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Exercise capacity in the Bidirectional Glenn Physiology: coupling cardiac index, ventricular function and oxygen extraction ratio

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Abstract

In Bi-directional Glenn (BDG) physiology, the superior systemic circulation and pulmonary circulation are in series. Consequently, only blood from the superior vena cava is oxygenated in the lungs. Oxygenated blood then travels to the ventricle where it is mixed with blood returning from the lower body. Therefore, incremental changes in oxygen extraction ratio (OER) could compromise exercise tolerance. In this study, the effect of exercise on the hemodynamic and ventricular performance of BDG physiology was investigated using clinical patient data as inputs for a lumped parameter model coupled with oxygenation equations. Changes in cardiac index, Q_p/Q_s , systemic pressure, oxygen extraction ratio and ventricular/vascular coupling ratio were calculated for three different exercise levels. The patient cohort ($n=29$) was sub-grouped by age and pulmonary vascular resistance (PVR) at rest. It was observed that the changes in exercise tolerance are significant in both comparisons, but most significant when sub-grouped by PVR at rest. Results showed that patients over 2 years old with high PVR are above or close to the upper tolerable limit of OER (0.32) at baseline. Patients with high PVR at rest had very poor exercise tolerance while patients with low PVR at rest could tolerate low exercise conditions. In general, ventricular function of SV patients is too poor to increase CI and fulfill exercise requirements. The presented mathematical model provides a framework to estimate the hemodynamic performance of BDG patients at different exercise levels according to patient specific data.

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Conflict of Interest Statement

None of the authors have potential conflicts of interest in relation to the presented work.

Keywords

Congenital heart disease; single ventricle heart; Fontan; Pulmonary vascular resistance; Lumped parameter Modeling; exercise capacity

1. Introduction

The bidirectional Glenn (BDG) is characterized by the anastomosis of the superior vena cava (SVC) to the pulmonary arteries, diverting superior systemic blood flow directly to the lungs. The BDG is the second stage of a set of palliative surgeries for single ventricle diseases which result in the total cavopulmonary connection (TCPC) (Bridges et al., 1990; Procelewska et al., 2007). The overall goal of the TCPC is to reroute venous blood flow directly to the pulmonary arteries, minimizing the mixing of oxygenated and deoxygenated blood in the single ventricle (SV) (De Leval et al., 1988; Fogel et al., 2004; Fontan et al., 1971).

BDG patients remain cyanotic with 80-85% systemic oxygen saturation (SO_2) due to systemic-pulmonary communications that ensure an adequate blood flow in the SV (Bin et al., 2001; Guyton et al., 1997; Tanoue et al., 2003). BDG circulation is a particular topic of study because only the superior systemic flow is oxygenated, and the overall SO_2 is highly dependent on the division between upper and lower circulations (Salim et al., 1995; Whitehead et al., 2009). Patients who have high surgical risk factors remain at this second stage BDG physiology living with moderate cyanosis (Day et al., 2006; Salim et al., 1995).

Several studies focus on the TCPC palliated single ventricle and its exercise capacity; however, the effect of physical activity in BDG patients is still unclear. It remains questionable whether patients whose cardiac output is sensitive to pulmonary vascular resistance could tolerate even low levels of exercise (Mahle et al., 2009; Arena et al., 2009; Mahle et al., 2012; Madan et al., 2013; Driscoll et al., 1986, 1984; Cordina et al., 2013; Prakash et al., 2010). The main conflict is the additional oxygen demand during exercise while oxygenated and deoxygenated blood continue to mix in the SV. Ventricular function is often studied to assess SV palliation outcomes (Day et al., 2006; Freedom et al., 1998; Hussain et al., 2008; Petrucci et al., 2010; Walker et al., 2004). Colan showed that the systolic function decays after BDG even though contractility is unchanged (Colan, 2002). Tanoue and Joh investigated ventricular function by measuring arterial (E_a) and ventricular (E_{es}) elastances before and after BDG, finding that end diastolic volume (EDV) is decreased after BDG resulting in E_{es} improvement (Tanoue et al., 2003). Ventricular function on palliated SV patients is poor with increased afterload and decreased cardiac function (Fogel et al., 1993; McHannon 2001; Pekkan et al., 2005; Senzaki et al., 2002; Senzaki et al., 2006).

The effect of exercise on ventricular function for BDG patients has not yet been investigated to our knowledge. This study is motivated by three key points: (1) the mixing of blood in the SV will affect systemic oxygenation and consequently affect exercise performance, (2) the BDG operation generally occurs between 6 months to two years of age when patients begin to rapidly increase physical activity, and (3) some patients will remain at the BDG stage at

the expense of cyanosis and therefore an increased oxygen demand during exercise would be a long-term problem (Freedom et al., 1998; Walker et al., 2004; Yuan et al., 2009).

The goal of this study was to investigate the effect of exercise on the ventricular function and oxygenation parameters of BDG circulation. Exercise was modeled by increasing heart rate and decreasing pulmonary and systemic resistances from the resting values. A mathematical framework was developed to estimate the changes in cardiac index, ventricular function and oxygen extraction ratio (OER) for three different exercise levels.

2. Methodology

2.1 Patient cohort

Catheterization data of 39 BDG patients from four different participating centers was collected (Table 1).

Informed consent was obtained from all patients and all study protocols complied with the Institutional Review Boards of all participating institutions. Catheterization data was taken while the patients were at stabilized oxygen conditions (FiO_2 approximately 0.9). Therefore, any environmental effects (elevation or FiO_2 at room temperature) were neglected for this model.

Patients were grouped using two different criteria: (1) PVR at rest and (2) age at BDG operation. For the analysis based on PVR, the cohort was divided into 2 groups based on their baseline PVR values as has been reported in literature for BDG patient hemodynamic analysis (Hussain et al., 2008): group A_{pvr} ($n=19$) with $\text{PVR} > 3.5$ WU, and group B_{pvr} ($n=20$) with $\text{PVR} \leq 3.5$ WU. The effects of exercise on oxygenation and ventricular function parameters were then compared between groups ($p > 0.05$).

The cohort was then divided into 2 groups based on the age at BDG operation. Group A_{age} ($n=25$) with age > 2 years, and group B_{age} ($n=14$) with age ≤ 2 years. This criterion was chosen because at 2 years of age the lung vasculature could be more mature and able to adapt to the circulation imposed by BDG palliation (Day et al., 2006, Hussain et al., 2008). This age also offers greater physical activity due to increased use of lower limbs.

2.2 Description of the mathematical lumped parameter model

A lumped parameter model (LPM) (Love, 2007) was developed for BDG physiology, representing it as a closed electric circuit (Figure 1). The general approach is based on previous LPMs (Penati et al. 1997; Penati et al. 2000; Peskin et al., 1986; Pekkan et al., 2005; Sundareswaran et al., 2008; Vallecilla et al. 2014) where vascular structures are modeled as transient compliant chambers and valves as switches. Baseline systemic resistance, baseline PVR, hemoglobin content, baseline SaO_2 , and BSA were used as input variables for each patient (Table 1). Systemic resistances, pressures and flows were taken from the individual patient catheterization data.

The compliances in the system were adapted as constant parameters from previous reported studies; see Table 2 (Pekkan et al., 2005; Penati et al. 1997; Penati et al. 2000).

Upper and lower circulations are divided as two loops in parallel. Initial resistances simulate physiology at rest, and all baseline oxygenation parameters were calculated using this configuration. The values assigned for upper and lower resistances were determined by each patient's body surface area (BSA) (see equations 1 and 2; Whitehead et al., 2009).

$$\frac{Q_{IVC}}{Q_s} = 0.2 \ln(BSA) + 0.57 \quad (1)$$

$$R_{down} = \frac{\left(1 + \frac{b}{a}\right)^* R_{sys}}{\frac{b}{a}} \quad (2)$$

2.3 Simulating exercise conditions

To simulate exercise, three levels have been considered: low, moderate and high. The levels were adjusted according to previous reported studies of exercise capacity in single ventricle patients. These studies state that SV patients after the Fontan surgery are able to double their cardiac index and decrease their systemic resistance (Whitehead et al., 2007, Mahle et al., 2012, Stringer et al., 1997, Arena et al., 2009, Cordina et al., 2013).

Under exercise conditions, increases in pulmonary blood flow and small increases in pulmonary artery pressure are seen, along with an increase in left atrial pressure. This effect is unique to the lung circulation and is progressive with exercise intensity. Due to vascular compliance in the lung microcirculation, the increase in left atrial pressure will help distend the small vessels, contributing to the fall in pulmonary vascular resistance during exercise (Bonow et al., 2012)

Therefore, the parameters chosen to model exercise in this study are the increase in heart rate and the decrease in systemic and pulmonary resistances. We have also taken into account the increase in oxygen consumption (VO_2) during exercise through the inputs to the model. Exercise will increase the body's oxygen requirements because there is no immediate energy available in the skeletal muscle. The ventilatory oxygen consumption is an indirect measure of the energy consumed, which depends directly on the cardiac output and the arterio-venous oxygen difference and indirectly on the oxygen delivery (DO_2) (Bonow et al., 2012). In this model an increment of VO_2 has been included for all exercise levels. VO_2 at baseline was taken from patient data and increased by 50% for each exercise level (Mahle et al., 1999, Stinger et al., 2012, Arena et al., 2009). See Table 3 for details related to exercise levels.

2.4 Analysis of oxygenation parameters

In this study, the arterial SO_2 (SAO_2) and venous SO_2 (SVO_2), oxygen delivery (DO_2), and oxygen extraction ratio (OER) were calculated by coupling the LPM with the following oxygenation equations (equations 3-6) where Hb is hemoglobin content, PaO_2 is the partial pressure of oxygen, and Q_p , Q_{sdown} , and Q_s are pulmonary, lower systemic, and systemic flow rates respectively.

In BDG circulation, the pulmonary flow is oxygenated (about 95%), and mixed in the single ventricle with the deoxygenated IVC flow. Since only the superior systemic flow is oxygenated in the lungs, the overall oxygen saturation is highly dependent on the flow split between the superior and inferior systemic circulations. Changes in PVR in the model will alter this flow split. Consequently, the overall SaO_2 content will also change. The new SaO_2 content was calculated using equation 3. Additionally, PO_2 values will also change in the mixed systemic blood.

The inclusion of CO_2 in the model is not explicit but is taken into consideration. According to equation 3, the new SO_2 in the mixed blood is a function dependent on the flow split between upper and lower circulations, SaO_2 and SvO_2 . SvO_2 in equation 4 was calculated using the model of global oxygen transport where PCO_2 is used to calculate the alveolar oxygen tension (Farrel et al., 2009). DO_2 was calculated based on oxygen partial pressure (PO_2) and Hb count of each patient (equation 5). It is important to note that for BDG patients the source of oxygen is the pulmonary flow, thus Q_s is equal to Q_p . OER is finally calculated using equation 6 and then compared with baseline (rest).

$$SaO_2 = (Q_p/Q_s) * SaO_{2p} + (Q_{sdown}/Q_s) * SvO_2 \quad (3)$$

$$SvO_2 = 80.302 \exp(0.008 DO_2/VO_2) - 85.298 \exp(-0.499 DO_2/VO_2) \quad (4)$$

$$DO_2 = 10Q_s [(1.36Hb \times SaO_2) + (0.003PaO_2)] \quad (5)$$

$$OER = \frac{VO_2}{DO_2} \quad (6)$$

2.5 Ventricular function analysis

Ventricular performance is the main result used to evaluate the success of SV palliation. (Day et al., 2006; Freedom et al., 1998; Hussain et al., 2008; Petrucci et al., 2010; Walker et al., 2004). The following hemodynamic parameters were calculated in this study to assess ventricular performance: cardiac index, mean systemic pressure (MSP), pulmonary to systemic flow ratio (Q_p/Q_s), and ventricular vascular coupling ratio (E_a/E_{es}).

2.6 Statistical analysis

All the parameters were presented as mean values with standard deviation unless otherwise stated. The comparison was made between groups A_{pvr} vs. B_{pvr} and A_{age} vs. B_{age} with a non-parametric non-paired test (Mann-Whitney test). Differences were considered significant for p-values less than 0.05.

3. Results

As mentioned, data was grouped by patient age at the time of surgery and by PVR at rest. The changes in hemodynamics, ventricular function and oxygenation parameters are further discussed in the following sections.

3.1 Effect on cardiac flows

The current model simulates the expected change in CI during exercise. Analyses by both PVR and age showed significant differences between groups ($p < 0.05$) compared to baseline values for all exercise levels (see Figure 2).

The A_{pvr} vs B_{pvr} comparison showed significant changes ($p < 0.05$) in cardiac flows. The mean CI in group A (4.37 ± 1.08 l/min/m² at baseline) was significantly ($p < 0.05$) smaller than the mean CI in group B (6.34 ± 1.96 l/min/m² at baseline) at all exercise levels. CI increased by $21.0 \pm 2.7\%$ at low exercise levels, $42.5 \pm 5.4\%$ at moderate exercise levels, and $82.6 \pm 11.3\%$ at high exercise levels for the A_{pvr} group. Group B_{pvr} showed increases in CI of $19.9 \pm 1.3\%$, $39.9 \pm 2.4\%$ and $76.5 \pm 4.4\%$ for the low, moderate and high levels of exercise respectively.

The same behavior was found when comparing by age. CI increased by $21.3 \pm 2.2\%$ at low exercise levels, $42.8 \pm 4.5\%$ at moderate exercise levels, and $82.3 \pm 9.8\%$ at high exercise levels for group A_{age} . Group B_{age} showed increases in CI of $18.9 \pm 0.9\%$, $38.3 \pm 1.5\%$ and $74.3 \pm 3.1\%$ for the low, moderate and high levels of exercise respectively.

Qp/Qs is strongly affected by exercise (see Figure 3). At moderate and high levels Qp/Qs is below 0.44 ± 0.06 for the A_{pvr} group. For the B_{pvr} group, Qp/Qs decreased to 0.43 ± 0.05 at the high exercise level. When compared by age, patients younger than 2 years have a decreased Qp/Qs of 0.40 ± 0.06 at high levels of exercise and patients older than 2 years have a decreased Qp/Qs of 0.43 ± 0.06 at high levels of exercise.

3.2 Effect on Mean Systemic Pressure and Ea/Ees

The change in MSP between exercise and rest was not significant for all groups (see Figure 4). At high levels of exercise the decrease in MSP is related to reduction in the systemic resistance.

Differences in Ea/Ees were not statistically significant for any group analyzed. In addition, Ea/Ees changes were not significant ($p > 0.05$) for the complete group ($n=39$) at any exercise level. The average Ea/Ees value was higher than 1.0 for all groups at all exercise levels and in a global analysis ($Ea/Ees=1.14 \pm 0.38$). An Ea/Ees above 1.0 shows that the ventricular elastance is lower than the arterial elastance which can be considered poor ventricular function, see Figure 5.

3.3 Effect on oxygen extraction ratio, OER

OER increased for all groups at all exercise levels compared with the rest condition (Figure 6). The normal range of OER in a healthy individual is between 0.21 and 0.32 (McGee et al., 2011). Patients younger than 2 years and patients with low PVR at baseline (rest condition)

were within the range of normal OER values at rest. However, as exercise increases all patients had OERs above the healthy range. A more critical situation occurs for patients older than two years and for patients with PVR higher than $3.5 \text{ WU} \cdot \text{m}^2$ at rest. These patients are already above the healthy range for OER at rest and therefore any increase in physical activity would result in an OER above the tolerable range.

4. Discussion

In this study the effect of three exercise conditions on hemodynamics and oxygenation within the BDG physiology was investigated. The results show that increasing exercise activity has a significant impact on CI, Qp/Qs and OER. Changes in flow between upper and lower circulation can cause deleterious oxygenation problems and afterload/preload mismatch in BDG patients. According to oxygenation parameters, the patients who are older than 2 years and had a PVR lower than $3.5 \text{ WU} \cdot \text{m}^2$ at rest could best tolerate exercise. This is in part due to older patients having more mature pulmonary vasculature. For all other patients, the increased oxygen demand was not supplied by the increased CI. The results for CI show the ability of each patient (linked to his/her ventricular function parameters) to maintain the desired oxygen level by increasing their cardiac index (Figure 2) while keeping OER levels within the normal range. Stroke work must increase in order to maintain an adequate cardiac output that will promote exercise tolerance. However, the capability of the system to increase output power depends on ventricular performance in each patient. If cardiac output cannot be maintained or increased, the individual will have a low exercise capacity and the development of congestive heart failure and ventricle hypertrophy may occur. It has been shown by several studies that Fontan patients have impaired aerobic capacity due to their limited ability to increase cardiac output and the passive blood flow through the lungs even with 95% SaO_2 at rest. (Mahle et al., 1999, 2012, Madan et al., 2013) For BDG patients who experience the mixing of blood in the single ventricle and have values of SaO_2 around 85% at rest, exercise capacity is greatly reduced.

The results showed significant decreases in Qp/Qs ratio as exercise increased (Figure 3). Since only the upper systemic flow is oxygenated in BDG circulation, SO_2 of systemic blood flow is compromised when the lower systemic (deoxygenated) blood flow is greater than the upper systemic (oxygenated) blood flow.

The mean OER in groups B_{pvr} (baseline PVR $3.5 \text{ WU} \cdot \text{m}^2$) and B_{age} (age ≥ 2 years) remained in the normal range (0.21-0.32) at rest, while all other groups at all rest and exercise conditions were above the healthy range for OER.

It should also be noted that if OER is not adequate and declines with exercise, the cerebral blood flow oxygenation is also low. Low cerebral flow or poorly oxygen-saturated cerebral blood flow is linked to neurological development resulting in poor long term neurological outcomes in BDG patients (Agarwall et al., 2006; Cassidy, 2000; Fogel et al., 2004; Hancock et al., 2002).

Ventricular-vascular coupling ratio (E_a/E_{es}) is the capacity of the ventricle to eject the proper amount of blood required for the system to overcome the imposed preload and

afterload. In both analyses, the changes in Ea/Ees were related to changes in Ea since the variations in Ees with exercise were not significant. It has been reported that although ventricular function improves after BDG operation, preload still remains higher than normal (Colan, 2002). The current results suggest that the mean Ea/Ees is not well coupled for this group of BDG patients even at rest. Ea/Ees mean values in all subgroups is greater than 1 and increased slightly with exercise. This means that ventricle contractility could not be increased to compensate for the increased preload and afterload during exercise (Tanoue et al., 2003). However, it should be noted that each patient's physiological condition determines their capability to overcome this limitation. Nevertheless, in both analyses, mean Ea/Ees was still greater than 1 for all groups at baseline and increased slightly with exercise.

The distribution of left vs right functional ventricles within the divisions used for analysis is an important consideration. We found that the percentage of functional left ventricles in the group with PVR higher than 3.5 W.U. is 75%, while the group with PVR lower than 3.5 W.U. is 67%. For the age based analysis, the percentage of functional left ventricles for the younger than 2 group was 50%, while the group older than 2 had 83% functioning left ventricles.

Upon further evaluation, we realized that the “best performing” groups in the two analyses were not consistently the groups with the greater prevalence of functioning left ventricles. For example, the group with PVR lower than 3.5 W.U. showed better performance than the above 3.5 W.U. group, even though it had 67% functioning left ventricles compared to 75%. Based on the results from this study, our analysis does not seem to be biased due to the varying prevalence of left vs right functional ventricles between the groups. As this study was focused on age and PVR at rest for inputs into the model, we did not include additional parameters related to the initial ventricular performance at rest such as stroke volume or ejection fraction. We believe that the inclusion of these parameters could show a stronger baseline condition for patients with functioning left ventricles. However, this prediction needs further thought and should be included in future analysis.

In general, even for healthy individuals, exercise tolerance depends on each patient's physiology, ventricular function and PVR at rest. Studies have shown that for Fontan patients with a more mature pulmonary system than BDG patients, high values of PVR can have detrimental effects including significant impairment to exercise performance, decreases in oxygen pulse, and compromised oxygen delivery (Darst et al., 2010; Gottlieb et al., 2012; Hosseinpour et al., 2006; Johnson et al., 2013; Malhotra et al., 2008, Mahle et al., 2012, Madan et al., 2013, Driscoll et al., 1984, Driscoll., 1986). These results are in complete agreement with the results of this model.

SV patients already have a limited ventricular capacity due to the constant challenge of supplying blood to a circulation in parallel with a single pump. This shortcoming, along with the current predictions of poor ventricular performance and low oxygenation under exercise conditions, suggest that BDG patients have even more difficulties, especially those with elevated PVR at rest.

4.1 Limitations

One of the biggest limitations of mathematical models for physiological systems is the inclusion of adaptation responses and complex biological changes and the availability of patient specific data as input parameters to fully validate the model. Although improvements have been made over time, there will always be many shortcomings in mathematically modeling physiological systems. This model serves as a preliminary framework to investigate the effect of exercise on the hemodynamic and oxygenation performance of BDG patients.

Some studies have shown that volume unloading at an earlier age could increase aerobic capacity in SV palliated patients. Although this point is still controversial, we did not make any comparison in this aspect, and this could be an interesting analysis for future research (Mahle et al., 2012, Madan et al., 2013).

In addition, it is unlikely that children under two years of age will perform any kind of traditionally defined exercise. With this term, we refer to any kind of movement that implies an additional oxygen requirement that could be classified as moderate or high according to the age and the activities of the subject.

The regulation of blood flow and oxygenation in BDG circulation is controlled by many biochemical factors which are not fully understood or characterized. However, a major effect of exercise performance is the increase in cardiac output through increased HR and the increase in VO_2 which are included in the present model. As a future work, an analysis including VO_2 max should be considered to establish a threshold for each patient's exercise capacity according to the resulting CI.

5. Conclusions

In this study, for the first time to our knowledge, the effect of exercise was included in modeling the performance of BDG circulation coupled with oxygenation parameters. Data from 39 BDG patients were included in this study and the results of the model were compared between sub-groups divided by the patient's PVR at rest and the patient's age at BDG surgery. The present results showed a significant change in ventricular function and oxygenation parameters (CI, Qp/Qs, MSP, Ea/Ees, and OER) in all patients at all exercise levels.

The ventricular capacity and the OER predicted in this analysis suggest that patients with lower PVR at baseline ($\text{PVR} < 3.5 \text{ WU} \cdot \text{m}^2$) showed acceptable performance at low to moderate levels of exercise but performed poorly at high levels of exercise. The same findings are true for patients older than 2 years. Tolerance to low exercise levels will depend on each patients' ventricular capacity.

It was also shown that CI increases as an obvious effect of imposed increased HR. Moderate exercise levels require increments of CI more than 45%. For patients with PRV above $3.5 \text{ WU} \cdot \text{m}^2$, a 70% increase in CI is required at high exercise levels. Therefore, it is concluded

that PVR at baseline is a key determining factor of a patient's capability for exercise performance.

The results presented here can help clinicians understand the influence that BSA (related to age) and PVR at rest have on BDG circulation during exercise. This methodology can be a useful tool to determine a patient's ventricular limitations and show how the amount of mixed blood affects oxygenation parameters. Additionally, this could potentially be used as a tool for surgical planning when moving to the TCPC operation where the mixing of blood is restricted in most cases.

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Figure 1.

Schematic of the lumped parameter model. CLA: compliance of left atrium, Csa: compliance of systemic arterial vessels, CSvdown: compliance of systemic venous bed for lower body, CSvup: compliance of systemic venous bed for upper body, AO: aorta, IVC: inferior vena cava, LA: left atrium, LSR: systemic vascular resistance of lower body, LV: left ventricle, PVR: pulmonary vascular resistance, RA: right atrium, Rasd: resistance of atrial septal defect, Rbdg: resistance of bidirectional Glenn, Rmi: resistance of mitral valve, SVC: superior vena cava, USR: systemic vascular resistance of upper body. *Arrows indicate flow direction.

Figure 2. Cardiac Index. Left: comparison by PVR at rest, Right: Comparison by age. *=p<0.05 compared between each other at the same exercise level.

Figure 3.
Qp/Qs. Left: comparison by PVR at rest, Right: Comparison by age. *=p<0.05 compared between each other at the same exercise level.

Figure 4.
MSP. Left: comparison by PVR at rest, Right: Comparison by age. $\ast=p<0.05$ compared between each other at the same exercise level.

Figure 5. Ea/Ees. Left: comparison by PVR at rest, Right: Comparison by age. $\ast=p<0.05$ compared between each other at the same exercise level.

Figure 6.
OER. Left: comparison by PVR at rest, Right: Comparison by age.

Table 1

Patient data used in the model. Data was obtained from cath reports.

Patient	diagnostic	Age [years]	HR [bpm]	BSA [m ²]	PVR [WU* ³ m ²]	Rsys [WU* ³ m ²]	PA pressure [mmHg]	Hb [g blood/dl]	SaO ₂ [%]	VO ₂ [ml O ₂ /min]
FCI 1	HRV, PA	0.75	130	0.30	2.78	8.22	18	13.00	86	37.50
FCI 2	UNK	9.00	80	1.00	5.78	63.84	13	20.00	79	140.00
FCI 3	TA, PS	0.42	150	0.31	5.11	31.00	17	16.00	87	38.75
FCV 1	TGA, VSD	1.00	90	0.56	7.43	21.55	15	12.80	84	84.00
FCV 2	TA-TGA	0.85	150	0.35	2.30	21.16	11	13.10	86	43.75
FCI 4	DIDOV, TGA	1.00	120	0.44	4.18	23.93	15	13.00	85	53.68
FCI 5	DIDOV, TGA	1.17	118	0.51	2.06	18.29	15	14.00	83	86.70
FCI 6	UNK	2.00	120	0.53	5.93	32.35	15	12.50	80	79.50
FCI 7	ASD, LRS, PA, HRV	2.00	130	0.45	6.04	54.99	12	13.00	85	54.90
FCI 8	TA, DOV, LA, PS	0.92	130	0.39	1.66	9.05	17	13.70	73	48.75
FCI 9	SV, TA, PS	14.34	125	1.35	4.05	14.80	12	15.80	68	189.00
FCI 10	SV,TA	10.94	85	0.90	3.50	26.00	27	18.10	71	126.00
FCI 11	SV,TA	7.04	125	0.70	4.50	12.40	24	16.00	75	92.40
FCI 12	SV, TA, CIA, PA	10.54	120	0.98	5.69	17.34	17	26.70	73	137.20
FCI 13	SV,TA	9.59	120	1.00	13.00	45.49	22	22.20	76	140.00
FCI 15	SV,TA	4.19	120	0.76	4.64	12.95	15	19.00	83	100.32
FCI 18	TA	3.58	120	0.61	3.50	21.00	16	22.11	77	62.22
FCI 19	TA, PS	4.12	120	0.73	2.00	13.10	14	22.00	73	96.36
FCI 20	SV,TA	17.93	120	1.50	20.05	10.00	13	17.70	80	210.00
FCI 21	SV,TA	11.79	125	0.63	6.60	4.80	14	22.00	75	64.26
FCI 22	SV,TA,SPS	15.46	90	1.46	9.76	8.26	15	18.90	80	204.40
FCI 23	TA, PS	9.00	120	0.83	2.70	43.00	12	23.70	75	103.75
FCI 24	SV,TA	10.44	90	1.05	2.00	7.20	11	15.20	73	147.00
FCI 26	SV,TA,TGA	6.62	120	0.72	1.60	19.00	17	17.00	81	95.04
FCI 27	TA, LPS, VD	4.49	90	0.65	5.00	39.80	17	19.30	74	71.50
FCI 28	PA, TH	7.31	130	0.96	1.80	7.50	18	16.90	78	134.40
FCI 29	SV, DIDOV, PA, TGA	3.24	130	0.63	2.50	7.90	16	16.30	80	64.26
FCI 32	SV, DIDOV, PA	3.95	110	0.75	2.70	21.12	14	20.20	78	99.00

Patient	diagnostic	Age [years]	HR [bpm]	BSA [m ²]	PVR [WU*m ²]	Rsys [WU*m ²]	PA pressure [mmHg]	Hb [g blood/dl]	SaO ₂ [%]	VO ₂ [ml O ₂ /min]
FCI 33	SV,TA	12.54	120	1.23	4.32	15.02	13	19.80	71	172.2
FCI 34	SV,TA	7.38	130	0.89	2.10	18.20	15	17.60	73	124.6
FCI 35	SV,TGA,PS	3.75	110	0.63	4.15	52.70	22	22.70	81	64.26
CHOA55	CAVC, RA isomerism, SP, dTGA, DORV	1.75	120	0.52	3.42	17.00	17	13.00	89	88.40
CHOA005	HRV, TA, VSD, PS, abnormal right lung	4.00	130	0.77	6.06	24.90	12	16.70	80	101.64
CHOA003	HLHS	2.10	116	0.50	2.76	21.36	10	15.30	86	92.00
CHOA00d	TGA	3.00	95	0.59	3.96	16.86	15	13.80	90	60.18
CHOA00c	TGA	2.00	85	0.54	1.94	21.73	10	13.90	88	55.08
CHOP013	HLHS	1.33	115	0.44	0.69	8.96	15	15.50	79	53.68
CHOP026	HLHS	1.10	120	0.54	1.79	11.20	11	11.30	84	81.00
CHOP030	TA, VSD	1.58	130	0.51	2.32	31.59	10	16.00	90	76.50
mean	-	5.49	117	0.72	4.42	21.94	15	16.98	80	96.77
SD	-	4.71	17	0.30	3.52	14.30	4	3.82	6	48.87

ASD: atrial septal defect; BDC: bidirectional Glenn; DOV: double outlet ventricle; DIDOV: double inlet-double outlet ventricle; HF: hemifontan; HLHS: hypoplastic left heart syndrome; HRV: hypoplastic right ventricle; LA: aorta with "L" shape; LRS: left to right shunt; PA: pulmonary atresia; PAB: pulmonary artery banding; PS: pulmonary stenosis; RA: right atrium; TA: tricuspid atresia; TGA: transposition of great arteries; VSD: ventricular septal defect; UNK: unknown. FCI: Fundación Cardioinfantil Instituto de Cardiología. Bogotá, Colombia. FCV: Fundación Cardiovascular de Colombia. Bucaramanga, Colombia. CHOP: Children's Hospital of Philadelphia. Philadelphia, USA. CHOA: Children's Healthcare of Atlanta. Atlanta, USA.

Table 2

Vascular parameters used in the model.

Parameter	value [l/mmHg]
Csa	0.000271
Cpa	0.00412
Cpv	0.08
CLA	0.0003
CSvup	0.16625
CSvdown	0.16625
CLVS	0.0067
CLVD	0.0005

Csa: systemic arterial compliance, Cpa: systemic pulmonary compliance, Cpv: pulmonary venous compliance, CLA: left atrium compliance, CSvup: systemic venous upper compliance, CLVS: systolic compliance of the left ventricle, CLVD: diastolic compliance of the left ventricle, CSvdown: systemic venous lower compliance.

Table 3

Exercise conditions.

Parameter	Rest	EXE1	EXE2	EXE3
HR	1×	1.25×	1.5×	2.0×
SVR	1×	0.7×	0.5×	0.3×
PVR	1×	0.95×	0.9×	0.85×
VO ₂	1×	1.5×	2.0×	3.0×

EXE1: low exercise level, EXE2: moderate exercise level, EXE3: High exercise level. HR: heart rate, SVR: systemic vascular resistance, PVR: pulmonary vascular resistance, VO₂: oxygen consumption.