Cardiology in the Young (2010), **20**, 485–494
doi:10.1017/S1047951110000454

Original Article

Optimised rate-responsive pacing does not improve either right ventricular haemodynamics or exercise capacity in adults with a systemic right ventricle

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Abstract *Background:* Inappropriate heart rate response to exercise – chronotropic incompetence – and exercise intolerance are common in patients with a systemic right ventricle. We aimed to assess the relationship between heart rate increase, oxygen consumption, and timing of the right ventricular cardiac cycle in this cohort. *Methods:* We prospectively studied nine patients with systemic right ventricles and pre-existing pacemakers using Doppler-echocardiography and treadmill exercise testing. Echocardiography was performed at increasing heart rates. Exercise tests were performed with baseline pacemaker settings and with optimised heart rate response in random order. In addition, eight age- and gender-matched controls underwent exercise testing using a similar exercise protocol. *Results:* Patients with a systemic right ventricle had significantly lower peak oxygen consumption compared to controls – 12.6 plus or minus 6.8 versus 31.4 plus or minus 6.6 metres per kilogram per minute ($p = 0.0006$) – at baseline and active pacemaker reprogramming failed to increase peak oxygen consumption in this cohort – 12.6 plus or minus 6.8 versus 12.4 plus or minus 4.9 millilitres per kilogram per minute ($p = NS$) at baseline and with reprogramming, respectively. We found not only a marked increase in total isovolumic time but also a significant reduction in total filling time and the aortic velocity time integral, p-value is less than 0.001 for all, at higher heart rates compared to baseline conditions. *Conclusion:* This study suggests that despite chronotropic incompetence at baseline, rate-responsive pacing does not improve exercise capacity in patients with a systemic right ventricle. It further indicates that high heart rates may be detrimental in these patients by reducing diastolic filling and stroke volume. These findings may have clinical implications when considering implantation of a permanent pacemaker in this cohort.

Keywords: Chronotropic incompetence; systemic right ventricle; pacemaker therapy; exercise physiology

Received: 12 September 2009; Accepted: 21 February 2010; First published online: 11 May 2010

Adult patients with a systemic right ventricle often have an inappropriate heart rate response to exercise – chronotropic incompetence – and reduced exercise capacity.[1–4] It can therefore be hypothesised that chronotropic incompetence contributes to the limitation in exercise capacity in these patients. However, the filling of the systemic right ventricle might be limited at high heart rates, especially in patients after atrial switch operation for transposition of the great arteries, mainly as a result of impaired atrio-ventricular transport consequent to the abnormal intra-atrial pathways.[5] Artificially increasing heart

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rate to exercise might thus not be beneficial for some of these patients, as it may compromise ventricular filling.

An increasing number of patients with a systemic right ventricle are fitted with a permanent pacemaker for bradycardia,[6] and therefore it is of clinical importance to delineate the relationship between heart rate response to exercise and exercise capacity in these patients. We therefore investigated whether an artificial heart rate increase by reprogramming a pre-existing pacemaker during exercise leads to improved exercise capacity in patients with a systemic right ventricle. To assess the impact of heart rate increase on the physiology and filling of the systemic right ventricle, echocardiography was performed at rest and at higher heart rates.

Materials and methods

Patients

We performed a prospective exercise and echocardiographic study. From our institutional database, we identified 180 patients with a systemic right ventricle – 81 patients with congenitally corrected transposition of the great arteries, 88 patients with transposition of the great arteries after Mustard repair, and 11 patients with transposition of the great arteries after Senning repair. Of these, 19 patients (10.6%) had a permanent pacemaker implanted more than 6 months ago and were considered candidates for the study. Three patients could not be contacted as they had moved abroad. The remaining 16 patients were invited to take part in the study. However, five patients refused participation and two were considered too sick for exercise testing. Therefore, nine patients with a systemic right ventricle could be examined. Control subjects matched for age and free of any history of heart disease were also studied with treadmill exercise testing. All subjects gave prior written informed consent for this study, which was approved by the institutional ethics committee.

Cardiopulmonary exercise testing

In the group of patients with a systemic right ventricle, we performed two symptom-limited cardiopulmonary exercise tests on a treadmill on a single day. Recovery time between the tests was at least 3 hours. One test was carried out with the patient's pre-existing pacemaker settings. In those patients fitted with a rate-responsive pacemaker, rate responsiveness was not switched off for the baseline test. The other test was carried out while the pacemaker was actively reprogrammed to simulate a normal heart rate response to exercise. Tests were performed in a randomised order with the patients blinded to the actual test protocol. Healthy volunteers underwent a single exercise test using the same treadmill protocol.

We performed all tests according to a ramp protocol that uses a linear increase in walking speed coupled with a curvilinear increase in treadmill grade yielding a linear increase in work rate, as described previously.[7]

First, the treadmill exercise protocol was individually adjusted for each patient by predicting the peak work rate according to the patient's height, age, and gender.

We calculated the peak work rate according to the formulae developed by Jones et al[8]:

$$\text{Male: Peak work rate (Watts)} = 1506 \times \text{Height (m)}^{2.70} \times \text{Age (years)}^{-0.46}/6.12 \quad (1)$$

$$\text{Female: Peak work rate (Watts)} = 969 \times \text{Height (m)}^{2.80} \times \text{Age (years)}^{-0.43}/6.12 \quad (2)$$

Second, the treadmill velocity range was determined. Starting speed was set at 0.5 miles per hour; maximum speed after 10 minutes of exercise was set at 3.5–4 miles per hour to allow the subject to walk comfortably during the entire test period and to avoid a change in the gait pattern leading to a steeper rise of metabolic rate per calculated work rate than established over a slower speed range. Changes in work rate and speed were then spread linearly over 20 stages to reach the target work rate after 10 minutes of exercise.

Finally, we calculated the time course of inclination of the treadmill on the basis of the subject's body weight, the desired initial and 10-minute speed, the initial grade, and the predicted 10-minute work rate according to the formula[7]:

$$\text{Grade}(t) = \frac{\left[\left[(\text{WR}_{\text{peak}}/m \times g \times V_0) - \text{grade}_0\right] \times t + 10 \times \text{grade}_0\right]}{\left[\left[(V_{\max}/V_0) - 1\right] \times t + 10\right]} \quad (3)$$

WR_{peak} = predicted peak work rate in Watts, m = body mass in kilograms, g = gravitational acceleration (9.81 metres per second), V_0 and $V_{\max}$ = desired initial and final treadmill speeds, grade_0 = initial treadmill grade.

We chose this treadmill ramp protocol as it provides a linear increase in work rate and allows the prediction of a normal heart rate response, as heart rate relates in a predictable linear fashion to work rate. The pacemaker was programmed to simulate a normal heart rate response according to the data provided by Kindermann et al[9] on the basis

https://doi.org/10.1017/S1047951110000454 Published online by Cambridge University Press

of the relationship between work rate and heart rate response.

All subjects were encouraged to exercise to exhaustion regardless of the maximal heart rate achieved. Ventilation, oxygen uptake, and carbon dioxide production were measured continuously using a respiratory mass spectrometer (Amis 2000, Innovision, Odense, Denmark). Heart rate was recorded by continuous electrocardiography and arterial blood pressure was recorded manually by a sphygmomanometer.

Resting heart rate measured after 30 seconds in a seated position and maximal heart rate achieved during exercise testing were recorded. Exercise duration, peak oxygen consumption, ventilatory response to exercise expressed as the slope of the relationship between minute ventilation and carbon dioxide production, and arterial oxygen saturation at rest and at maximum exercise were also recorded.

Echocardiography

A single experienced operator using a standardised transthoracic approach with a Philips Sonos 7500 echocardiograph interfaced with a multifrequency MHz transducer performed transthoracic echocardiography in all patients with a systemic right ventricle. Transtricuspid – systemic atrioventricular valve – pulsed-wave Doppler recordings were obtained from the apical four-chamber view and aortic pulsed-wave Doppler recordings were acquired with anterior angulation of the transducer with the sample volume at the tips of the respective valve leaflets. All recordings were made simultaneously with an electrocardiogram and phonocardiogram and stored digitally for offline analysis using Medcon software (Medcon Telemedicine Technology, Whippany, New Jersey, United States of America).

The timing of the systemic right ventricular cardiac cycle was measured from aortic and tricuspid valve pulsed-wave Doppler recordings at resting heart rate, 68 plus or minus 8 beats per minute, as well as at 106 plus or minus 10 beats per minute and 140 plus or minus 9 beats per minute. Systemic ventricular ejection time was measured as the interval from the onset to the end of forward flow across the aortic valve. Filling time of the systemic ventricle was measured from the transtricuspid flow recording as the interval from the onset of the E wave to the end of the A wave. Time intervals were multiplied by heart rate and expressed as seconds per minute as these values are independent of heart rate. Total isovolumic time, the time of the cardiac cycle where the ventricle is neither filling nor ejecting, also expressed in seconds per minute, was calculated as 60 − total ejection time + total filling time, where total ejection and filling are expressed in seconds per minute. The aortic velocity time integral was calculated from the aortic valve Doppler tracings.

To assess ventricular long-axis function, M-mode and tissue Doppler recordings of the lateral wall of the systemic right ventricle, the ventricular septum, and the free wall of the subpulmonary ventricle were obtained from the apical four-chamber view with the sample volume positioned at the right and septal angles of the mitral valve ring and the left angle of the tricuspid valve ring as previously described.[4,10] Lissin et al[10] report the maximal diastolic inlet width of the systemic right ventricle to be a good correlate of end diastolic ventricular volume from cardiovascular magnetic resonance imaging, and it was therefore obtained from the apical four-chamber view to quantify systemic right ventricular size. We also used a qualitative, subjective assessment of systemic right ventricular size and function from multi-view two-dimensional echocardiography as described previously.[11] Systolic ventricular function was graded as normal, mildly, moderately, or severely impaired. Ventricular size was graded similarly as normal, mildly, moderately, or severely enlarged. A corresponding numerical grading from 1 to 4 was used for calculations.

Statistical analysis

For all measured variables, values are expressed as mean plus or minus standard deviation or median and range. Comparisons between groups were made using Mann–Whitney U test (unpaired samples), Wilcoxon test (paired sample), and chi-squared test as appropriate. Statistical analysis was performed using MedCalc for Windows, version 9.2.0.0 (MedCalc Software, Mariakerke, Belgium).

Results

Patient characteristics

There was no significant difference between patients and controls regarding age, 36.4 plus or minus 9.4 versus 32.7 plus or minus 5.0 ($p = 0.37$), and gender distribution ($p = 0.74$). Individual patients' characteristics are outlined in Table 1.

Exercise capacity and heart rate response to exercise

Complete exercise data with two tests at different pacemaker settings could be obtained in seven of nine patients. We report one patient who refused repeat testing after an uneventful first test without

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Table 1. Demographic and exercise data of the study population.

										Pre-existing PM settings			PM reprogramming			
Number	Gender (M/F)	Age at study (years)	Diagnosis	Medication	Order of tests	NYHA (1–4)	PM indication	PM mode at baseline	Upper tracking rate (bpm)	Peak HR (bpm)	Peak VO_2 (ml/kg/min)	PM Mode at Peak HR	Peak HR (bpm)	Peak VO_2 (ml/kg/min)	PM Mode at peak HR	Notes
1	M	35	TGA, Mustard	A	P, R	3	Symptomatic Bradycardia	DDDR	140	140	19.0	As Vp	160	19.0	Ap Vp	
2	M	35	TGA, Mustard	B	R, P	1	Symptomatic Bradycardia	VVI	–	140	25.6	Vs	166	21.0	occ. Vp	
3	F	27	TGA, Mustard		P, R	2	Symptomatic Bradycardia	DDIR	120	169	13.8	Ap Vs	169	10.7	Ap Vs	
4	M	50	ccTGA		R, P	2	Symptomatic Bradycardia	DDDR	150	176	10.1	As Vp	151	12.0	Ap Vp	AT at 2nd test
5	F	50	ccTGA	A, B, D	P, R	3	Complete cardiac block	VVIR	150		5.1	Vp				AT at first test, no second test
6	F	39	TGA, Mustard	A, B, D	P, R	2	Symptomatic Bradycardia	DDDR	120	114	9.5	Ap Vs	106	8.9	Ap Vs	
7	M	39	TGA, Mustard		R, P	2	Complete cardiac block	DDDR	145	127	6.8	As Vp	150	7.9	Ap Vp	
8	F	23	TGA, Mustard	A, B, D	R, P	3	Complete cardiac block	DDDR	130			As Vp	127	11.0	As Vp	Refused second test
9	M	30	TGA, Mustard	B	P, R	2	Complete cardiac block	DDDR	140	82	10.7	As Vp	162	8.9	Ap Vp	

A, ACE-inhibitor; B, beta-blocker; Ap, atrial pacing; As, atrial sensing; AT, atrial tachycardia; bpm, beats per minute; ccTGA, congenitally corrected TGA; D, diuretics; HR, heart rate; NYHA, New York Heart Association functional class; P, pre-existing pacemaker settings; PM, pacemaker; R, active reprogramming of the pacemaker to optimise heart rate response to exercise; TGA, transposition of the great arteries; VO_2, oxygen consumption; Vp ventricular pacing; Vs, ventricular sensing

explanation. A second patient developed symptomatic atrial tachycardia after 2 minutes of the initial test, and therefore no repeat testing was performed.

Peak heart rate, exercise duration, and peak oxygen consumption were significantly reduced and the slope of relationship between minute ventilation and carbon dioxide production was abnormally elevated in patients with a systemic right ventricle compared to controls (Table 2).

Pacemaker reprogramming resulted in an increase in peak heart rate during exercise from 135 plus or minus 32 to 149 plus or minus 22 beats per minute. However, due to large inter-individual variability and the development of atrial tachyarrhythmia during the exercise test with the pre-existing pacemaker settings in one patient, this increase was not statistically significant. Overall, active reprogramming did not result in an increase in peak oxygen consumption, 12.6 plus or minus 6.8 versus 12.4 plus or minus 4.9 millilitres per kilogram per minute ($p = 0.44$). In fact, a clinically relevant improvement in peak oxygen consumption was not achieved in any patient with active pacemaker reprogramming (Fig 1). Interestingly, even in the patient with the largest improvement in heart rate response, 82–162 beats per minute (see Table 1, patient no. 4), peak oxygen consumption decreased from 10.7 to 8.9 millilitres per kilogram per minute.

Table 2. Exercise testing.

	Patients with SRV	Controls	p
Exercise duration (s)	494 ± 179	758 ± 125	0.005
Peak HR (bpm)	135 ± 32	186 ± 11	0.0006
Peak VO_2 (ml/kg/min)	12.6 ± 6.8	31.4 ± 6.6	0.0006
VE/VCO_2 slope	57.4 ± 12.3	36.6 ± 7.7	0.002

Data from patients with systemic right ventricle (SRV) obtained from tests with pre-existing pacemaker settings; bpm, beats per minute; HR, heart rate; VO_2, oxygen consumption; VE, minute ventilation; VCO_2, carbon dioxide production

Pacemaker reprogramming led to an increase in heart rate in four of seven patients from 122 plus or minus 28 to 160 plus or minus 7 beats per minute ($p = 0.12$) – but registered no increase in peak oxygen consumption even in this subgroup – 15.5 plus or minus 8.4 versus 14.2 plus or minus 6.8 millilitres per kilogram per minute ($p = NS$). Furthermore, none of these four patients showed a relevant increase in oxygen consumption resulting from pacemaker reprogramming (Table 1 and Fig 1).

On linear regression analysis of the data from all 15 exercise studies, peak oxygen consumption was not related to peak heart rate ($r = 0.23$, $p = 0.39$).

In all control subjects, oxygen consumption increased linearly with heart rate, while a markedly non-linear oxygen consumption to heart rate relationship was observed in six of eight patients as illustrated in Figure 2.

Systemic right ventricular size and function

Data on ventricular size and function of the patients with a systemic right ventricle are given in Table 3.

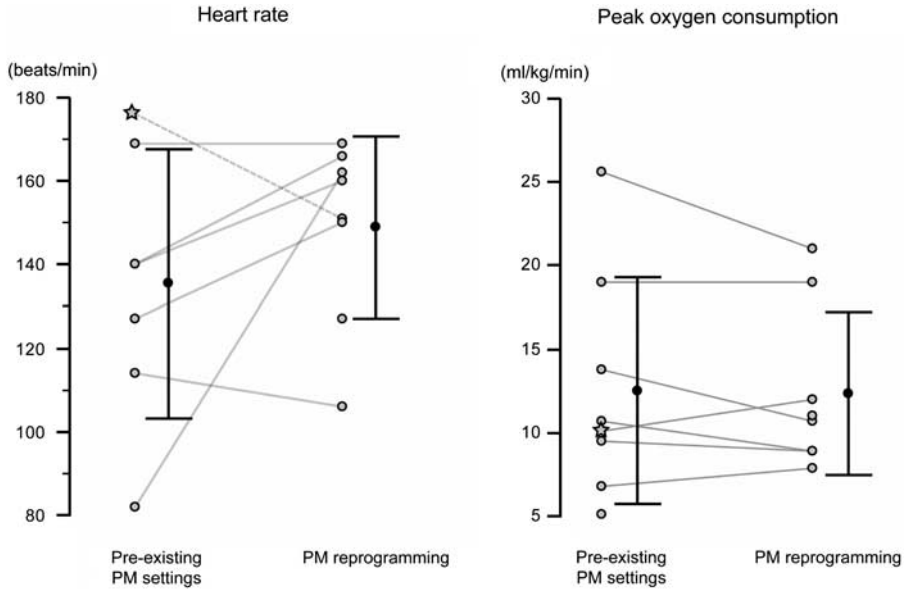

Figure 1.
Heart rate and peak oxygen consumption with pre-existing pacemaker settings and after active reprogramming. One patient, marked with an asterisk, developed atrial tachycardia at the test with pre-existing pacemaker settings; PM, pacemaker.

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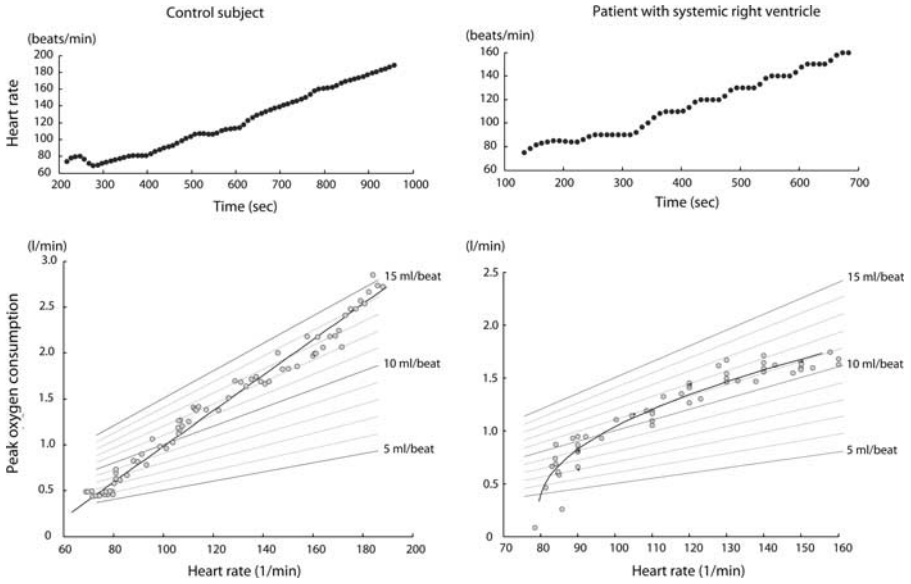

Figure 2.

Heart rate versus time and oxygen consumption versus heart rate plots, including oxygen pulse isopleths with corresponding oxygen pulse values given on the right, recorded from a healthy control subject (left panel) and a patient with systemic right ventricle (right panel). The plots illustrate the normal, expected linear relationship between heart rate and oxygen consumption in the control subject and pathological heart rate-to-oxygen-uptake kinetics in the patient. Despite an increase in the heart rate, the patient is unable to increase oxygen uptake above a heart rate of approximately 130 beats per minute resulting in a curvilinear heart rate-to-oxygen-uptake kinetics.

Physiology of systemic right ventricular cardiac cycle and heart rate

An increase in heart rate resulting from pacemaker reprogramming markedly altered the timing of the systemic right ventricular cardiac cycle. A significant increase in total isovolumic time was accompanied by a marked reduction in total filling time and aortic velocity time integral with increasing heart rate (Figs 3 and 4). In fact, these two parameters decreased in all the patients studied. In addition, total ejection time increased significantly from baseline to maximum heart rate – 18.3 plus or minus 2.3 versus 21.9 plus or minus 2.3, p is equal to 0.008 at 68 plus or minus 8 and 140 plus or minus 9 beats per minute, respectively, whereas peak aortic velocity remained unchanged – 82.7 plus or minus 16.1 versus 76.8 plus or minus 16.1 centimetres per second, p is equal to 0.55 at 68 plus or minus 8 and 140 plus or minus 9 beats per minute, respectively.

The mathematical product of the aortic velocity time integral and heart rate can be regarded as a surrogate parameter of cardiac output. It increased non-significantly with the increase in heart rate from 68 plus or minus 8 beats per minute at baseline to 106 plus or minus 10 beats per minute – 1164 plus or minus 288 versus 1335 plus or minus 430 centimetres per minute ($p = 0.30$) – but fell to baseline levels when further increasing the heart rate to the maximum of 140 plus or minus 9 beats per minute – 1335 plus or minus 430 versus 1086 plus or minus 380 centimetres per minute ($p = 0.03$).

Discussion

Our study suggests that active reprogramming of a pre-existent pacemaker that aims to optimise heart rate response to exercise does not result in improved exercise capacity in patients with a systemic right ventricle. This may be explained by marked alterations of the timing of the systemic right ventricular cardiac cycle resulting in impaired diastolic filling.

Sinus node dysfunction, complete cardiac block, and symptomatic bradycardia are common rhythm disturbances in patients with a systemic right ventricle. In published series, approximately 10% of patients after atrial switch operation and up to 50% of patients with congenitally corrected transposition require pacemaker implantation during long-term follow-up.[12–15] In our cohort, we found a comparable prevalence of pacemaker patients (10.6%). Our patients required pacemaker implantation because of symptomatic bradycardia or complete cardiac block, as shown in Table 1.

Chronotropic incompetence is prevalent in this patient population and is associated with exercise intolerance.[2,16] Implantation of rate-responsive pacemakers, therefore, appears as an attractive option to

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Table 3. Echocardiographic data on ventricular size and function.

Number	Diagnosis	Diastolic inlet diameter SRV (mm)	Function SRV (1–4)	Size SRV (1–4)	Long-axis M-mode, systolic excursion (mm)			S′ (cm/s)			E′ (cm/s)			A′ (cm/s)		
					SRV	Septum	SPLV	SRV	Septum	SPLV	SRV	Septum	SPLV	SRV	Septum	SPLV
1	TGA, Mustard	70	4	4	4.0	4.0	10.0	2.5	2.3	10.2	3.9	4.1	10.3	1.9	3.4	6.1
2	TGA, Mustard	55	2	2	12.0	8.0	15.0	5.0	3.7	7.2	8.2	5.2	15.3	2.3	2.3	2.3
3	TGA, Mustard	47	2	1	9.0	7.0	18.0	4.3	2.4	5.5	5.3	3.2	8.7	1.6	4.4	6.7
4	ccTGA	62	3	3	8.0	4.0	17.0	3.3	2.4	6.8	2.7	1.6	10.3	1.6	5.4	8.5
5	ccTGA	46	2	2	11.0	5.0	14.0	2.7	1.6	4.7	6.2	3.4	10.3	–	–	–
6	TGA, Mustard	62	2	3	12.0	8.0	20.0	5.7	3.7	7.1	6.5	4.1	13.3	3.0	2.4	2.5
7	TGA, Mustard	49	3	3	8.0	4.0	13.0	3.3	1.8	6.1	2.6	2.3	5.5	3.4	1.5	4.3
8	TGA, Mustard	44	2	2	12.0	8.0	12.0	3.5	4.9	6.8	6.5	5.4	6.8	1.9	2.8	10.5
9	TGA, Mustard	63	2	3	11.0	7.0	16.0	3.7	1.6	3.4	2.7	1.7	7.9	2.1	4.8	11.6
Mean ± SD		55.3 ± 9.3			9.7 ± 2.7	6.1 ± 1.8	15.0 ± 3.1	3.8 ± 1.0	2.7 ± 1.1	6.4 ± 1.9	5.0 ± 2.1	3.4 ± 1.4	9.8 ± 3.1	2.2 ± 0.7	3.4 ± 1.4	6.6 ± 3.5
Median (range)			2 (2–4)	3 (1–4)												

A′, peak late diastolic myocardial lengthening velocity on TDI; E′, peak early diastolic myocardial lengthening velocity on TDI; S′, peak systolic myocardial shortening velocity on tissue Doppler imaging (TDI); SPLV, subpulmonary left ventricle; SRV, systemic right ventricle; TGA, transposition of the great arteries

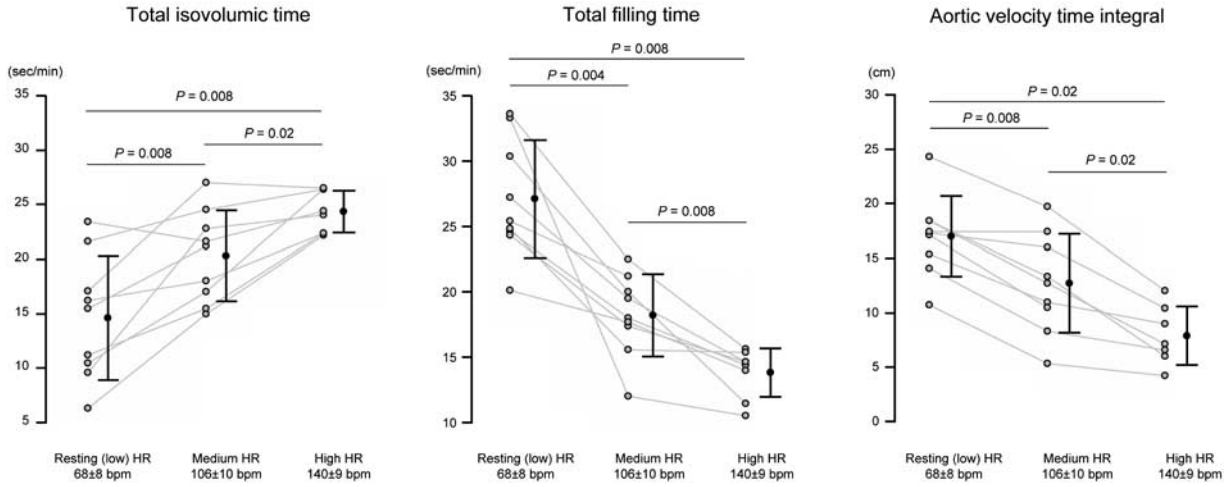
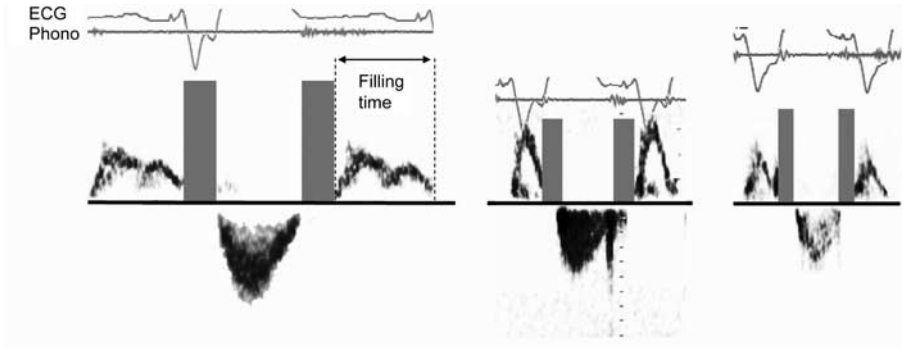


Figure 3.
Comparison between systemic right ventricular total isovolumic time, total filling time, and aortic velocity time integral at three different heart rates. We used non-parametric Wilcoxon tests (paired samples) to compare data.



Heart rate	68 bpm	110 bpm	140 bpm
Total isovolumic time	17.1 s/min	27.0 s/min	28.0 s/min
Total filling time	24.8 s/min	15.6 s/min	13.9 s/min
Aortic velocity time integral	10.7 cm	5.3 cm	4.2 cm

Figure 4.
Superimposed aortic and tricuspid Doppler recordings from a patient with a systemic right ventricle (patient no. 9) at three different heart rates. The two components of total isovolumic time are shaded. ECG indicates electrocardiogram; Phono, phonocardiogram.

improve exercise capacity. However, there are no established criteria for patient selection and it is unclear whether exercise limitation is causally related to chronotropic incompetence, especially as systemic right ventricular dysfunction, impaired coronary flow reserve, and ventricular filling abnormalities are described in these patients, potentially limiting exercise capacity irrespective of the heart rate.[4,5,17]

In order to investigate whether lower peak heart rate is indeed responsible for reduced peak oxygen consumption in this population, we chose to optimise heart rate response to exercise by pacemaker reprogramming. We found that artificially increasing the peak heart rate is complicated in some of these patients and could successfully be augmented in four of seven patients only (Fig 1). However, in none of these patients did this intervention lead to a clinically relevant increase in peak oxygen consumption. Furthermore, we could not show a relationship between peak heart rate and peak oxygen consumption, irrespective of the pacing mode in our group of patients with a systemic right ventricle.

The lack of improvement in exercise capacity with increase in heart rate in patients with a systemic right ventricle is in line with a recent study by Giardini et al.[18] The study shows that beta-blocker treatment improves exercise tolerance in this population potentially by modulating heart rate at peak exercise promoting right ventricular filling by prolonging filling time.

https://doi.org/10.1017/S1047951110000454 Published online by Cambridge University Press

The echocardiographic assessment of the timing of the cardiac cycle at baseline and during higher heart rates provides an opportunity to investigate mechanisms potentially responsible for the discrepancy between adequate exercise heart rates and low oxygen consumption in these patients. We found that heart rate increase leads to a significant reduction in total filling time and a significant increase in total isovolumic time accompanied by a marked reduction in aortic velocity time integral. This is in contrast to data published in healthy individuals showing an increase in total filling time and a reduction in total isovolumic time with increasing heart rate during dobutamine stress.[19]

Total isovolumic time – the time where the ventricle neither ejects nor fills – is shown to be prolonged in patients with myocardial ischaemia and to be linked to mechanical incoordination.[20] Both limited coronary flow reserve and mechanical incoordination during pharmacological stress are reported previously in patients with a systemic right ventricle.[4,17] It appears likely, therefore, that the increase in total isovolumic time with increasing heart rate in our patients reflects myocardial ischaemia and mechanical incoordination. This notion is supported by the fact that increasing heart rate during exercise was not accompanied by an increase in oxygen consumption in the majority of patients (Fig 2), a well recognized feature of myocardial ischaemia in acquired heart disease.[21] The increase in total isovolumic time in turn leads to a reduction in total filling time finally resulting in a reduction in stroke volume as indicated by reduced aortic velocity time integral (Fig 3). Derrick et al[5] reported a limitation in stroke volume augmentation during exercise and dobutamine stress resulting from impaired atrio-ventricular transport potentially reflecting anatomical and functional abnormalities of the atrio-ventricular pathways after the Mustard operation. This suggests that there may be two mechanisms limiting stroke volume during heart rate increase in patients with a systemic right ventricle.

Limitations

Of necessity, the number of patients in the study is small. Furthermore, we included two patients with congenitally corrected transposition of the great arteries who, in contrast to the seven patients with previous atrial switch procedure, did not have atrial surgery potentially limiting their atrio-ventricular transport capacity. There were no differences, however, between these two patients and the remaining patients with a systemic right ventricle.

Pacemaker reprogramming did not result in a statistically significant difference in peak heart rate at exercise, an effect we might have achieved comparing non-rate responsive pacing with optimized pacing. However, post-hoc analysis of the data of patients who showed an increase in peak heart with pacemaker reprogramming demonstrates that increasing peak heart rate at exercise does not increase peak oxygen consumption in patients with a systemic right ventricle.

We performed echocardiographic assessment at resting heart rate and after artificially increasing the heart rate by pacemaker reprogramming. The findings may therefore not fully reflect the physiological changes occurring during physical exercise, such as inotropic activation, peripheral vasodilatation, and increased venous return. Nevertheless, our findings are consistent with previous data in patients with a systemic right ventricle studied during pharmacological stress and exercise showing comparable abnormalities.

Conclusions

Our study suggests that despite inappropriate heart rate response to exercise – chronotropic incompetence – optimised rate-responsive pacing does not improve objective exercise capacity in patients with a systemic right ventricle. Our results rather indicate that higher heart rates may be detrimental in these patients by prolonging isovolumic time and reducing diastolic filling time. These findings may have clinical implications when considering implantation of a permanent pacemaker in a patient with a systemic right ventricle.

Acknowledgement

The Royal Brompton Adult Congenital Heart Centre, AU and MAG acknowledge the support received from the Clinical Research Committee and the Waring Trust both at the Royal Brompton Hospital and from the British Heart Foundation. GPD has received support, in part, through an educational grant from Actelion, United Kingdom. The authors have no conflict of interest.

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