to the new left bundle branch block produced by standard pacing. It is as important to try to synchronize as it is not to dyssynchronize.

The aim of the study is to evaluate the electrical, mechanical and hemodynamic behavior in patients with severe intraventricular conduction disorders, some with dilated cardiomyopathy, treated with high-energy septal pacing with an average of 7.5 V of total energy at the septal level, and to compare it with other pacing sites in the RV.

## METHODS

Thirty patients whose average age was 65 years were continuously analyzed. They were divided into: Group I (n=15),



**Fig. 1.** Left: Radioscopy showing catheters in His, coronary sinus and right atrial or right ventricular (movable) zones and Millar catheter in the left ventricular apex. Right: dP/dt<sub>max</sub> assessment with on/off high-energy septal pacing cycles. Upper and inferior panels: Electrocardiogram. Middle panel: Pressure tracing for dP/dt<sub>max</sub> assessment showing increase with on pacing.

with severe conduction disorders, complete left bundle branch block (LBBB) or complete right bundle branch block (RBBB) associated to left anterior hemiblock (LAHB), all with dilated cardiomyopathy and ejection fraction (EF) <35%, and Group II or control (n=15), without conduction disorders and preserved ejection fraction.

All patients underwent an electrophysiological study to evaluate different types of arrhythmias, sinus node disease, to study conduction disorders, or for possible resynchronization therapy. Tissue Doppler echocardiography and invasive hemodynamic measurements were performed. All variables were assessed at baseline (without pacing), with high-energy septal pacing (HESP), RV apical pacing (RVAP) and RV outflow tract pacing (RVOTP).

Definitions: Septal pacing is defined as that whose capture is performed in the presence of maximum intracavitary His bundle activity. Parahisian pacing consists in capture with minimum His bundle activity, with large ventricular electrogram and no atrium, nor right bundle branch potential, always under radioscopy observation.

Right ventricular apical pacing and RVOTP are defined as standard pacing in the free wall, always under radioscopy control (Figures 1 and 2).

During the electrophysiological study, the following acute parameters were assessed:

- Total QRS duration in ms: acquired from at least three simultaneous channels by surface ECG measurement.
- R-LV distance in ms: measurement performed between the onset of surface QRS or spike (in paced patients)

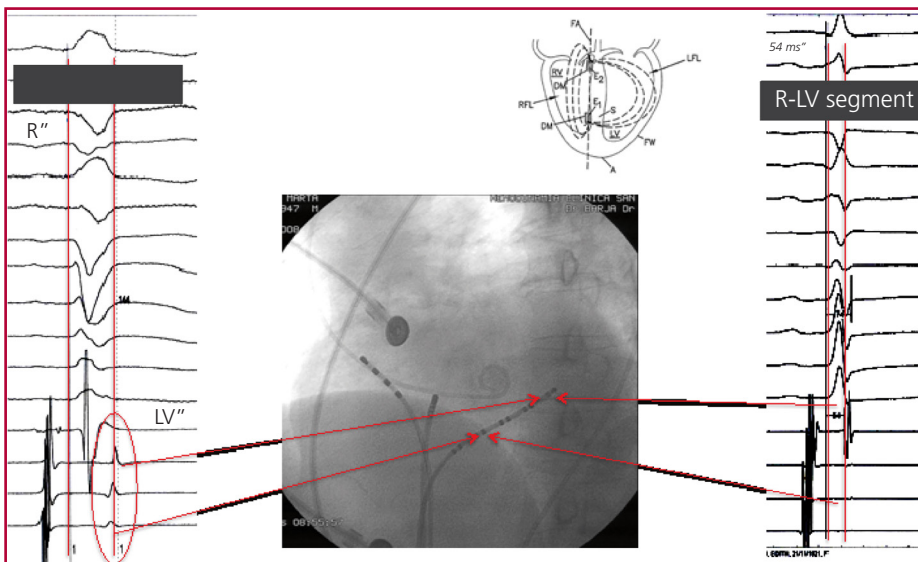
and intracavitary electrogram obtained from the most distal parts of the LV basal wall through the coronary sinus, in general, the posterobasal or laterobasal area.

c. Tissue Doppler echocardiogram was performed during the same procedure, with isovolumic contraction time (ICT) in ms, Doppler LV ejection fraction, and subjective evaluation of paradoxical septal motion recordings in each of the pacing sites. All this parameters were assessed off-line by a specialist.

d. Hemodynamic parameters were evaluated through LV catheters: Millar-type catheter with intraventricular pressure transducer to assess LV dP/dt<sub>max</sub> (only 18 patients were evaluated with this associated method). dP/dt<sub>max</sub> was analyzed averaging 4/5 consecutive beats, with or without pacing in several on/off cycles, and then averaging the sequences among them (see Figures 1 and 2).

#### Measurements

- Ventricular conduction time measured on baseline QRS.
- Conduction time from QRS onset to the most distal part of the left ventricle through the intracavitary electrogram obtained in the coronary sinus (R-LV).
- ICT measured by beat to beat tissue Doppler echocardiography.
- EF.
- Left ventricular dP/dt<sub>max</sub> evaluated in a group of patients with LBBB.
- Other parameters as paradoxical interventricular septum motion.



**Fig. 2.** Evaluation of the R-LV segment or distance between QRS or spike to the left ventricular (LV) deflection obtained through the most distal coronary sinus. To the left: Patient with complete left bundle branch block. To the right: Patient with narrow QRS. The two cursors (red vertical lines) show in the first patient the distance and delay from QRS to the left ventricle seen from the coronary sinus (144 ms and 54 ms, respectively). Center, below: Radioscopy showing the catheters and above, graphical outline of high energy as possible "virtual electrode".

### High-energy septal wave characteristics

Pacing was performed with a specially designed pacemaker capable of delivering high energy in the distal and proximal electrodes. High energy provides a virtual wave or electrode.

Energy released was 7.5 V with pulse width of 1 ms, and 350 ohm catheter resistance for the 4 mm catheter used (Blazer II EPT, Boston Scientific). Narrowing energy was also evaluated, assessing the different degrees of pulse narrowing associated with energy. Its placement was performed recording His bundle activation without atrial electrogram, under radioscopic control.

### Patient characteristics

Patient clinical characteristics are detailed in Table I. Eleven of the 15 Group I patients presented high degree LBBB, half of them with dilated cardiomyopathy, and the rest with RBBB associated with LAHB, 3 of whom had associated Chagas disease. Group II patients were without bundle branch block, with narrow QRS, and generally associated to supraventricular arrhythmias that had to undergo ablation, as atrial flutter, atrial fibrillation or supraventricular tachycardia (see Table I).

### Statistical analysis

Qualitative data were expressed as absolute values and percentages and quantitative values as mean and standard deviation. The goodness of fit test was used to evaluate normality of metric variables. Qualitative variables were compared with the chi-square test and quantitative variables with Student's t test.

### Ethical considerations

Protocols were accepted and approved by the Instituto Lariani Ethics Committee and the Clínica San Camilo Scientific Committee. Patients were requested to sign a personal informed consent to participate in the study.

### RESULTS

Results were evaluated at: 1) baseline conditions, with patient sinus rhythm or baseline rhythm at that moment; 2) with HESP; 3) with RVOTP and 4) with RVAP (Table 2 and Figure 3).

### Group I with LBBB or RBBB +LAHB

In Group I patients with conduction disorders, average

**Table 1. Patient clinical characteristics**

N	Sex	Age	QRS				Underlying disease	Treatment
			Normal	LBBB	RBBB	LAHB		
1	M	82	1				Sinus node disease	Without treatment
2	F	62	1				Paroxysmal 2:1 AV Block	ACEI
3	M	55	1				Hypertrophic cardiomyopathy	BB
4	M	63	1				Tachycardia-bradycardia syndrome	Without treatment
5	F	76		1			Tachycardia-bradycardia syndrome	Digoxin
6	M	94			1	1	Syncope	ASA-Amiodarone
7	F	85		1			Coronary artery disease	ASA-Amiodarone
8	M	44			1		Atrial flutter	Propafenone
9	M	67	1				Tachycardia-bradycardia syndrome	Amiodarone
10	F	54		1			Coronary artery disease	Carvedilol - ACEI - ASA - Diuretics
11	F	62	1				PSVT	ASA-Amiodarone
12	F	46	1				PSVT	Atenolol - ASA - Verapamil
13	M	64			1	1	Trifascicular block	Atenolol - ASA
14	F	75	1				Atrial flutter	Amiodarone - ASA - Dicumarinic agents
15	M	54		1			Non-ischemic dilated cardiomyopathy	ACEI- Digitalis - Diuretics - Spironolactone
16	M	67		1			Non-ischemic dilated cardiomyopathy	ACEI - Digitalis - Diuretics - BB - Spironolactone
17	M	61		1			Non-ischemic dilated cardiomyopathy	ACEI - Diuretics - BB - Spironolactone
18	M	52		1			Non-ischemic dilated cardiomyopathy	ACEI - Diuretics - BB - Spironolactone - Digoxin
19	F	58		1			Non-ischemic dilated cardiomyopathy	Amiodarone - Diuretics- BB - Spironolactone - Digoxin
20	M	70			1	1	Chagasic cardiomyopathy	ACEI - Amiodarone
21	F	65	1				PSVT	BB
22	M	78	1				Atrial flutter	Amiodarone - ASA - Dicumarinic agents
23	M	64	1				Atrial fibrillation	Amiodarone - ASA - Dicumarinic agents
24	F	78			1	1	Chagasic cardiomyopathy	Amiodarone - Diuretics - BB - Spironolactone - Digoxin
25	F	79		1			Coronary artery disease	ACEI- Digitalis - Diuretics - Spironolactone
26	M	81		1			Non-ischemic dilated cardiomyopathy	ACEI- Digitalis - Diuretics - Spironolactone
27	F	65		1			Non-ischemic dilated cardiomyopathy	ACEI- Digitalis - Diuretics - BB - Spironolactone
28	M	57	1				PSVT	BB
29	M	68	1				Atrial flutter	Amiodarone - ASA - Dicumarinic agents
30	F	67	1				Syncope	ASA

M: Male. F: Female. LBBB: Left bundle branch block. RBBB: Right bundle branch block. LAHB: Left anterior hemiblock. AV: Atrioventricular. PSVT: Paroxysmal supraventricular tachycardia. ACEI: Angiotensin-converting enzyme inhibitors. BB: Betablockers. ASA: Acetylsalicylic acid (aspirin).

QRS width was  $176 \pm 30.7$  ms at baseline,  $118 \pm 19.1$  ms with HESP,  $200.3 \pm 27$  ms with RVAP and  $180.6 \pm 56.7$  ms with RVOTP.

Results of the R-LV temporal analysis in the same pacing sequence described above were:  $115.5 \pm 30.9$  ms at baseline,  $64.6 \pm 12.5$  ms with HESP,  $134 \pm 22.7$  ms with RVAP and  $124.9 \pm 36.3$  ms with RVOTP.

Isovolumic contraction time by tissue Doppler echocardiography during pacing was  $150.9 \pm 22.7$  ms at baseline,  $148.1 \pm 14.9$  ms with HESP,  $201.5 \pm 24.7$  ms with RVAP and  $203.1 \pm 32.5$  ms with RVOTP (Figure 3).

Significant differences were found between QRS narrowing and R-LV under HESP pacing compared with baseline QRS and the other pacing sites ( $p < 0.01$ , chi-square test). A similar response was found for ICT.

#### Group II with normal QRS

In group II patients without conduction disorders, average QRS width was  $89.5 \pm 8$  ms at baseline,  $87.9 \pm 11.8$  ms with HESP,  $149.5 \pm 16$  ms with RVAP and  $147.7 \pm 10$  ms with RVOTP.

R-LV times analyzed in the same pacing sequen-

**Table 2.**

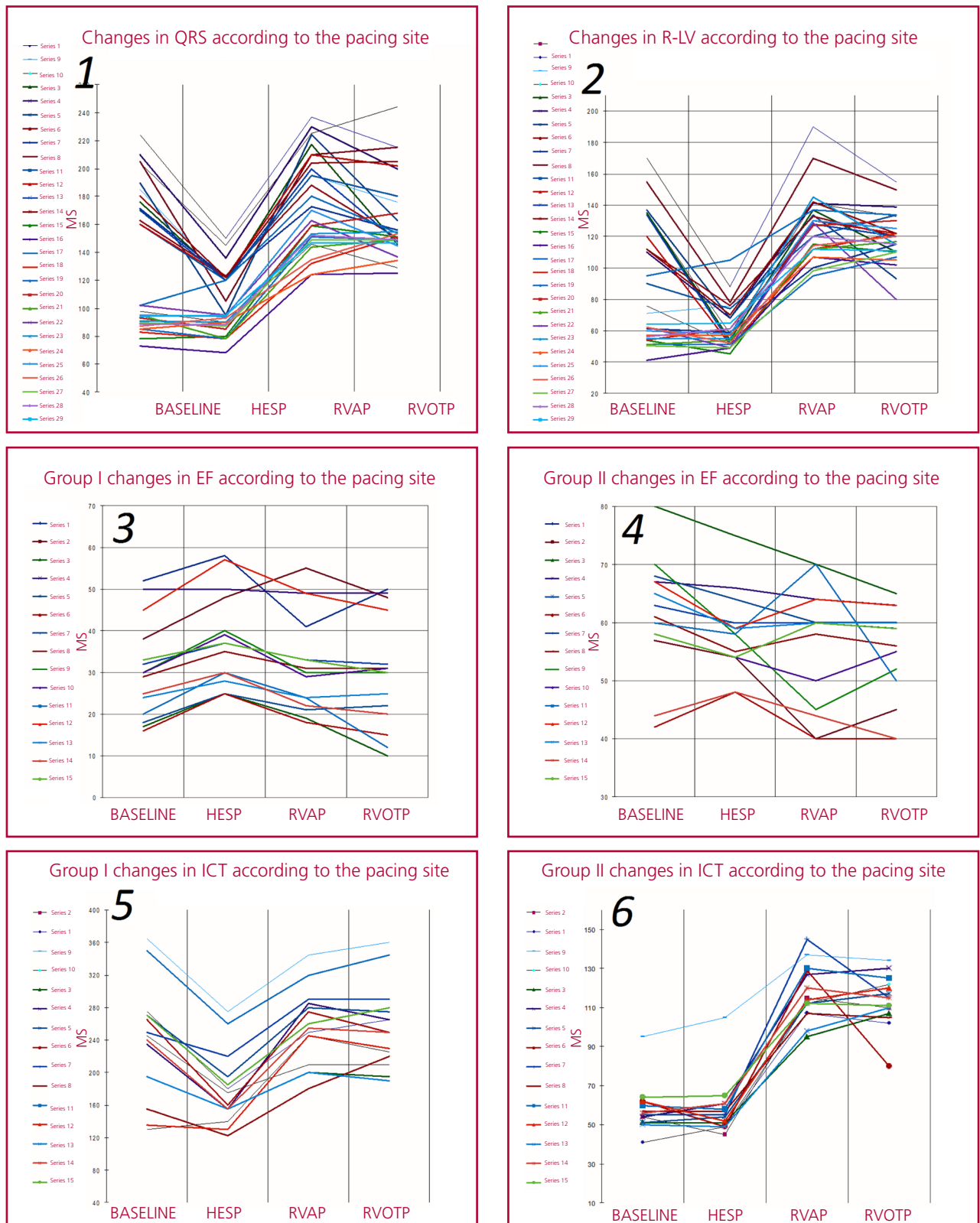
Group I (with conduction disorders)

	Baseline		HESP		RVAP		RVOTP		Ejection fraction				Isovolumic contraction time			
	QRS	R-LV	QRS	R-LV	QRS	R-LV	QRS	R-LV	Baseline	Septal > E	RV apex	RVOT	Baseline	Septal > E	RV apex	RVOT
1	144	115	80	115	151	117	No	No	52	58	41	0	245	175	210	No
2	98	76	90	76	146	107	129	102	38	48	55	48	275	180	250	265
3	224	170	150	170	237	190	215	155	17	25	19	10	365	275	345	360
4	185	71	120	71	195	120	176	134	50	50	49	49	130	140	245	225
5	204	135	145	135	225	141	244	133	18	25	21	22	195	155	200	195
6	176	135	120	135	217	137	146	110	16	25	18	15	235	155	285	265
7	210	110	136	110	230	141	200	139	32	37	33	32	270	195	280	275
8	190	137	95	137	224	134	163	93	29	35	31	31	265	160	275	250
9	163	112	123	112	188	133	150	120	30	40	No	No	250	220	290	No
10	171	61	122	61	173	100	156	115	30	39	No	No	155	122	180	220
11	205	155	105	155	210	170	215	150	20	30	24	12	350	260	320	345
12	160	90	120	90	195	120	180	134	45	57	49	45	135	130	245	230
13	160	120	122	120	210	130	202	122	24	28	24	25	195	155	200	190
14	170	134	120	134	200	128	148	120	25	30	22	20	240	155	255	250
15	180	112	122	112	204	142	205	122	33	37	33	30	270	185	260	280
<b>M</b>	<b>176,0</b>	<b>115,5</b>	<b>118,0</b>	<b>115,5</b>	<b>200,3</b>	<b>134,0</b>	<b>180,6</b>	<b>124,9</b>	<b>30,6</b>	<b>37,6</b>	<b>32,2</b>	<b>26,1</b>	<b>238,3</b>	<b>177,5</b>	<b>256,0</b>	<b>257,7</b>
<b>SD</b>	<b>30,7</b>	<b>30,9</b>	<b>19,1</b>	<b>30,9</b>	<b>27,0</b>	<b>22,7</b>	<b>56,7</b>	<b>36,3</b>	<b>11,5</b>	<b>11,2</b>	<b>16,3</b>	<b>16,8</b>	<b>68,6</b>	<b>44,4</b>	<b>45,8</b>	<b>102,1</b>

Group II (without conduction disorders)

	Baseline		HESP		RVAP		RVOTP		Ejection fraction				Isovolumic contraction time			
	QRS	R-LV	QRS	R-LV	QRS	R-LV	QRS	R-LV	Baseline	Septal > E	RV apex	RVOT	Baseline	Septal > E	RV apex	RVOT
1	78	54	80	45	159	115	151	110	60	58	45	5	200	175	255	270
2	73	41	68	49	124	107	125	102	57	54	40	0	125	150	175	175
3	102	95	120	105	180	137	154	134	80	75	70	65	165	140	210	200
4	83	50	78	49	132	112	151	122	67	66	64	63	155	160	195	217
5	85	51	78	51	151	95	149	107	68	64	60	60	130	135	190	175
6	93	54	85	61	159	127	168	130	42	48	40	40	165	155	205	220
7	95	51	78	54	144	112	149	117	63	60	60	59	140	135	175	160
8	102	62	95	49	163	129	137	80	61	55	58	56	145	130	210	210
9	91	55	90	55	153	145	155	115	70	58	45	52	190	175	252	260
10	85	57	90	57	124	107	134	105	58	54	50	0	120	145	178	180
11	95	60	94	58	170	130	145	125	60	58	75	65	155	138	208	200
12	87	62	93	52	135	114	153	120	67	59	64	63	153	161	195	218
13	90	50	87	49	149	98	149	110	65	59	60	60	128	133	194	174
14	89	56	88	61	152	120	149	115	44	48	44	40	150	154	206	220
15	94	64	95	65	147	112	147	111	58	54	60	59	142	135	175	168
<b>M</b>	<b>89,5</b>	<b>57,5</b>	<b>87,9</b>	<b>57,3</b>	<b>149,5</b>	<b>117,9</b>	<b>147,7</b>	<b>113,5</b>	<b>61,3</b>	<b>58,0</b>	<b>55,3</b>	<b>48,9</b>	<b>150,9</b>	<b>148,1</b>	<b>201,5</b>	<b>203,1</b>
<b>SD</b>	<b>8,0</b>	<b>11,5</b>	<b>11,8</b>	<b>14,3</b>	<b>16,0</b>	<b>16,0</b>	<b>10,0</b>	<b>13,0</b>	<b>9,5</b>	<b>6,8</b>	<b>6,8</b>	<b>10,4</b>	<b>22,7</b>	<b>14,9</b>	<b>24,7</b>	<b>32,5</b>

HESP: High energy septal pacing. RVAP: Right ventricular apical pacing. RVOTP: Right ventricular outflow tract pacing. R LV: Coronary sinus. RV: Right ventricular. RVOT: Right ventricular outflow tract. E: Energy. M: Mean. SD: Standard deviation.



**Fig. 3.** 1 and 2. QRS and R-LV measurements in Groups I and II analyzed together. QRS narrowing and R-LV shortening are observed in patients with wide QRS and their preservation with narrow QRS during high energy septal pacing (HESP). Standard apical and right ventricular outflow tract pacing worsens both

parameters. 3 and 4 illustrate ejection fraction (EF) assessment. Group I shows improvement and Group II, no changes during HESP. 5 and 6 depict changes in isovolumic contraction time (ICT). Group I shows improvement with HESP, and Group II shows no deterioration with HESP but worsening with standard pacing.

ce described above were:  $57.5 \pm 11.9$  ms at baseline,  $57.3 \pm 14.3$  ms with HESP,  $117.3 \pm 14$  ms with RVAP and  $113.5 \pm 13$  ms with RVOTP.

Isovolumic contraction time by tissue Doppler echocardiography during pacing was:  $238 \pm 67$  ms at baseline,  $177 \pm 44$  ms with HESP,  $256 \pm 46$  ms with RVAP and  $257 \pm 102$  ms with RVOTP.

No significant differences were found between baseline and HESP, but significant differences were obtained between these data and those obtained from RVAP and RVOTP, both for QRS, R-LV and ICT. Thus, with RVAP and RVOTP there are significant differences with respect to baseline.

Results of EF planimetric analysis by tissue echocardiography in Group I with conduction disorders and most patients with cardiomyopathies were  $30.6\% \pm 11.5\%$  at baseline (without pacing),  $37.6\% \pm 11.2\%$  with HESP,  $32.2\% \pm 16.3\%$  with RVAP and  $26.1\% \pm 16.8\%$  with RVOTP, whereas in Group II, these values were  $61.35\% \pm 9.5\%$ ,  $58\% \pm 6.8\%$ ,

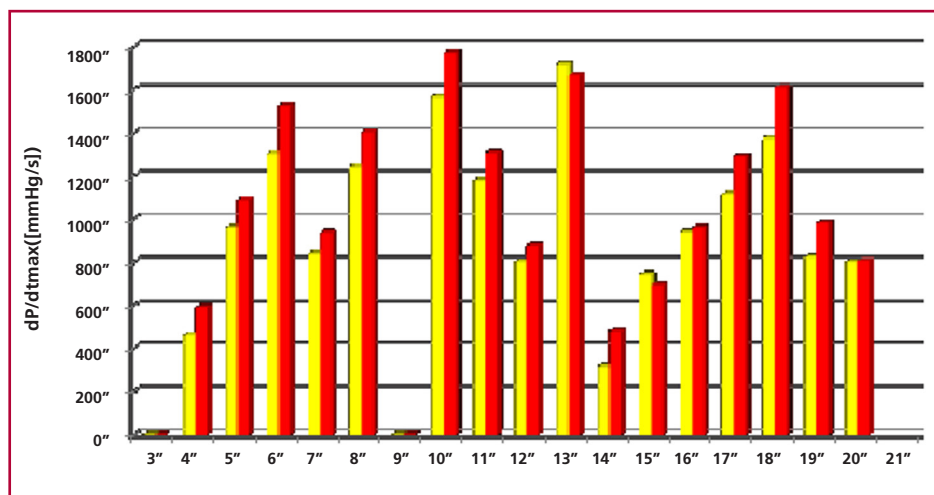
$55.3\% \pm 10.4\%$  and  $48.9\% \pm 21.3\%$ , respectively.

In Group I, baseline EF improved 23% with HESP, showing a trend to worsening with the other pacing sites.

In patients with normal QRS without cardiomyopathy (where many were subjected to an electrophysiological study for paroxysmal supraventricular tachycardia or other type of arrhythmia with preserved ventricular function), HESP did not impair ventricular function, whereas the other pacing sites did, as shown in Figures 2 and 3.

dP/dtmax was analyzed in 18 patients through direct acquisition with Millar catheter pressure transducer in the left ventricle. It was assessed in a subgroup of patients with LBBB or RBBB+high degree LAHB, evaluating changes with on/off HESP, and in 5 patients without conduction disorders. Independently of the initial dP/dtmax value, 14% increase and improvement was observed in 16 of 18 patients. (Figure 4).

In Group I patients with severe conduction disorder



**Fig. 4.** Patient dP/dt<sub>max</sub> changes at baseline versus high energy septal pacing.

Below: Baseline and pacing (p) dP/dt absolute values; cut-off point for normality: 1,200 mmHg/s.

#	dP/dt	dP/dt p	%
14	314	481	53.18%
4	465	592	27.31%
15	743	694	-6.59%
20	801	807	0.75%
12	802	876	9.23%
19	825	982	19.03%
7	840	936	11.43%
16	938	960	2.35%
5	960	1088	13.33%
17	1116	1288	15.41%
11	1178	1305	10.78%
			14.20%
8	1241	1403	13.05%
6	1302	1525	17.13%
18	1372	1610	17.35%
10	1566	1770	13.03%
13	1717	1667	-2.91%
			11.53%

ders HESP narrowed the QRS, shortened the time between QRS onset and the delayed distal portions or R-LV, improved EF, shortened ICT measured by tissue Doppler echocardiography and improved dP/dtmax. Therefore, there is resynchronization with electrical and mechanical parameter improvement. The remaining pacing sites did not present changes.

In Group II or control with narrow QRS and preserved LV function, HESP did not change with respect to baseline, but RVAP and RVOTP worsened QRS and R-LV electrical synchrony and electromechanical ICT synchrony, though without changes in EF.

On the other hand, in all patients, ICT changes correlated with R-LV delay, and also with "shortening" changes or difference, with mean shortening duration of approximately 70 ms.

As an example, in one patient with high degree LBBB, dilated cardiomyopathy and prolonged QRS times, as well as 120 ms. R-LV and 245 ms ICT, HESP narrowed QRS, shortening R-LV to 46 ms and ICT to 175 ms. This is a typical example of QRS narrowing with positive resynchronization and similar R-LV and ICT shortening, increasing acute EF.

## DISCUSSION

As previously discussed, RV apical pacing produces multiple deleterious effects, disrupting electrical synchronization by generating left bundle branch block, which in some cases leads to mechanical dyssynchrony. (2, 3) Numerous multicenter studies and sub-studies have been developed examining the effects of chronic RV apical pacing. The DAVID trial examined patients with low EF who had indication for implantable cardioverter-defibrillator (ICD). Patients were randomized into two groups: one group with dual-chamber ICD in DDDR mode at 70 beats per min, and the other group with single-chamber ICD in VVI mode at 40 beats per min. None of these patients had indication for permanent cardiac pacing. This study showed that patients constantly paced in the RV apex had higher mortality and hospitalization rate for heart failure. (10) A sub-study of the MADIT II trial arrived to similar conclusions as those of the DAVID trial. With a 20-month follow-up period, patients with higher rate of RV apical pacing had higher incidence of decompensated heart failure, arrhythmia and mortality. (11) A sub-study of the MOST trial analyzed patients with sinus node dysfunction and permanent pacemaker implant with two pacing modes: VVIR and DDDR, where, unlike the two studies mentioned above, all patients had preserved ventricular function. However, despite the optimization of AV synchrony in DDDR mode, a higher rate of hospitalization for heart failure was found in those with long-term RV apical pacing, regardless of pacing mode. (12) Loss of pacing sequence, change in axis pattern, non-simultaneous contraction, loss of rotation, among other things, are the deleterious effects of non-physiological RV apical and outflow tract pacing. This prompted the search for alternative

methods of pacing trying to ensure as much as possible a physiologic cardiac mechanical behavior, and avoiding above all not to dyssynchronize the patient.

As seen in this study, HESP generates an activation front which takes into account not only the physiological activation vectors as QRS narrowing and the distance to the most distal portions of the left ventricle (R-LV), but improved mechanical parameters such as isovolumic ejection time, LV dP/dtmax and EF, especially in patients with greater myocardial involvement, there by enabling electrical and mechanical synchrony. This may be interpreted as a wavefront input into the bundle of His trunk generated by the special characteristics of this type of pacing.

It is worth noting that this pacing has a double benefit: On the one hand it prevents the electromechanical impairment of conventional pacing in patients without intraventricular conduction disorder or prior dyssynchrony, especially in those whose EF is on the verge of severity, and in other circumstances, in which previous QRS presents conduction delay due to the presence of bundle branch block, this special pacing technique generates a significant QRS narrowing by following the physiological pathways of cardiac activation, as evidenced in the results.

Even in the presence of complete AV block, septal pacing ensures ventricular capture with narrow QRS and preserved intraventricular conduction sequence. The pacing performed in this work allows its safe use in pacemakers usually implanted due to complete AV block after ablation of the AV node, or spontaneous ones. This is due to the greater energy allowed by this type of pacing.

HESP is useful by ensuring, with the same 7.5 V output of conventional pacing, greater efficiency in the capture and absence of symptoms despite higher output (two opposing waves). If the use of "screw in" catheters is added, security during the implantation is significantly greater and easier. (19)

Finally, HESP presents no contraindications, regardless the degree of AV or intraventricular block, replacing standard pacing and eventually catheter resynchronization therapy in the coronary sinus. Its only contraindication would be in dynamic hypertrophic cardiomyopathy, where conventional pacing produces a dyssynchrony decreasing the subvalvular gradient by paradoxical septal motion.

## CONCLUSIONS

The present study poses the question of how physiological pacing should be implemented. By following the orientation of the heart's normal depolarization pathway HESP becomes the most appropriate pacing approach. The possibility of having a wave that allows using only one catheter in the para-Hisian region makes this method technically much simpler than the one currently used. According to the results, in patients with severe conduction disorders and poor



EF, HESP allows electro-mechanical resynchronization and EF and dP/dtmax improvement. In patients without conduction disorders HESP does not alter electrical synchrony, while pacing at other sites as the apex and outflow tract impair it.

#### Conflicts of interests:

None declared.

(See authors' conflict of interest forms in the web/ Supplementary material)

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