Assessment of central venous physiology of Fontan circulation using peripheral venous pressure

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ABSTRACT

Objective: Elevated central venous pressure is a major cause of morbidity and mortality after the Fontan operation. The difference between mean circulatory filling pressure and central venous pressure, a driving force of venous return, is important in determining dynamic changes in central venous pressure in response to changes in ventricular properties or loading conditions. Thus, noninvasive central venous pressure and mean circulatory filling pressure estimation may contribute to optimal management in patients undergoing the Fontan operation. We tested the hypothesis that central venous pressure and mean circulatory filling pressure in those undergoing the Fontan operation can be simply estimated using peripheral venous pressure and arm equilibrium pressure, respectively.

Methods: This study included 30 patients after the Fontan operation who underwent cardiac catheterization (median 8.6, 3.4–42 years). Peripheral venous pressure was measured at the peripheral vein in the upper extremities. Mean circulatory filling pressure was calculated by the changes of arterial pressure and central venous pressure during the Valsalva maneuver. Arm equilibrium pressure was measured as equilibrated venous pressure by rapidly inflating a blood pressure cuff to 200 mm Hg.

Results: Central venous pressure and peripheral venous pressure were highly correlated (central venous pressure = $1.6 + 0.68 \times$ peripheral venous pressure, $R = 0.86$, $P < .0001$). Stepwise multivariable regression analysis showed that only peripheral venous pressure was a significant determinant of central venous pressure. Central venous pressure was accurately estimated using regression after volume loading by contrast injection ($R = 0.82$, $P < .0001$). In addition, arm equilibrium pressure measurements were highly reproducible and robustly reflected invasively measured mean circulatory filling pressure (mean circulatory filling pressure = $9.1 + 0.63 \times$ arm equilibrium pressure, $R = 0.88$, $P < .0001$).

Conclusions: Central venous pressure and mean circulatory filling pressure can be noninvasively estimated by peripheral venous pressure and arm equilibrium pressure, respectively. This should help clarify unidentified Fontan pathophysiology and the mechanisms of Fontan failure progression, thereby helping construct effective tailor-made approaches to prevent Fontan failure. (J Thorac Cardiovasc Surg 2017;153:912–20)

Estimation of central venous hemodynamics using PVP in the Fontan procedure.

Central Message

Central venous hemodynamics can be accurately estimated by less-invasive monitoring of PVP in the Fontan procedure.

Perspective

The minimum invasiveness and simplicity of our approach using the peripheral vein make it feasible to repeatedly measure central venous hemodynamics on an outpatient basis. This should help clarify unidentified Fontan pathophysiology and the mechanisms of Fontan failure progression, thereby helping construct effective tailor-made approaches to prevent Fontan failure.

See Editorial Commentary page 921.

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Abbreviations and Acronyms

CI	= cardiac index
CVP	= central venous pressure
MAP	= mean aortic pressure
Parm-occ	= arm equilibrium pressure
Pmcf	= mean circulatory filling pressure
PVP	= peripheral venous pressure
Rp	= pulmonary resistance index
Rs	= systemic resistance index
SaO ₂	= arterial oxygen saturation
TPG	= transpulmonary gradient

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The Fontan operation is a surgical completion for patients with single ventricular circulation.¹ Although it resolves cyanosis and improves prognosis, Fontan circulation has an inherent disadvantage,² represented by venous congestion.^{3,4} Central venous pressure (CVP), or Fontan pressure, is an important hemodynamic parameter that reflects this abnormal venous physiology of Fontan circulation, and elevated Fontan pressure is a major cause of increased morbidity and mortality in both the early and late periods after Fontan operation.⁵⁻⁷ Mean circulatory filling pressure (Pmcf) is another important parameter that characterizes venous hemodynamics, although less attention has been paid to it compared with CVP. Pmcf is the pressure anywhere in the circulation during circulatory arrest^{8,9} and reflects effective blood volume and systemic vascular capacitance.¹⁰⁻¹² The difference between Pmcf and CVP is a driving force of venous return and is important in determining dynamic changes in CVP in response to changes in ventricular properties or loading conditions. Even in the same cardiac index (CI) and CVP at rest, higher Pmcf indicates higher venous return resistance, which predicts a greater increase in CVP at a given decrease in ventricular contractility or a given increase in ventricular afterload.^{13,14} If combined with circulatory blood volume data, Pmcf further provides information about venous capacitance, which determines CVP variations in response to changes in volume status.¹² Thus, venous hemodynamics and therapeutic responses can differ markedly depending on Pmcf even with the same CVP and CI at rest. Therefore, it is not only useful but also important to monitor these venous parameters to better understand Fontan physiology and to determine the therapeutic strategy accordingly.^{12,15}

However, CVP and Pmcf measurement generally require invasive catheter placement and thus cannot be easily or repeatedly performed in the clinical setting. In contrast, peripheral venous pressure (PVP) can be obtained less invasively, more easily and safely, and repeatedly. If central venous hemodynamics can be accurately estimated using PVP, it would be valuable for patients' management and clarification of the venous physiology in patients undergoing the Fontan. The present study was conducted to test our hypothesis that CVP (Fontan pressure) and Pmcf in those undergoing the Fontan could be accurately estimated by using the PVP measured at rest and during transient forearm obstruction.

MATERIALS AND METHODS**Patients**

This study included 40 consecutive patients who had undergone Fontan surgery and diagnostic or interventional cardiac catheterization at Saitama Medical Center. As a general clinical practice in Japan, including at our institution, catheter examination is routinely performed 1 year after Fontan surgery to check the Fontan status, regardless of the presence or absence of symptoms. Furthermore, many Japanese institutions, including ours, subsequently perform Fontan evaluation catheterization every 5 to 10 years on the basis of the understanding that a treatable failure process (so-called the failing Fontan) can progress even in asymptomatic patients. Written informed consent was obtained from the parents of all patients, and the study was approved by the institutional review board of Saitama Medical Center, Saitama Medical University (no. 972).

Data Collection

Peripheral venous pressure and central venous pressure. Data were collected during cardiac catheterization. CVP was measured at the superior vena cava level using a 5F to 7F wedge pressure catheter. A 24-gauge venous cannula was inserted into the peripheral vein in the upper extremities before catheterization and was used for PVP measurement during catheterization. The peripheral venous line and CVP line were connected to a common pressure transducer using a 3-way stopcock to avoid any errors introduced by differences in transducer quality or pressure zero level. To assess whether the relationship between PVP and CVP can be retained in different volume statuses, the CVP and PVP measurements were repeated after volume loading by contrast media injection for angiography. In addition, we further tested the validity of the estimation in a separate cohort of 7 patients (validation cohort) who underwent catheterization after the initial enrollment of 33 patients.

Mean circulatory filling pressure. In a subgroup of 20 patients after the start of Pmcf and Parm-occ measurements, Pmcf was calculated during the Valsalva maneuver with simultaneous measurements of aortic pressure and CVP, as previously reported.¹⁶ Briefly, the Valsalva maneuver was applied with 30 cm H₂O of endotracheal pressure for 15 seconds under endotracheal anesthesia (n = 15)¹⁶ or with maximal breath-holding in patients who had spontaneous breathing without endotracheal anesthesia (n = 5). When CVP and mean aortic pressure (MAP) during the control state before the Valsalva maneuver (CVPcon and MAPcon, respectively) change to those during the Valsalva maneuver (CVPval and MAPval, respectively), Pmcf can be calculated as $Pmcf = (MAPval \times CVPcon - MAPcon \times CVPval) / (MAPval - MAPcon + CVPcon - CVPval)$ (Figure 1, A).¹⁶ Because this method relies only on the changes in CVP and MAP during the Valsalva maneuver, which reflect blood volume redistribution, in the circulatory system where venous and arterial system have capacitance,

FIGURE 1. Representative recordings of (A) arterial and CVP during the Valsalva maneuver and (B) PVP before and during arm circulation occlusion by cuff. MAP, Mean arterial pressure; *con*, control; *Parm-occ*, arm equilibrium pressure; CVP, central venous pressure; ECG, electrocardiography; *val*, Valsalva; PVP, peripheral venous pressure.

the method can be applicable to patients undergoing the Fontan who have capacitance vessels (veins and arteries).

Pmcf also was estimated from PVP as an arm equilibrium pressure (*Parm-occ*), which is a transient stop-flow forearm arterial and venous equilibrium pressure.^{8,11,17} As illustrated in Figure 1, B, *Parm-occ* was obtained as an equilibrated venous pressure during the rapid inflation of a blood pressure cuff to the pressure level of 200 mm Hg, to simultaneously occlude both arteries and veins in the arm to stop the circulation as in a circulatory arrest.¹⁷ The *Parm-occ* measurements were repeated to test data reproducibility. The estimated Pmcf from PVP (ie, *Parm-occ*) was compared with Pmcf obtained during the Valsalva maneuver.

Hemodynamic parameters and morphologic consideration. The CI was measured with the Fick method by using the estimated oxygen consumption.¹⁸ As a part of routine evaluation for patients undergoing the Fontan, we performed venography from the innominate vein or superior vena cava to assess the presence of systemic venous to pulmonary venous collaterals or stenosis in the venous to pulmonary arterial route. These factors were evaluated to assess the relationship between CVP and PVP.

Statistical Analysis

Data were summarized as means $\pm$ standard deviation. The relationships between 2 measurements were tested using the Pearson correlation coefficient and the Bland–Altman plot analysis for the differences. To determine factors other than PVP and *Parm-occ* that affect CVP and Pmcf, a stepwise multivariate linear regression analysis (a variable increase method with a minimum Bayesian information criterion) was performed by selecting hemodynamic and demographic variables that could affect CVP and Pmcf in Fontan circulation, including age, heart rate, CI, pulmonary resistance index (*R_p*), systemic resistance index (*R_s*), arterial oxygen saturation (*SaO₂*), transpulmonary gradient (TPG), and patency of fenestration. Because the included patients had no apparent lung disease, *SaO₂* should represent the degree of the right-to-left shunt through fenestration or systemic venous to pulmonary venous collaterals. We used JMP version 9.0.2 for the stepwise regression analysis and GraphPad Prism version 5.04 for other statistics.

RESULTS

There were 2 patients without clear PVP waveform¹⁹ and 1 patient with significant stenosis at the superior vena cava and pulmonary arterial junction. These patients were excluded from data analysis. Thus, data from 30 patients were finally included for the analysis of the relationship

between PVP and CVP, and to determine the estimation equation. Patients' demographic and hemodynamic data are summarized in Tables 1 and 2, respectively. Although a fenestrated Fontan operation was applied to all patients, fenestration was patent in 14 patients (47%) at the time of catheterization.

Relationship Between Peripheral Venous Pressure and Central Venous Pressure

Average CVP was 11.0 ± 3.3 mm Hg, and average PVP was 13.8 ± 4.2 mm Hg. CVP and PVP were highly correlated (Figure 2, A) ($R = 0.86$, $P < .0001$), with a regression equation given by $CVP = 1.6 + 0.68 \times PVP$. A Bland–Altman plot for PVP and CVP showed a significant positive tendency of difference between PVP and CVP to their average ($P < .05$), indicating an overestimation of CVP by PVP (Figure 2, B). A stepwise multivariable regression analysis showed that only PVP was a significant determinant of CVP (Table 3). Thus, the linear correlation ($CVP = 1.6 + 0.68 \times PVP$) shown in Figure 2, A seems necessary and sufficient for CVP estimation. Because *SaO₂* was not a significant determinant, the effects of venovenous collaterals or fenestration on the CVP–PVP relationship seemed to be insignificant.

To further validate the estimation of CVP by PVP from the equation in Figure 2, A, we measured CVP and PVP after volume loading with contrast injection in 20 randomly selected patients as a validation cohort. After contrast injection (4.8 ± 2.0 mL/kg), CVP increased from 10.9 ± 3.3 mm Hg to 13.0 ± 4.1 mm Hg ($P < .005$), and PVP increased from 13.6 ± 4.2 mm Hg to 16.2 ± 5.4 mm Hg ($P < .05$). Estimated CVP using the aforementioned regression equation significantly correlated with measured CVP (Figure 3, A, measured CVP = $1.3 + 0.93 \times$ estimated CVP, $R = 0.82$, $P < .0001$). The Bland–Altman plot for the estimated and measured CVP showed no significant tendency of difference to average ($P = .37$), and standard deviation of bias

TABLE 1. Demographic data

	Development cohort	Validation cohort	P value
No. of patients	30	7	
Male gender (%)	18 (60%)	7 (100%)	.072
Age (y)	8.6 (3.4-42)	10.0 (6.6-33)	.181
Body weight (kg)	21.3 (11.3-80.3)	30.0 (19.1-71.8)	.074
Body length (cm)	120 (89-167)	129 (118-173)	.112
Body surface area (m ²)	0.84 (0.53-1.9)	1.05 (0.81-1.9)	.108
Years after Fontan (y)	5.1 (1.0-23)	6.7 (5.0-25)	.126
Type of Fontan surgery	N	N	
Atriopulmonary connection	1	2	.086
Lateral tunnel	5	0	.560
Extracardiac conduit	24	5	.631
Underlying disease	N	N	
Univentricular connection of RV type	12	3	1.000
Univentricular connection of LV type	1	0	1.000
DORV	7	0	.306
PA IVS	3	3	.068
TA	3	0	1.000
PS hypoplastic RV	1	0	1.000
TGA + VSD + PS	1	1	.347
VSD + hypoplastic RV	1	0	1.000
HLHS	1	0	1.000

Data are median (range) or number of patients. RV, Right ventricle; LV, left ventricle; DORV, double outlet right ventricle; PA IVS, pulmonary atresia with intact ventricular septum; TA, tricuspid atresia; PS, pulmonary stenosis; TGA, transposition of the great arteries; VSD, ventricular septum defect; HLHS, hypoplastic left heart syndrome.

was 2.3 mm Hg (Figure 3, B). In addition, an excellent correlation between the measured CVP and the estimated CVP was obtained even in a separate cohort of 7 patients whose demographic data were not significantly different from those of the main group (measured CVP = $-2.6 + 1.3 \times$ estimated CVP, $R = 0.92$, $P = .0031$).

Relationship Between Mean Circulatory Filling Pressure and Arm Equilibrium Pressure

In a subgroup of 20 patients, P_{mc} obtained with the Valsalva maneuver ranged from 20.1 to 43.6 mm Hg (27.7 ± 6.3 mm Hg). By rapidly occluding circulation in

the arm with a high-pressurized cuff, PVP (12.9 ± 3.5 mm Hg) significantly increased in all cases (Parm-occ, 29.5 ± 8.8 mm Hg, $P < .0001$), with high reproducibility ($R = 0.986$, root mean square error = 2.23). There was a significant correlation between P_{mc} and Parm-occ (Figure 4, A) ($P_{mc} = 9.1 + 0.63 \times$ Parm-occ, $r = 0.88$, $P < .0001$), but the Bland-Altman plot for Parm-occ and P_{mc} showed a significant positive tendency of difference between Parm-occ and P_{mc} to their average (Figure 4, B) ($\Delta = -8.1 + 0.35 \times$ average, $r = 0.57$, $P = .0086$). Stepwise multivariate regression revealed that only Parm-occ was a significant determinant of P_{mc}

TABLE 2. Hemodynamic data

	Development cohort	Validation cohort	P value
Fenestration patent (%)	14 (47%)	2 (29%)	.675
Qp/Qs	0.85 ± 0.14	0.88 ± 0.08	.660
SaO ₂ (%)	91.9 ± 3.7	94.6 ± 2.8	.081
Rp (unit·m ²)	1.5 ± 0.6	1.7 ± 0.3	.612
Rs (unit·m ²)	19.5 ± 7.4	15.0 ± 6.8	.142
Cardiac index (L/min/m ²)	3.23 ± 0.77	3.41 ± 1.18	.613
CVP (mm Hg)	11.0 ± 3.3	10.3 ± 1.2	.867
PVP (mm Hg)	13.8 ± 4.2	12.8 ± 2.1	.473
PCWP (mm Hg)	6.3 ± 3.2	5.6 ± 1.6	.592
TPG	4.0 ± 1.7	4.5 ± 1.2	.555
P _{mc} (mm Hg)	27.7 ± 6.3	34.9 ± 3.3	.019*
Parm-occ (mm Hg)	28.9 ± 9.0	38.9 ± 7.1	.013*

Data are mean $\pm$ standard deviation. Qp/Qs, Pulmonary to systemic output ratio; SaO₂, arterial oxygen saturation; Rp, pulmonary resistance index; Rs, systemic resistance index; CVP, central venous pressure; PVP, peripheral venous pressure; PCWP, pulmonary capillary wedge pressure; TPG, transpulmonary gradient; P_{mc}, mean systemic filling pressure; Parm-occ, arm equilibrium pressure. *P < .05.

FIGURE 2. CVP estimation by PVP. A, CVP was positively correlated with PVP ($CVP = 1.6 + 0.68 \times PVP$, $P < .0001$, $R = 0.86$). B, Bland–Altman plot of PVP and CVP. The differences were positive and positively correlated with average ($P < .05$). Dashed lines indicate 95% limits of agreement. CVP, Central venous pressure; PVP, peripheral venous pressure.

(Table 3). Thus, the linear regression equation shown in Figure 4, A was necessary but sufficient to estimate Pmcf by Parm-occ. Of note, the regressions were not significantly different between patients with and without general anesthesia ($P = .18$ by analysis of covariance).

DISCUSSION

We demonstrated for the first time that CVP and Pmcf can be accurately estimated by measuring PVP in patients undergoing the Fontan. Because these 2 are important hemodynamic parameters for venous physiology that should be closely associated with morbidity and mortality in

Fontan cases, our approaches using PVP may contribute to better understanding of Fontan pathophysiology, thereby optimizing patients' management to improve prognoses.

Peripheral Venous Pressure and Central Venous Pressure Relationship

Because the peripheral veins have continuity with the central vein with a small vascular resistance, it may be intuitive that PVP reflects CVP. In fact, many researchers have tried to validate this assumption mostly in biventricular circulation and indeed consistently demonstrated significant associations between the 2 pressures.^{20–23} However, correlation coefficients were not high enough, and differences between the 2 pressures were not always small enough to accurately estimate CVP using PVP.²² In contrast, one previous study performed in patients with single ventricular circulation showed an excellent correlation between the 2 pressures.²⁴ Although the study included only 9 Fontan cases, PVP and CVP in a total of 19 patients including 10 Glenn cases were highly correlated ($R = 0.97$), and the difference between PVP and CVP was small (1.5 ± 1.5 mm Hg). The present results conducted in Fontan cases were consistent with the study by Milhoan and colleagues²⁴ in that correlation between PVP and CVP is better and differences between the 2 pressures are smaller than in previous reports in biventricular circulation. It was reported that the difference between PVP and CVP decreases with increasing CVP in biventricular circulation,²⁵ and the mechanism was proposed that high CVP prevents venous collapse.²⁵ In this aspect, the current study and the study of Milhoan and colleagues²⁴ were conducted in patients with superior vena caval-pulmonary connection in which high CVP is mandatory^{26,27} and appears to induce venous distension and reduce venous resistance. Of note, the abolition of the pressure difference between venous systems was first seen in another region of interest in the Fontan venous physiology: the splanchnic circulation.²⁸

TABLE 3. Stepwise multivariate linear regression analysis

	<i>P</i> value	β
CVP (mm Hg)		
PVP (mm Hg)	<.0001	0.860
Age (y)	.271	
Heart rate (beats/min)	.864	
Cardiac index (L/min/m ²)	.678	
Rp (unit•m ²)	.202	
Rs (unit•m ²)	.375	
SaO ₂ (%)	.932	
TPG (mm Hg)	.381	
Patency of fenestration	.812	
Pmcf (mm Hg)		
Parm-occ (mm Hg)	<.0001	0.876
Age (y)	.244	
Heart rate (beats/min)	.815	
Cardiac index (L/min/m ²)	.243	
Rp (unit•m ²)	.608	
Rs (unit•m ²)	.618	
SaO ₂ (%)	.397	
TPG (mm Hg)	.726	
Patency of fenestration	.267	

CVP, Central venous pressure; PVP, peripheral venous pressure; Rp, pulmonary resistance index; Rs, systemic resistance index; SaO₂, arterial oxygen saturation; TPG, transpulmonary gradient; Pmcf, mean systemic filling pressure; Parm-occ, arm equilibrium pressure.

FIGURE 3. Validation of CVP estimation by PVP. A, Estimated CVP using the obtained regression equation significantly correlated with measured CVP after contrast injection (measured CVP = $1.3 + 0.93 \times \text{estimated CVP}$, $P < .0001$, $R = 0.82$). B, Bland–Altman plot for estimated and measured CVP showed no significant tendency of difference to average ($P = .37$); standard deviation of bias was 2.3 mm Hg. *Dashed lines* indicate 95% limits of agreement. CVP, Central venous pressure.

Whereas a normal transhepatic venous pressure gradient of 2 to 3 mm Hg existed in normal subjects, its absence in Fontan cases signified a loss of resistance and capacitance in the hepatic sinusoids.²⁸

The close association between PVP and CVP in our study supports the important notion that CVP can be easily evaluated by using PVP in Fontan cases. Yet, unlike a previous study with only a limited number of patients, the Bland–Altman plot showed that it is inappropriate to use PVP per se as a substitute for CVP because of the dependency of the difference on the average. Instead, the use of a regression equation improved the estimation of CVP by using PVP (Figure 2). The regression equation also provided an accurate estimation of CVP both in a different condition where preload volume was increased and in a separate cohort of patients, further confirming the validity of the estimation equation.

In addition to CVP, the TPG, or atrial pressure, is an important hemodynamic parameter in Fontan circulation. Unfortunately, to the best of our knowledge, there is no peripheral hemodynamic measurement applicable to all Fontan cases that could reflect the TPG or atrial pressure. However, in Fontan cases with fenestration, echocardiography offers a pressure gradient across the fenestration that is equal to TPG. Atrial pressure can then be calculated as the difference between CVP based on peripheral hemodynamics and TPG based on echocardiography.

Venous Physiology Assessed by Mean Circulatory Filling Pressure and Arm Equilibrium Pressure

Pmcf measurement had been considered difficult in the clinical setting because it is an intravascular pressure during circulatory arrest. Ohishi and colleagues¹⁶ developed a method to estimate Pmcf in a living human body, but this

FIGURE 4. Pmcf estimation by Parm-occ. A, Pmcf was linearly correlated with Parm-occ ($\text{Pmcf} = 9.1 + 0.63 \times \text{Parm-occ}$, $P < .0001$, $R = 0.88$). B, Bland–Altman plot for Parm-occ and Pmcf showed a significant tendency of difference to average ($P < .01$). *Dashed lines* indicate 95% limits of agreement. Pmcf, Mean circulatory filling pressure; Parm-occ, arm equilibrium pressure.

still required invasive monitoring of aortic pressure and CVP during the Valsalva maneuver and has never been applied to Fontan circulation. The present study showed for the first time that Pmcf can be estimated by measuring PVP during transient forearm obstruction in Fontan circulation. The measurements were highly reproducible and robustly reflected invasively measured Pmcf. The subjects included in this study easily tolerated the tightness sensation induced by the acute and rapid insufflation of 200 mm Hg pressure on the forearm.

High CVP is a key driver of developing late complications in patients after the Fontan operation. However, we often realize the diversity of clinical outcomes among patients with similar levels of CVP measured in a resting condition during catheterization,²⁹⁻³¹ suggesting an importance of knowing dynamic changes in CVP. When we also know Pmcf other than resting CVP and CI, we can obtain a venous return curve, which enables us to predict CVP changes in response to changes in ventricular function or afterload condition.³² In addition, when combined with circulatory blood volume data, which are noninvasively obtainable by dye-dilution technique,¹² venous capacitance can be calculated. Venous capacitance appears to be generally reduced in Fontan circulation as an adaptive mechanism to preserve preload^{12,33,34} and is important to determine the CVP variation. The lower the capacitance, the larger the change in CVP in response to a given change in preload volume. Therefore, hemodynamic responses greatly depend on Pmcf even with the same CVP and CI at rest. In an animal model of Fontan circulation, Mace and colleagues¹⁴ found that Pmcf was elevated in Fontan circulation to maintain preload and discussed in detail how the changes in Pmcf affect the Fontan hemodynamics. We have also shown that a pharmacologic increase in venous capacitance, and thus a reduction of Pmcf, by using nitrates and angiotensin-converting enzyme inhibitors is associated with Fontan circulation with lower levels of CVP compared with in the absence of such treatment.¹² The modulation of venous capacitance with the same medications also was reported in an animal model of heart failure.³⁵ In addition, Ohishi and colleagues¹⁶ reported that in anesthetized patients, Pmcf was reduced by nitroglycerin and reversed by volume loading. Thus, obtaining Pmcf by using a less-invasive measurement of PVP has the potential to contribute to the selection of appropriate therapies based on the individualized Fontan pathophysiology.

Considering the progressively increasing morbidity, which is mostly related to abnormal venous physiology, with time after the Fontan surgery, it is our current approach at outpatient follow-up to assess serial changes in venous physiology and to check for related complications, including protein-losing enteropathy, hepatic disorder, or abnormal coagulability. For this purpose, we perform a blood examination at least once a year at our outpatient

clinic. At the time of blood examination, the use of an indwelling needle enables us to assess the venous hemodynamics by using PVP and Parm-occ in the outpatient setting (Video 1). If there is a significant elevation of PVP or Parm-occ, further assessment or initiation of tailor-made therapy may be suggested. Such a management protocol may deserve a prospective evaluation.

Study Limitations

The present study has several limitations that warrant further discussion. First, although Pmcf is an important determinant of venous pressure and cardiac output, no study has clearly demonstrated the clinical importance of Pmcf specifically in the Fontan prognosis, and this remains to be further explored in future studies. Special attention should be paid to avoid air embolization whenever the peripheral venous route is used. We used a regular blood pressure cuff to obtain Parm-occ. Cuff inflation to increase cuff pressure to 200 mm Hg for stop-flow took approximately 2 seconds in our study. During this inflation time, the stop of arterial flow (inflow to arm compartment) should occur after the stop of venous flow (outflow from arm compartment), which potentially induces

VIDEO 1. PVP and Parm-occ measurement in the outpatient clinic. After the insertion of a regular venous catheter (24G JELCO [Smiths Medical, Dublin, Ohio] intravenous catheter in this example), the peripheral venous line was connected to a pressure transducer. The pressure zero level should be carefully calibrated before the measurement. First, PVP was measured (15 mm Hg). Then, Parm-occ was obtained (23 mm Hg) as an equilibrated venous pressure during the rapid inflation of a blood pressure cuff to the pressure level of 200 mm Hg to simultaneously occlude both arteries and veins in the arm to stop the circulation as in a circulatory arrest. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(16\)31800-1/addons](http://www.jtcvsonline.org/article/S0022-5223(16)31800-1/addons).

TABLE 4. Estimated central venous pressure by peripheral venous pressure

PVP (mm Hg)	Estimated CVP (mm Hg)
7	6.4
8	7.0
9	7.7
10	8.4
11	9.1
12	9.8
13	10.4
14	11.1
15	11.8
16	12.5
17	13.2
18	13.8
19	14.5
20	15.2
21	15.9
22	16.6
23	17.2
24	17.9
25	18.6
26	19.3
27	20.0
28	20.6
29	21.3
30	22.0

PVP, Peripheral venous pressure; CVP, central venous pressure.

overestimation of P_{mc}f by Parm-occ. To address this, we tested the effect of the cuff inflation timing on Parm-occ values in an additional 6 patients, in whom Parm-occ measurement was repeated with 2 different inflation timings (2 and 5 seconds). We found that the obtained Parm-occ values were similar between the 2 different cuff inflation timings (Parm-occ by 5 seconds = $2.5 + 0.93 \times$ Parm-occ by 2 seconds, $R = 0.98$, $P = .0008$). Therefore, the effects of the timing of cuff inflation seemed to be minimum at least within 5 seconds. In addition, the time lag between venous and arterial occlusion can be shortened by using a specially designed device to more quickly occlude arm vessels.¹¹ Nevertheless, our study rather validated the way to measure Parm-occ for P_{mc}f estimation with wide applicability by using a regular blood pressure cuff. This study included several types of Fontan circuits (Table 1), although most of them were extracardiac conduit Fontan circuits. Because the type of Fontan is an issue between lower-body circulation and pulmonary circulation, it would be unlikely that the types of Fontan surgery have an impact on the relationship between CVP and PVP of the upper arm. Although this study demonstrated the close relationships between CVP and PVP and between P_{mc}f and Parm-occ, some biases remained. Efforts to reduce the factors that potentially affect the

continuity of the venous system may be needed to further improve the estimation quality. These would include compression of the vessel due to patient positioning, soft tissue, or muscular obstruction as the vein passes from the surface to the deeper connecting system, or even a pathologic process leading to venous obstruction.²³

CVP values corresponding to a measured PVP based on the regression equation are provided in Table 4 for clinical use and for external validations, as well to establish further refined regression equations in future study including a larger cohort.

CONCLUSIONS

Central venous hemodynamics can be accurately estimated by less-invasive monitoring of peripheral venous hemodynamics in patients undergoing the Fontan procedure. Despite the well-recognized importance of central venous hemodynamics in the development of late complications after Fontan surgery, information for central venous hemodynamics has never been obtainable on an outpatient clinical assessment basis. The minimum invasiveness and simplicity of our approach make it feasible to repeatedly measure central venous hemodynamics on an outpatient basis. This may help clarify an unidentified Fontan pathophysiology and the mechanisms of Fontan failure progression, thereby possibly helping construct effective tailor-made approaches to prevent Fontan failure.

Conflict of Interest Statement

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