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Adverse impact of chronic subpulmonary left ventricular pacing on systemic right ventricular function in patients with congenitally corrected transposition of the great arteries

Wee Tiong Yeo [a,b,1], Julian W.E. Jarman [a,1], Wei Li [a,1], Michael A. Gatzoulis [a,1], Tom Wong [a,*,1]

[a] Royal Brompton & Harefield NHS Foundation Trust and Imperial College London, United Kingdom
[b] National University Heart Centre, Singapore

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ABSTRACT

Background: Patients with congenitally corrected transposition of the great arteries (ccTGA) are at high risk of heart block requiring subpulmonary left ventricular (LV) pacing. Long-term right ventricular (RV) pacing in congenitally normal hearts is associated with LV dysfunction. We examined the effects of univentricular subpulmonary LV pacing on the systemic RV in a ccTGA cohort.

Methods: ccTGA patients with two echocardiographic studies at least 6 months apart were included. Records of 52 patients, 22 with pacing, were retrospectively reviewed. Seven patients with biventricular pacing were included for comparison.

Results: The LV-Paced Group experienced deterioration in the RV fractional area change (RVFAC) (28.7 ± 10.0 vs. 21.9 ± 9.1%; $P = 0.003$), systemic atrioventricular valve regurgitation ($P = 0.019$) and RV dilatation (end-diastolic area 32.7 ± 8.7 vs. 37.2 ± 9.0 cm^2; $P = 0.004$). There was a corresponding deterioration in NYHA class ($P = 0.013$). Multivariate Cox regression analysis showed that pacing was an independent predictor of deteriorating RV function and RV dilation (hazard ratio 2.7(10–7.0) and 4.7(1.1–20.6) respectively). None of these parameters changed significantly in the Un-paced Group. The CRT Group showed improvement in RVFAC (22.0% to 30.7% ($P = 0.030$) and NYHA class ($P = 0.030$), despite having lower baseline RVFAC (22.0 ± 5.7 vs. 31 ± 9.7%; $P = 0.025$) and greater dyssynchrony (RV total isovolumic time 13.4 ± 2.1 vs. 9.3 ± 4.2 s/min; $P = 0.016$) when compared to the Un-Paced Group.

Conclusions: Univentricular subpulmonary LV pacing in patients with ccTGA predicted deterioration in RV function and RV dilatation over time associated with deteriorating NYHA class. Alternative primary pacing strategies such as biventricular pacing may need consideration in this vulnerable group already highly prone to mortality from systemic RV failure.

1. Introduction

Congenitally corrected transposition of the great arteries (ccTGA) is a structural congenital heart defect in which life expectancy is usually determined by development of progressive heart failure from deteriorating function of the systemic right ventricle (RV) [1]. The condition has a high incidence of heart block, thought to relate to anterior displacement of the atrioventricular (AV) node altering its functional properties [2,3]. The prevalence of heart block reaches 10% to 15% by adolescence, and 30% in early–mid adulthood [4]. Epicardial or endocardial pacing of the subpulmonary left ventricle (LV) has been the mainstay of treatment. Extensive evidence exists that RV pacing in structurally normal hearts leads to deleterious effects on LV function [5,6]. However, the effects of subpulmonary LV pacing on the systemic RV in ccTGA have not been well examined. Potential sequential changes in systemic RV size and function related to LV pacing in these patients have not been reported. We tested the hypothesis that systemic RV function declines in patients with ccTGA who received univentricular subpulmonary LV pacing when compared with a control group of ccTGA patients who had no pacing over a similar period.

2. Methods

We identified all adult patients with ccTGA in our institutional database. Clinical, echocardiographic and pacing data were carefully evaluated retrospectively. Patients were categorized into two principal groups for comparison: an "LV-Paced Group" with univentricular subpulmonary LV pacing and an "Un-paced Group" without pacing. In addition, we examined a third group of patients with cardiac resynchronization therapy (CRT) in whom both ventricles were paced: the "CRT Group".

* Corresponding author at: Heart Rhythm Centre, NIHR Cardiovascular Biomedical Research Unit, Royal Brompton & Harefield NHS Foundation Trust Sydney Street, London, SW3 6NP, United Kingdom. Tel.: +44 20 7351 8619; fax: +44 20 7351 8629.
E-mail address: tom.wong@imperial.ac.uk (T. Wong).
[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Table 1
Classification of RVFAC and RVEDA.

	Reference range	Mildly abnormal	Moderately abnormal	Severely abnormal
RV end-diastolic area (RVEDA), cm^2	11–28	29–32	33–37	≥38
RV fractional area change (RVFAC), %	32–60	25–31	18–24	≤17

Adapted from Lang et al. [8].

2.1. Clinical data

Clinical characteristics including age, gender, height, weight, associated cardiac defects, pulmonary hypertension, arrhythmia, cardiac surgery, New York Heart Association (NYHA) functional classification and maximal oxygen consumption (VO_2max) on cardiopulmonary testing [7] were recorded. Pacing data including pacemaker type, duration of implantation and percentage pacing were also recorded.

2.2. Echocardiographic data

Two sequential transthoracic echocardiographic studies at least 6 months apart were a prerequisite for inclusion. In the LV-Paced Group, both studies followed permanent pacemaker (PPM) or implantable cardiac defibrillator (ICD) implantation. Where three or more studies were available, the two with the longest interval between them were selected. Studies performed within 1 year of cardiac surgery or intervention were excluded, and no patient underwent cardiac surgery between studies. In the Un-paced Group no pacing device was present during the interval between studies, even if the patient later underwent device implantation. Similarly, in the LV-Paced Group no CRT device was present during the study period, even if a device was later upgraded to CRT. In the CRT Group, both studies were performed subsequent to initiation of CRT pacing. A single independent assessor blinded to the order of the studies derived all measurements.

Systemic RV function and size were determined by the American Society of Echocardiography recommendations on chamber quantification [8] and assessment of the pulmonary RV [9]. RV size was assessed by planimetry area in end-diastole (RVEDA) and end-systole (RVESA) in the 4-chamber view. In keeping with the guidelines, these values were not indexed to body surface area. RV fractional area change (RVFAC) was used as a global index of RV function and derived by the formula (RVEDA − RVESA) / RVEDA. Classification of RVFAC and RVEDA is given in Table 1. Tricuspid plane systolic excursion (TAPSE) and systolic tissue Doppler velocity (RVLat S′) of the lateral RV wall were used as indices of RV longitudinal function.

Subpulmonary LV size was assessed by left ventricular end-systolic (LVESV) and end-diastolic volume (LVEDV) using the modified Simpson's rule in the 4-chamber view. This was indexed to the body surface area calculated by the Morstella formula [10]. Subpulmonary LV function was assessed by left ventricular ejection fraction (LVEF) using the formula (LVEDV − LVESV) / LVEDV. With atrial fibrillation, at least two readings of each index were taken and averaged. Systemic and pulmonary atrioventricular (AV) valve regurgitation was graded qualitatively using Doppler into none, mild, moderate and severe categories [11]. Ventricular asynchrony was assessed with right ventricular total isovolumic time (RVIVT) [12].

2.3. Statistical methods

SPSS version 13.1 was used. Normally distributed data were summarized using mean ± standard deviation (SD), and other data with median and inter-quartile range (IQR). Differences between groups were assessed by Pearson's χ^2 test, the Fisher exact test, the two-sided, two-sample *t* test and Mann–Whitney *U* test. Comparison of parameters between the two echocardiographic studies was performed with the paired *t* test for continuous variables and the Wilcoxon signed ranks test for ordinal variables. The outcome measures of interest were deterioration in systemic RV function (RVFAC), systemic

Table 2
Baseline clinical characteristics.

	LV-Paced Group $n = 22$		Un-paced Group $n = 30$		*P*-value for difference between groups
	Mean ± SD		Mean ± SD		
Age at initial study, years	39 ± 16		36 ± 15		0.317
Interval between studies, months	46 ± 25		39 ± 23		0.329
VO_2max, ml O_2/kg/min [a]	17.7 ± 7.7		23.0 ± 7.3		0.030[b]
	Number	%	Number	%	*P*-value
Male sex	12	54.5	19	63.3	0.523
Atrial fibrillation	8	36.4	7	23.3	0.306
Atrial tachycardia	5	22.7	4	13.3	0.468
Supraventricular tachycardia	1	4.5	5	16.7	0.226
Ventricular tachycardia	2	9.1	3	10.0	1.000
Ventricular septal defect	13	59.1	20	66.7	0.575
Atrial septal defect	3	13.6	5	16.7	1.000
Atrioventricular septal defect	1	4.5	1	3.3	1.000
Patent foramen ovale	2	9.1	2	6.7	1.000
Valvular pulmonary stenosis	7	31.8	10	33.3	0.908
Subvalvular pulmonary stenosis	5	22.7	9	30.0	0.559
Ebstien malformation of systemic AV valve	6	27.3	4	13.3	0.290
Pulmonary hypertension	2	9.1	3	10.0	1.000
Isolated ccTGA without other defects	5	22.7	5	16.7	0.737
Tricuspid valve surgery	5	22.7	6	20.0	0.661
Any cardiac surgery	13	59.1	13	43.3	0.206
NYHA class[c]					
Class 1	11	52.4	18	66.7	0.385
Class 2	9	42.9	7	25.9	
Class 3	0	0.0	2	7.4	
Class 4	1	4.8	0	0.0	
	Median	IQR			
Ventricular pacing, %	99	98–100	–	–	–
Duration of ventricular pacing, years	7	4–13	–	–	–
Type of device					
Single chamber pacemaker (subpulmonary ventricle pacing)	3		–		–
Dual chamber pacemaker (right atrial and subpulmonary ventricle pacing)	16		–		–
Dual chamber defibrillator (right atrial and subpulmonary ventricle pacing)	3		–		–

IQR: interquartile range, NYHA: New York Heart Association, SD: standard deviation.
[a] VO_2max data were only available for 20 patients in the LV-Paced Group and 21 in the Un-paced Group.
[b] $P < 0.05$.
[c] NYHA class was only available for 21 patients in the LV-Paced Group and 27 in the Un-paced Group.