## ORIGINAL PAPER



# Partial cavopulmonary assist from the inferior vena cava to the pulmonary artery improves hemodynamics in failing Fontan circulation: a theoretical analysis

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Received: 24 June 2015/Accepted: 23 October 2015/Published online: 6 November 2015 © The Physiological Society of Japan and Springer Japan 2015

**Abstract** Cavopulmonary assist (CPA) for failing Fontan patients remains a challenging issue in the clinical setting. To evaluate the effectiveness of a partial CPA from the inferior vena cava (IVC) to the pulmonary artery (PA), we performed a theoretical analysis using a computational model of the Fontan circulation. Cardiac chambers and vascular systems were described as the time-varying elastance model and the modified three-element Windkessel model, respectively. A rotational pump described as a nonlinear function was inserted between the IVC and the PA. When pulmonary vascular resistance index varied from 2.1 to 5.9 Wood units m<sup>2</sup>, the partial CPA maintained cardiac index as efficiently as total CPA and markedly reduced the IVC pressure compared with total CPA. However, the partial CPA increased the superior vena cava pressure substantially. The modification from total to partial CPA is potentially an effective alternative in failing Fontan patients suffering from high IVC pressure.

 $\begin{tabular}{ll} \textbf{Keywords} & Fontan circulation \cdot Assist device \cdot Pulmonary \\ vascular resistance \cdot Cavopulmonary assist \cdot Inferior vena \\ cava \cdot Computational model \\ \end{tabular}$ 

#### Introduction

Since Fontan and Baudet [1] reported the first successful procedure of diverting systemic venous blood to the pulmonary artery (PA) without using the right ventricle (RV)

in 1971, the Fontan procedure has been the goal of surgical palliation for patients with functionally single ventricle physiology [2, 3]. After the Fontan operation, elevation in pulmonary vascular resistance (PVR) may decrease venous return to the single ventricle and consequently reduce cardiac output. Furthermore, elevated PVR may increase the inferior vena cava (IVC) pressure. In patients who have undergone the Fontan operation, high IVC pressure often causes critical complications such as protein-losing enteropathy and cirrhosis [4].

To restore hemodynamics in the case of failing Fontan circulation due to elevated PVR, a mechanical cavopulmonary assist (CPA) may be useful [5]. However, to establish total CPA from both venae cavae to the PA, a take-down of the cavopulmonary anastomosis may be necessary in patients who had a Fontan procedure with total cavopulmonary connection (TCPC) [6], thus limiting the use of CPA in these patients.

In patients with hypoplastic RV, one and a half ventricular repair (1.5 VR) has been reported to be a surgical alternative [7]. In this procedure, the superior vena cava (SVC) is anastomosed directly to the PA and the hypoplastic RV pumps venous blood from the IVC to the PA. In patients with Fontan circulation, use of an assist device that pumps blood from the IVC to the PA would artificially establish a circulation equivalent to the 1.5 VR. If this mode of CPA from the IVC to the PA, i.e., partial CPA, improves hemodynamics of the failing Fontan circulation, the indication of CPA in failing Fontan patients may be expanded.

In this study, we performed a theoretical analysis using computational models aiming to clarify the hemodynamic effects of a partial CPA from the IVC to the PA on the Fontan circulation under high PVR condition. We compared three conditions: the Fontan circulation (control),



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Fontan circulation with partial CPA, and Fontan circulation with total CPA.

#### Materials and methods

Schematic representations of total CPA and a partial CPA from the IVC to the PA are shown in Fig. 1. The electrical analog used to simulate the cardiovascular system of the Fontan circulation is shown in Fig. 2. Details of this model have been described previously [8]. In the present study, a 75-kg man with a body surface area of 1.9 m<sup>2</sup> was simulated according to previously published reports [8, 9].

#### Heart

The ventricular and atrial chambers are represented by the time-varying elastance model [8–11]. Pressure and volume of each chamber are related by:

$$P_{\rm cc}(t) = \left[P_{\rm es,cc}(V_{\rm cc}) - P_{\rm ed,cc}(V_{\rm cc})\right] e_{\rm cc}(t) + P_{\rm ed,cc}(V_{\rm cc})$$

$$\tag{1}$$

$$P_{\rm ed,cc} = A_{\rm cc} \left[ e^{B_{\rm cc}(V_{\rm ed,cc} - V_{0,cc})} - 1 \right]$$
 (2)

$$P_{\rm es,cc} = E_{\rm es,cc} [V_{\rm es,cc} - V_{0,cc}] \tag{3}$$

$$e_{cc}(t) = 0.5[1 - \cos(\pi t / T_{es.cc})] \quad (0 \le t < 2T_{es.cc})$$

$$e_{\rm cc}(t) = 0 \quad (2T_{\rm es,cc} \le t < T_{\rm c}) \tag{4}$$

where  $P_{\rm cc}$  and  $V_{\rm cc}$  are chamber pressure and volume, respectively [cc denotes single atrial (SA) or single ventricular (SV) chamber], and t is the time from the start of systole. The chamber pressure is modeled as the sum of end-diastolic pressure ( $P_{\rm ed,cc}$ , Eq. 2) and the developed pressure [difference between end-systolic pressure ( $P_{\rm es,cc}$ , Eq. 3) and

 $P_{\rm ed,cc}$ ] scaled by normalized elastance [ $e_{\rm cc}(t)$ , Eq. 4]. The parameters used in this model are listed in Table 1. Each valve is represented as an ideal diode connected serially to a small resistor ( $R_{\rm AV}$ ; aortic,  $R_{\rm AVV}$ ; atrioventricular).

#### Vascular system

Pulmonary and systemic vascular systems are modeled as modified three-element Windkessel models (Fig. 2). Each vascular system is modeled by lumped venous ( $C_v$ ) and arterial ( $C_a$ ) capacitances, a characteristic impedance ( $R_c$ ), arterial resistance ( $R_a$ ), and a resistance proximal to  $C_v$  ( $R_v$ ). For each variable, pulmonary circulation is denoted by adding the subscript ( $p_c$ , such as  $R_{a,p}$ ), superior systemic circulation by adding ( $s_s$ ) and inferior circulation by adding ( $s_s$ ). Linear relation between pressure drop and flow in each resistance, the relation between pressure ( $P_c$ ) and volume ( $V_c$ ) in each capacitance C (Eq. 5), and the change in volume in each capacitance [dV(t)/dt] calculated by the difference between inflow and outflow (Eq. 6) are used to describe each vascular system:

$$P_{\rm c} = \frac{V_{\rm c}}{C} \tag{5}$$

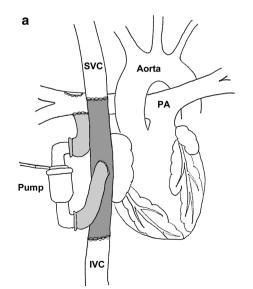
$$\frac{\mathrm{d}V(t)}{\mathrm{d}t} = \sum Q_{\mathrm{inflow}}(t) - \sum Q_{\mathrm{outflow}}(t) \tag{6}$$

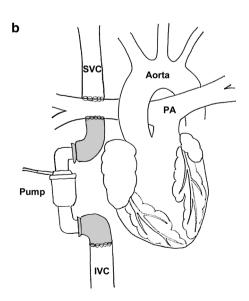
where  $Q_{\text{inflow}}(t)$  and  $Q_{\text{outflow}}(t)$  are volumetric inflow and outflow, respectively.

## Rotational pump model

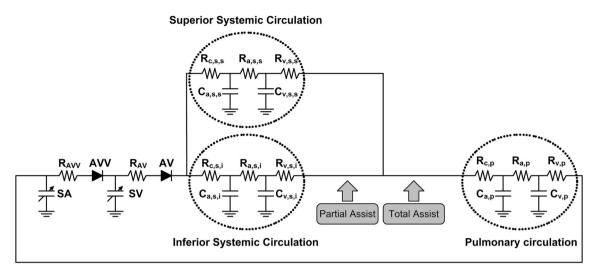
The flow of a rotational pump has been described as a function of pressure head ( $\Delta P$ ) and rotational frequency (r)

Fig. 1 Schematic representations of total cavopulmonary assist from both venae cavae to the pulmonary artery (a) and partial cavopulmonary assist from the inferior vena cava to the pulmonary artery (b). SVC superior vena cava, IVC inferior vena cava, PA pulmonary artery









**Fig. 2** An electrical analog of the Fontan circulation. In the partial cavopulmonary assist (CPA) model, a rotational pump is added between the inferior systemic venous resistance ( $R_{v,s,i}$ ) and the junction of superior and inferior systemic venous return. In the total

CPA model, a rotational pump is added between the junction of superior and inferior systemic venous return and the pulmonary characteristic impedance ( $R_{c,p}$ )

Table 1 Parameters used in the Fontan model

Valvular resistance (forward),

Heart rate (HR), beats/min	75			
Duration of cardiac cycle ( $T_c$ ), ms	800			
Time advance of atrial systole, ms	16			
	SV	SA		
Time to end systole $(T_{es})$ , ms	200	120		
End-systolic elastance ( $E_{\rm es}$ ), mmHg/ml	3.0	0.5		
Scaling factor of EDPVR (A), mmHg	0.35	0.06		
Exponent for EDPVR $(B)$ , ml <sup>-1</sup>	0.033	0.264		
Unstressed volume $(V_0)$ , ml	0	5		
	Aortic	Atrioventricular		

	Systemic		Pulmonary
	Superior (s, s)	Inferior (s, i)	(p)
Arterial resistance ( $R_a$ ), mmHg s ml <sup>-1</sup>	2.25	1.5	0.03
Characteristic impedance ( $R_c$ ), mmHg s ml <sup>-1</sup>	0.075	0.05	0.02
Venous resistance $(R_v)$ , mmHg s ml <sup>-1</sup>	0.0375	0.025	0.015
Arterial capacitance (C <sub>a</sub> ), ml/mmHg	0.528	0.792	13
Venous capacitance (C <sub>v</sub> ), ml/mmHg	28	42	8

0.001

0.001

SV single ventricle, SA single atrium, EDPVR end-diastolic pressure-volume relation

in a previous study [12]. Therefore, in the present study, a non-linear function is used to simulate the flow of the rotational pump ( $Q_{pump}$ ):

$$Q_{\text{pump}} = \frac{r}{6000} - \frac{500\Delta P}{r} \tag{7}$$

The simulated pump flow is shown in Fig. 3. This flow characteristic is almost similar to that of a Synergy micropump (CircuLite Inc., Saddle Brook, NJ, USA) [13].

# **Protocols**

First, the control state was simulated with  $R_{\rm a,p}$  set at 0.03 mmHg s ml<sup>-1</sup>. Total stressed blood volume ( $V_{\rm s}$ ), which is the sum of the stressed volumes in all capacitances and in all chambers, was set at 1224 ml.

$$V_{s} = V_{SA} + V_{SV} + V_{Ca,s,s} + V_{Cv,s,s} + V_{Ca,s,i} + V_{Cv,s,i} + V_{Ca,p} + V_{Cv,p}$$
(8)

The simultaneous differential equations (Eqs. 1–8) were solved using MATLAB/Simulink (MathWorks Inc., Natick, MA, USA).

To simulate elevated PVR,  $R_{\rm a,p}$  was increased stepwise from 0.03 to 0.15 mmHg s ml $^{-1}$  (from 0.95 to 4.75 Wood units m $^2$ ) in increments of 0.03 mmHg s ml $^{-1}$  (0.95 Wood units m $^2$ ). As a result, PVR index [PVRI =  $R_{\rm c,p}$  +  $R_{\rm a,p}$  +  $R_{\rm v,p}$  =  $R_{\rm a,p}$  + 1.11 (Wood units m $^2$ ), normal values < 2.0 Wood units m $^2$  [14] ] increased from 2.1 to 5.9 Wood units m $^2$ . Heart rate was fixed at 75 bpm, and mean systemic arterial pressure (SAP) was set at the same value as that in the control state, by adjusting  $V_{\rm s}$  in the control model or by adjusting the rotational frequency in



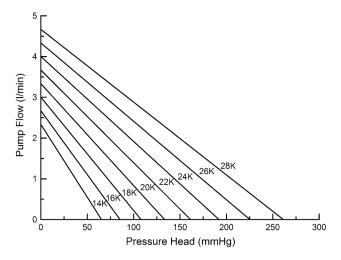


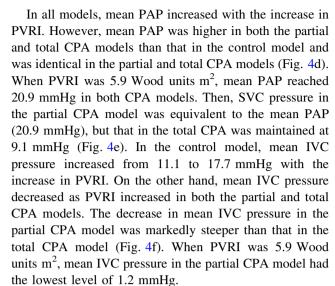
Fig. 3 The relations between pressure head and pump flow at rotational frequencies of  $14\ k$ ,  $16\ k$ ,  $18\ k$ ,  $20\ k$ ,  $22\ k$ ,  $24\ k$ ,  $26\ k$ , and  $28\ k$  rpm

both the total and partial CPA models. Cardiac index, SAP, pulmonary arterial pressure (PAP), SVC and IVC flows, SVC and IVC pressures, and atrial pressure were calculated for each model.

#### **Results**

With the stepwise increase of  $R_{\rm a,p}$ , PVRI increased from 2.1 to 5.9 Wood units m<sup>2</sup>. Mean SAP was maintained at the same magnitude of 80.3 mmHg in the control and both CPA models. In the control model, higher PVRI required larger stressed blood volume to maintain the mean SAP (Table 2). When PVRI was 5.9 Wood units m<sup>2</sup>, an additional stressed blood volume of 535 ml was required to maintain mean SAP of 80.3 mmHg in the control model. In both the partial and total CPA models, higher PVRI required higher rotational frequency to maintain the mean SAP without additional stressed blood volume. The rotational frequency was approximately 10,000 rpm lower in the partial CPA than that in total CPA (Table 2).

The increase in PVRI decreased cardiac index remarkably in the control model. On the other hand, cardiac indices were maintained in the range of 2.3–2.4 l/min/m² despite the increase in PVRI in both partial and total CPA models (Fig. 4a). The increase in PVRI did not affect SVC flow in the total CPA model, but decreased SVC flow from 0.9 to 0.8 l/min/m² in the control and partial CPA models (Fig. 4b). Although the increase in PVRI decreased IVC flow from 1.4 to 1.3 l/min/m² in the control model, the increase almost did not affect IVC flow in the total CPA model. In contrast, the partial CPA increased IVC flow from 1.4 to 1.6 l/min/m² against the increase in PVRI (Fig. 4c).



Although higher PVRI required larger stressed blood volume in the control model to maintain the mean SAP, mean atrial pressure decreased from 6.3 to 5.4 mmHg with the increase in PVRI. In both CPA models, mean atrial pressure remained almost unchanged as PVRI increased (Fig. 4g).

#### Discussion

This study using computational models reveals that in Fontan circulation, use of a partial CPA from the IVC to the PA is theoretically capable of maintaining cardiac index and reducing the IVC pressure under high PVRI conditions.

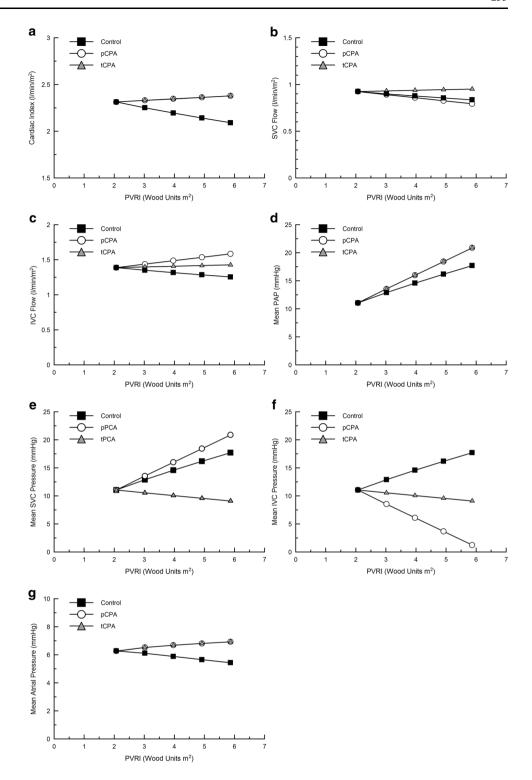
**Table 2** Stressed blood volume and rotational frequency to maintain mean arterial pressure at 80.3 mmHg

2.1	3.0	4.0	4.9	5.9			
80.3	80.3	80.3	80.3	80.3			
1224	1373	1509	1637	1759			
NA	NA	NA	NA	NA			
80.3	80.3	80.3	80.3	80.3			
1224	1224	1224	1224	1224			
15,840	16,400	16,960	17,510	18,070			
80.3	80.3	80.3	80.3	80.3			
1224	1224	1224	1224	1224			
26,390	26,570	26,750	26,940	27,120			
	80.3 1224 NA 80.3 1224 15,840 80.3 1224	80.3 80.3 1224 1373 NA NA 80.3 80.3 1224 1224 15,840 16,400 80.3 80.3 1224 1224	80.3 80.3 80.3 1224 1373 1509 NA NA NA 80.3 80.3 80.3 1224 1224 1224 15,840 16,400 16,960 80.3 80.3 80.3 1224 1224 1224	80.3 80.3 80.3 80.3 1224 1373 1509 1637 NA NA NA NA  80.3 80.3 80.3 80.3 1224 1224 1224 1224 15,840 16,400 16,960 17,510  80.3 80.3 80.3 80.3 1224 1224 1224 1224			

PVRI pulmonary vascular resistance index, MAP mean arterial pressure, SBV stressed blood volume, RF rotational frequency, pCPA partial cavopulmonary assist, tCPA total cavopulmonary assist, NA not applicable



Fig. 4 Relations between pulmonary vascular resistance index (PVRI) and hemodynamic variables. a Relation between PVRI and cardiac index. **b** Relation between PVRI and superior vena cava (SVC) flow. c Relation between PVRI and inferior vena cava (IVC) flow. d Relation between PVRI and mean pulmonary arterial pressure (PAP). e Relation between PVRI and mean SVC pressure. f Relation between PVRI and mean IVC pressure. g Relation between PVRI and mean atrial pressure. Closed square control model, open circle partial cavopulmonary assist (CPA) model, gray triangle total CPA model



# Advantages of partial cavopulmonary assist

Cavopulmonary assist for failing Fontan circulation with high PVR has recently become a popular research topic. A numerical model study has demonstrated that the highest cardiac output and SAP increment can be obtained with a right ventricular assist device (VAD) with the highest decrement of IVC pressure in the case of PVR increase [15]. Derk et al. [16] reported that an axial flow VAD restored normal hemodynamics and cardiac output when used as a pulmonary pump in a pig Fontan circulation model. However, CPA for failing Fontan patients remains a challenging issue in the clinical settings. To establish total CPA after TCPC, cannulation



into both venae cavae or take-down of the cavopul-monary anastomosis followed by re-anastomosis of the two venae cavae may be necessary [6]. Therefore, surgical establishment of total CPA may be too invasive for the failing Fontan patients. The present study demonstrates that a partial CPA from the IVC to the PA efficiently improves cardiac index comparable to that achieved by total CPA (Fig. 4a). Furthermore, the partial CPA reduces IVC pressure markedly compared with total CPA (Fig. 4f). Since the partial CPA can be implanted easily within the extra-cardiac conduit of the TCPC (Fig. 1), this modification may reduce the surgical invasion of CPA implantation.

Postoperative circulation of the partial CPA is hemodynamically equivalent to that after a 1.5 VR for hypoplastic RV. Because RV function greatly affects the postoperative hemodynamics of the 1.5 VR [8], RV dysfunction may decrease cardiac output (index) and increase IVC pressure in the 1.5 VR. On the other hand, with the partial CPA from the IVC to the PA, the RV is replaced with a rotational pump and RV function is dependent on the rotational frequency. Therefore, there may be no need to worry about RV dysfunction when using the partial CPA if the pump has sufficient power against the pressure head between the IVC and the PA.

# Disadvantages of partial CPA

A major disadvantage of the partial CPA, as well as the 1.5 VR, is elevation of the SVC pressure. Upon installation of the partial CPA, the SVC pressure is equal to the PAP. In the present study, when PVRI was set at 5.9 Wood units m<sup>2</sup>, the SVC pressure in the partial CPA model was elevated to 20.9 mmHg (Fig. 4e). This value was approximately twice as high as that in total CPA (9.1 mmHg). Such high SVC pressure may cause several complications such as significant pleural effusion [17] and SVC syndrome [18]. The SVC in the partial CPA may be loaded with the pressure from the assist device more directly than that from hypoplastic RV in the 1.5VR because the position and angle of the inflow to the PA are different between the partial CPA and the 1.5 VR. The partial CPA may cause SVC syndrome more easily than the 1.5 VR. Therefore, we need further investigations about the partial CPA including animal experiments.

A great difference between the SVC and the IVC pressures may promote the development of collaterals from the SVC to the IVC via the hemiazygos venous system and consequently increase venous return from the IVC. In 1.5 VR, increased venous return from the IVC may increase the RV preload, causing RV dysfunction. On the other hand, because the RV is replaced by a rotational pump in the partial CPA, the rotational frequency should be adjusted properly when these collaterals are patent.



Extracorporeal membrane oxygen support (ECMO) has been the most common mechanical circulatory support in failing Fontan patients, but high mortality has been reported [19]. Recently, several successful cases of VAD implantation in patients with failing Fontan circulation have been reported. Morales et al. [20] reported a successful case of VAD implantation with the Heart Mate II in a 15-year-old Fontan patient with protein-losing enteropathy. Hoganson et al. [21] reported successful bridge-toheart transplantation using a Berlin Heart VAD in a child. Niebler et al. [22] presented a successful case of using a HeartWare VAD as a bridge to transplantation. However, in these reports, VAD was used as systemic circulatory assist. There are few clinical reports on the use of CPA in failing Fontan patients. In the experimental settings, several papers have demonstrated the effectiveness of CPA in failing Fontan circulation. Giridharan et al. [23] reported that CPA improved failing Fontan circulation during diastolic dysfunction but preserved systolic function. Several researchers have recently tried to apply the Impella device (Abiomed Inc., MA, USA) to the failing Fontan circulation. Haggerty et al. [24] reported that a right-sided Impella device inserted from the IVC to the left PA restored hemodynamics of failing Fontan circulation in the experimental settings. However, this method has a demerit of a decreased contralateral (right) pulmonary flow. Furthermore, the Impella device may not be suitable for a destination therapy. Therefore, we need further investigations about the Impella device as well as the partial CPA.

Although CPA may potentially benefit patients with failing Fontan circulation, surgical invasions during implantation may limit the use of implantable CPA in the clinical settings. The present study demonstrates that a partial CPA from the IVC to the PA is theoretically able to maintain cardiac index against PVRI increase as efficiently as total CPA. The modification from total to partial CPA may reduce surgical invasion and expand the indication of implantable CPA in failing Fontan patients. In addition, although the partial CPA may cause SVC syndrome due to high SVC pressure, the partial CPA will reduce the IVC pressure more effectively than the total CPA. Therefore, the partial CPA may be beneficial for the Fontan patients suffering from protein-losing enteropathy or cirrhosis due to high IVC pressure.

## Limitations

This study has several methodological limitations. First, the parameters used in the present model were fixed except  $R_{\rm a,p}$ , stressed blood volume, and rotational frequency. A change in  $R_{\rm a,p}$  may affect other parameters such as  $C_{\rm a,p}$  in



the real-world clinical setting. Further experimental and clinical information is necessary to include interactions among parameters in our simulation. Second, we used the parameters of an adult patient, not a pediatric patient. Because pediatric patients have large variations in baseline parameters, individualized simulation may be necessary for evaluating the effectiveness of partial CPA in pediatric Fontan patients.

#### **Conclusions**

In Fontan circulation, higher PVRI decreases cardiac index and increases the IVC pressure, although it requires larger stressed blood volume. A partial CPA from the IVC to the PA is able to maintain cardiac index without extra stressed blood volume, and reduce the IVC pressure. This mode of partial CPA may expand the indication of implantable CPA in failing Fontan patients.

**Conflict of interest** The authors declare that they have no conflicts of interest.

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