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Simulation of the Fontan circulation during rest and exercise

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Abstract—**The Fontan palliation was introduced as surgical repair method for tricuspid atresia, creating a univentricular serial circulation. However, it is used as treatment for other life threatening complex congenital heart diseases as well. The variation of underlying pathologies treated with this palliation makes optimization difficult. To assist the optimization process, we adjusted a lumped parameter computational model of the biventricular circulation (CircAdapt) and evaluated the univentricular circulation. The model simulates beat-to-beat dynamics of the two cardiac chambers, the valves, and the systemic and pulmonary circulations. The univentricular circulation in rest and exercise was simulated. Exercise resulted in increased stroke volume, heart rate, pulse pressure, and stressed blood volume. Central venous pressure rose as a result of the constant pulmonary resistance, reducing systemic pressure drop. Reduced systemic pressure drop implies either reduction of systemic flow or further decrease of systemic resistance. Based on our simulation results, we conclude that exercise capacity in Fontan patients is limited due to increase of central venous pressure and the impossibility to reduce systemic resistance further, restricting systemic flow.**

I. Introduction

In 1971 Francis Fontan introduced a surgical repair method for tricuspid atresia (1). He created a bypass from the venae cavae via the right atrium to the pulmonary artery to create a serial circulation and to decrease the volume load of the univentricular heart. In the following decades the Fontan procedure was modified several times (2), with total or partial exclusion of the right atrium. Since the 1970s, many newborns with life threatening complex congenital heart disease underwent the Fontan procedure, or a modification of it, to create a functional univentricular serial circulation. Although the clinical management of severe and complex heart disease improved over the years, the diversity of underlying pathologies, e.g., valve atresia, abnormalities of the cardiac structure, or combinations, makes optimization of the Fontan procedure difficult.

Computer fluid dynamics, *in vivo* and *in vitro* experiments, and analytical models have been used to gain insight into the hemodynamics of the completed univentricular circulation and to design a more ideal Fontan circulation (2). Since the optimal Fontan circulation was supposed to have minimal turbulent blood flow in the connection towards the pulmonary vasculature and hence, energy losses, many of these models focused on fluid dynamics and energy efficiency (2-4). However, the Fontan physiology not only influences local blood flow patterns, but also impacts general pressures, workload of the ventricle and resistance of the pulmonary peripheral circulation. To assist the optimization of the Fontan palliation we introduce a multi-scale lumped parameter model of the circulation (CircAdapt) (5). The CircAdapt model includes contractile sheets representing the individual cardiac cavities, compliant tubes representing arteries and veins, and variable resistors mimicking the pulmonary and systemic peripheral resistance. It allows assessment of complex physiological principles in rest and exercise in a simplified environment and the evaluation of pressures, volumes, and flows that are unavailable in patients.

This paper shows the results of simulations of a Fontan circulation. The effects of exercise on flows, pressures, and volumes were evaluated and a perspective on the use of CircAdapt to investigate treatment options of hypoplastic left heart syndrome (HLHS) patients is given. Although exercise in patients with a Fontan circulation has been evaluated in the past (6-9), limited data and knowledge are available about the restricted exercise tolerance of these patients (8, 10). It is reported that limited exercise capacity is not a result of decreased venous return, but is more likely due to diminished diastolic function and restriction of pulmonary resistance decrease. In this study, simulations were used to evaluate the effect of a constant pulmonary resistance during exercise on pressures and volumes in the univentricular circulation.

A. Background on HLHS and the Fontan circulation

The present study focuses on the Fontan procedure as treatment for the HLHS. This pathology is characterized by an underdeveloped left ventricle and ascending aorta. *In utero*, HLHS is tolerated by the fetus as the blood is redirected from the left atrium through the foramen ovale to the right heart side. The right ventricle pumps the blood into the pulmonary artery. The ductus arteriosus connects the pulmonary artery to the aorta, facilitating systemic perfusion. The relative proportions of blood distributed to the pulmonary and systemic circulations are determined by the ratio of systemic to pulmonary resistance. *In utero*, because the fetus does not breathe, the pulmonary resistance is high, causing a preferential flow into the systemic circulation.

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After birth, the ductus arteriosus closes and the pulmonary resistance decreases, causing a preferential flow towards the pulmonary circulation. This results in a life threatening reduction of systemic perfusion pressure and systemic flow. Without treatment the infant dies shortly after birth.

The Fontan procedure for HLHS consists of multiple stages. In the first stage, directly after birth, the right ventricle is connected to the aorta, an atrial septal defect is created, and a systemic to pulmonary shunt is made. In the second stage, the upper vena cava is connected directly to the pulmonary artery. Finally, in the third stage the lower vena cava is connected to the pulmonary artery likewise, placing both the systemic and pulmonary circulation in series with one single pump, i.e., the univentricular heart. A major problem during this staged palliation is the volume load on the ventricle during the first stage, because shunt flow to the pulmonary circulation is overestimated at the time of surgery to prevent low pulmonary flow after growth of the child. However, high pulmonary blood flow increases pulmonary venous return and, hence, volume load on the ventricle. The ventricle adapts to this high volume load and develops a large cavity volume. Completion of the Fontan circulation in the second as well as the third stage unloads the dilated and adapted ventricle.

II. Methods

A. The CircAdapt model

The multi-scale CircAdapt model of the cardiovascular system was adjusted for investigation of hemodynamics in the completed Fontan circulation in rest and during exercise. The model allows simulation of beat-to-beat dynamics of the two cardiac cavities, i.e., atrium and ventricle, and the systemic and pulmonary circulations (5). The model includes myocardial walls, large blood vessels, peripheral resistances, the atrio-ventricular valve, and the ventricular outflow valve (Fig.1). An important characteristic of the CircAdapt model is the small number of required input parameters. This reduction is achieved by adaptation of cardiac and vascular wall size and mass to mechanical load (11). More specifically, parameters describing cardiac and vessel mechanics are adapted to obtain physiological stresses and strains. Extended description and model equations of CircAdapt are available in (5) and input parameters used in this study are shown in Table 1.

TABLE I Input parameters

Parameter	**Unit**	**Value** *rest*
Mean systemic arterial blood pressure (MAP)	kPa	12.2
Systemic peripheral resistance (R_{sys})	MPa·s/m^3	149
Pulmonary peripheral resistance (R_{pulm})	MPa·s/m^3	27.5
Mean systemic blood flow (CO)	ml/s	66
Heart rate (HR)	bpm	80
Ventricular wall volume	ml	75
Maximal active myofiber stress	kPa	110

B. Simulations set-up

In rest the stroke volume was set to 50 ml and heart rate to 80 beats/min (bpm), resulting in a cardiac output (CO) of 4 l/min (8). The pulmonary resistance (R_{pulm}) was 27.5 MPa·s/m^3 and the systemic resistance (R_{sys}) was set to 149 MPa·s/m^3 (8). Mean arterial pressure (MAP) was regulated at 12.2 kPa (92 mmHg) by variation of stressed blood volume (12, 13), which is the lumped effect of venoconstriction and renal retention. Venoconstriction is a short-term mechanism to increase stressed volume, where renal retention is a long-term adaptation resulting in increased total blood volume. The Frank-Starling mechanism is included in the model of cardiac cavity mechanics.

C. Exercise simulations

Exercise was simulated by incrementally increasing prescribed CO from 4 l/min to 8 l/min at either a constant heart rate of 80 bpm or a constant stroke volume. This paper concentrates on simulations with constant heart rate. R_{pulm} was kept constant and R_{sys} was regulated to the prescribed cardiac output. Stressed volume was allowed to change to regulate MAP. To touch upon the effect of heart rate during exercise, one simulation with an increased heart rate of 100 bpm at a CO of 8 l/min was performed.

III. Results

Fig. 2A shows ventricular pressure, systemic arterial pressure, and ventricular outflow in time at a heart rate of 80 bpm in rest in a univentricular circulation. Cardiac output was 4 l/min, systolic blood pressure (SBP) was 15.4 kPa (116 mmHg), and diastolic blood pressure (DBP) was 9.5 kPa (72 mmHg). The pressure volume loop of the ventricle in rest is shown in Fig. 2B (solid line). End diastolic volume was 76 ml and end systolic volume was 26 ml, resulting in a stroke volume of 50 ml and an ejection fraction of 66%.

A. Exercise simulations

Results of simulations with increased cardiac output are shown in Fig. 2B and Fig. 3. Increase of CO, due to larger stroke volumes, resulted in larger end diastolic volumes, while end systolic volume remained unchanged (Fig. 2B). In addition, end diastolic pressure and maximal ventricular

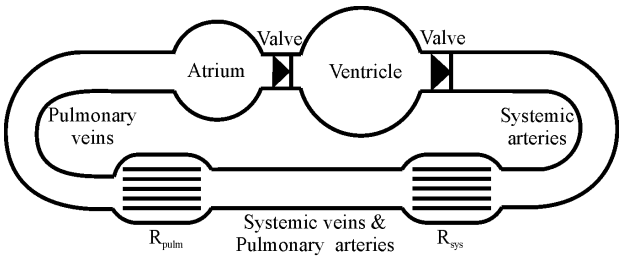

Figure 1. Scheme of the complete Fontan circulation including the ventricle and atrium, systemic arteries and veins, pulmonary arteries and veins, and the pulmonary (R_{pulm}) and systemic peripheral resistance (R_{sys}).

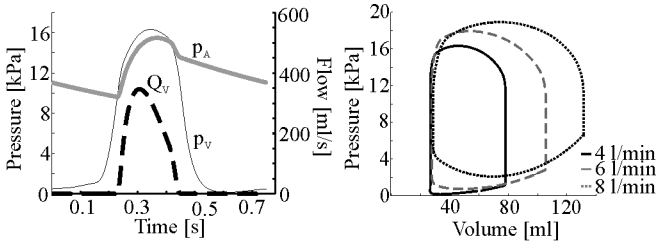

Figure 2 A) Ventricular pressure (p_v), systemic arterial pressure (p_A), and ventricular outflow (Q_v) for a Fontan circulation in rest. B) Pressure-volume loops for a Fontan circulation in rest (CO = 4 l/min) and exercise (CO = 6 l/min, CO = 8 l/min)

pressure were increased at high CO. Fig. 3A shows a biventricular systemic resistance (R_{BIV}) and univentricular systemic resistance (R_{UNIV}) for CO ranging from 4 l/min up to 8 l/min. R_{UNIV} decreased steeper with CO compared to R_{BIV}. Heart rate increase resulted in an increased R_{UNIV}. MAP, SBP, DBP, and CVP are shown in Panel 3B. Increase of CO led to increase of SBP and decrease of DBP and, hence, increase of pulse pressure. MAP was regulated to 12.2 kPa (92 mmHg) by increase of stressed blood volume (Fig. 3C). Stressed blood volume was increased concomitantly with an increase in CO to maintain MAP. The increase of stressed blood volume resulted in increase of CVP, thus reducing the pressure drop over the systemic resistance. Increase in heart rate to 100 bpm at a CO of 8 l/min reduced stroke volume as well as stressed blood volume, CVP, and R_{sys}.

IV. Discussion

The CircAdapt model of the cardiovascular system was successfully adjusted to simulate the Fontan circulation. Simulations of rest and exercise were performed to get more insight into the hemodynamics of the univentricular circulation.

Simulation of a Fontan circulation in rest with realistic hemodynamics was presented (Fig. 2). Pressures, volumes, and flows were available on significant locations, e.g., mean arterial pressure (MAP), central venous pressure (CVP) and cardiac output (CO), and did correspond to clinical data in literature (8, 14, 15). Only atrial pressure in the simulation was low compared to these clinical data. Low right atrial pressure implies low diastolic right ventricular pressure. This suggests that the right ventricle is more compliant in the model than in Fontan patients. Conceivably, simulating a less compliant ventricle would only amplify the presented results.

Exercise simulations showed that decrease of systemic resistance (R_{sys}) and increase of CO result in acute increase of CVP (Fig. 3). Increase of CVP is directly related to the absence of a separate ventricle for the pulmonary circulation and a constant pulmonary resistance (R_{pulm}), that is, the inability of Fontan patients to further decrease pulmonary resistance. According to Ohm's law an increase in flow through a resistor must be accompanied with an increase in pressure drop over the resistance, decrease of resistance, or a combination of both. In a biventricular circulation the right ventricle can compensate for an increase in pressure drop over the pulmonary resistance, leaving the CVP relatively unaffected. In a Fontan circulation, the increase in pulmonary pressure drop cannot be compensated for and it directly influences CVP, reducing the pressure drop over the systemic resistance. Because the decrease in R_{UNIV} during exercise is more rapid than the decrease of the systemic resistance in a biventricular circulation, minimal resistance and, consequently, maximum systemic flow is reached at lower exercise levels. Furthermore, high increase of CVP leads to too high filtration pressures for organs and may result in protein losing enteropathy (16).

It was assumed that the R_{pulm} of a Fontan patient is constant. However, in clinical studies a decrease of R_{pulm} to 79% of its original value was observed (8). Consequently, the pressure drop over R_{pulm} in Fontan patients might be less affected during exercise than shown in the simulation results. Therefore, it is plausible that CVP increases less extreme, and, consequently, that the systemic resistance will decrease to a lesser extent and lies in the grey area between R_{UNIV} and R_{BIV} in Fig. 3A. Conceivably, the demonstrated effects will be still present, though attenuated.

Doubling cardiac output during exercise causes an increase of stressed volume by 100% (Fig 3C). This increase is unrealistic compared to literature for the biventricular

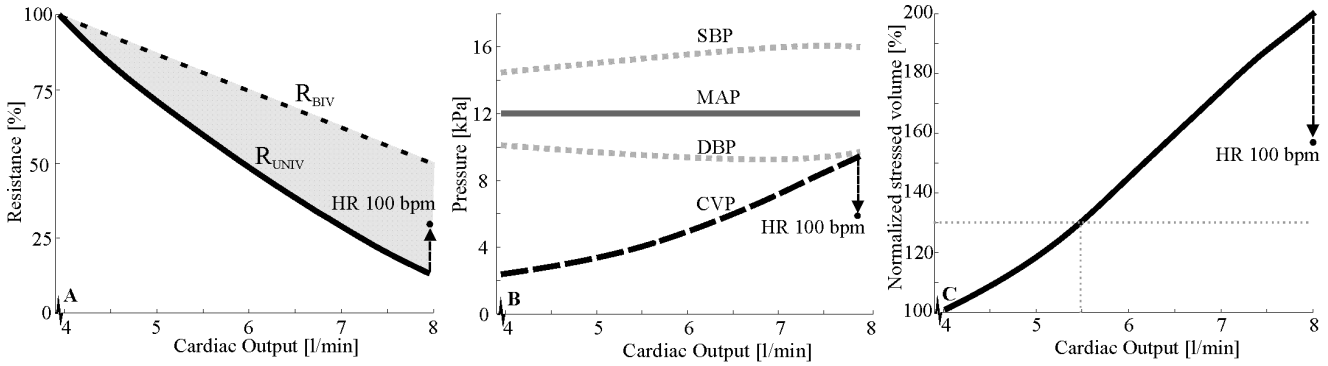

Figure 3 A) Systemic resistance of the univentricular (R_{UNIV}) and biventricular circulation (R_{BIV}) versus cardiac output. B) Systolic (SBP), mean (MAP), diastolic (DBP), and central venous blood pressure (CVP) versus cardiac output. C) Normalized stressed volume versus cardiac output.

circulation, which suggests an increase of stressed volume with maximal 30% (12, 13). If the limit of 130% stressed volume is applied to the simulation of a Fontan circulation, cardiac output cannot be increased beyond 5.5 l/min (Fig. 3C). Further decrease of the systemic resistance and increase of cardiac output in these patients, without the possibility to increase stressed volume, will result in decreased systemic blood pressure and loss of consciousness.

Despite the remarks above, the completed Fontan circulation could be simulated by the adjusted CircAdapt model. CircAdapt has the opportunities to evaluate adaptation of cardiac cavities and blood vessels to mechanical load during the respective stages of the Fontan palliation. Modeling the different stages of the Fontan palliation, including growth and adaptation of the cardiovascular system, will lead to more insight into the dominant and limiting factors of this treatment and will create the opportunity to improve patient specific treatment. In addition, CircAdapt enables simulation not only of HLHS, but also of a wide variety of cardiovascular disorders that are treated with a Fontan palliation, as the model allows for easy modification of the modeled anatomical structure.

V. Conclusion

This study shows the ability of the CircAdapt model to simulate a univentricular circulation. Simulations showed that increase of central venous pressure restrict a Fontan patient to further increase systemic flow during exercise. This will limit exercise capacity of these patients. CircAdapt has the potential to give insight in the hemodynamics of the different stages involved in the Fontan palliation and may create the opportunity to improve treatment strategy.

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