A preoperative estimate of central venous pressure is associated with early Fontan failure

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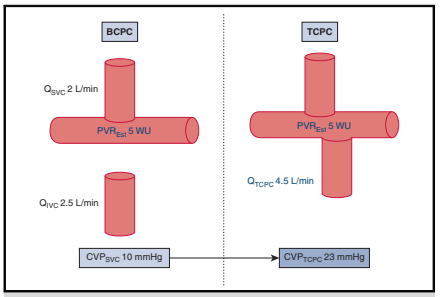
ABSTRACT

Objective: Early Fontan failure is a serious complication after total cavopulmonary connection, characterized by high central venous pressure, low cardiac output, and resistance to medical therapy. This study aimed to estimate postoperative central venous pressure in patients with total cavopulmonary connection using data routinely collected during preoperative assessment. We sought to determine if this metric correlated with measured postoperative central venous pressure and if it was associated with early Fontan failure.

Methods: In this retrospective study, central venous pressure in total cavopulmonary connection was estimated in 131 patients undergoing pre–total cavopulmonary connection assessment by cardiac magnetic resonance imaging and central venous pressure measurement under general anesthesia. Postoperative central venous pressure during the first 24 hours in the intensive care unit was collected from electronic patient records in a subset of patients. Early Fontan failure was defined as death, transplantation, total cavopulmonary connection takedown, or emergency fenestration within the first 30 days.

Results: Estimated central venous pressure in total cavopulmonary connection correlated significantly with central venous pressure during the first 24 hours in the intensive care unit ($r = 0.26$, $P = .03$), particularly in patients without a fenestration ($r = 0.45$, $P = .01$). Central venous pressure in total cavopulmonary connection was significantly associated with early Fontan failure (odds ratio, 1.1; 95% confidence interval, 1.01-1.21; $P = .03$). A threshold of central venous pressure in total cavopulmonary connection 33 mm Hg or greater was found to have the highest specificity (90%) and sensitivity (58%) for identifying early Fontan failure (area under receiver operating curve = 0.73; odds ratio, 12.4; 95% confidence interval, 2.5-62.3; $P = .002$). This association was stronger in patients with single superior vena cava.

Conclusions: Estimated central venous pressure in total cavopulmonary connection is an easily calculated metric combining preoperative pressure and flow data. Higher central venous pressure in total cavopulmonary connection is associated with an increased risk of early Fontan failure and is correlated with directly measured post–total cavopulmonary connection pressure. Identification of patients at risk of early Fontan failure has the potential to guide risk-mitigation strategies. (J Thorac Cardiovasc Surg 2021;161:1426-34)



CVP_{TCPC} is calculated as the product of estimated PVR and assumed TCPC flow.

CENTRAL MESSAGE

An estimate of the CVP after total cavopulmonary connection can be calculated from preoperative Glenn data and is associated with risk of EFF.

PERSPECTIVE

EFF is an infrequent but serious postoperative complication that may result in death or necessitate Fontan takedown or emergency fenestration. Estimated CVP may help clinicians select patients for mitigation strategies (eg, elective fenestration), a process currently hampered by a lack of clinically useful biomarkers.

See Commentaries on pages 1435 and 1436.

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Abbreviations and Acronyms

AUC = area under the curve
BCPC = bidirectional cavopulmonary connection
CI = confidence interval
CMR = cardiac magnetic resonance
CVP = central venous pressure
EFF = early Fontan failure
ICU = intensive care unit
IVC = inferior vena cava
OR = odds ratio
PA = pulmonary artery
PVR = pulmonary vascular resistance
Q_p = pulmonary blood flow
ROC = receiver operating characteristic
SPC = systemic to pulmonary collaterals
SVC = superior vena cava
TCPC = total cavopulmonary connection

Scanning this QR code will take you to the table of contents to access supplementary information.

EFF is a malignant hemodynamic state that occurs in the early postoperative period after total cavopulmonary connection (TCPC). EFF is primarily characterized by high CVP, low cardiac output, and resistance to medical therapy. EFF may result in death, take-down of the TCPC, emergency fenestration, or cardiac transplantation.[1,2]

It is recognized that mean CVP increases linearly with both Q_p and pulmonary vascular resistance (PVR) in patients with cavopulmonary connections. Thus, the transition from the BCPC to the TCPC must result in increased CVP due to the increase in Q_p. Patients who experience large increases in CVP may be at increased risk of EFF.

Unfortunately, preoperative biomarkers for EFF are lacking.[3,4] Given the pathophysiology of EFF, identification of a postoperative high CVP phenotype would be desirable to both inform surgical risk and guide mitigation strategies (eg, elective fenestration). One possibility is to use pressure and flow data, routinely acquired in the preoperative BCPC state, to derive an estimate of CVP after TCPC completion.

In this study we aimed to (1) estimate CVP in the immediate TCPC postoperative period using data routinely collected during preoperative cardiovascular magnetic resonance (CMR); (2) determine the association, if any, with CVP measured in the ICU; and (3) assess if metrics were associated with EFF.

MATERIALS AND METHODS

Study Population

The study cohort included all children between April 2005 and September 2017 who underwent elective pre-TCPC CMR assessment in whom a complete CMR flow and CVP dataset were available: 131 patients of a total population of 147. Demographic and clinical details were obtained from the medical records.

All patients subsequently underwent an extracardiac TCPC with or without elective fenestration. The decision to electively fenestrate the TCPC conduit was made by consensus of the cardiology and cardiac surgical staff at the time of case discussion, based on clinically available data. This did not include the investigational estimated TCPC pressure. The cardiac surgical team may also have decided to fenestrate based on intraoperative data, including high TCPC pressure.

Informed consent for the use of imaging data was obtained from all parents or guardians of the patients included in this study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the local committee of the UK national research ethics service (06/Q0508/124).

Cardiac Magnetic Resonance Protocol

All CMR studies were undertaken on a 1.5 T MR scanner (Avanto; Siemens Medical Systems, Erlangen, Germany) with the patient under general anesthetic, as is our institutional policy for all pre-TCPC CMR examinations. Ventilator parameters were adjusted to keep end-tidal carbon dioxide between 3.5 and 5.5 kPa, and supplemental oxygen was given as required to maintain oxygen saturations at the usual preanesthetic value for the patient.

Flow Imaging

Through-plane quantitative flow data were acquired using retrospectively gated, velocity-encoded, phase-contrast magnetic resonance. Images were acquired using a free breathing Cartesian sequence with 3 signal averages or a spiral sequence acquired during a short apneic period of 5 to 8 seconds. The spirals sequence has been validated against free breathing Cartesian phase-contrast magnetic resonance with good agreement.[5] Data were acquired in the following positions: superior vena cava (SVC) close to pulmonary artery (PA) anastomosis, inferior vena cava (IVC) at diaphragm level, pulmonary trunk (if present), proximal branch PAs, proximal pulmonary veins, and ascending aorta. Vessels were segmented using a semiautomatic vessel edge detection algorithm (OsiriX; OsiriX Foundation, Bernex, Switzerland) with manual operator correction. The following calculations were made using flow data: systemic-to-pulmonary collateral flow proportion = (total pulmonary venous return - total PA flow)/total pulmonary venous return, expressed as a percentage.[6]

Ventricular Volume and Function

Ventricular volumes were assessed using a retrospectively gated multi-slice, short-axis, steady-state free precession cine sequence.[7] Slices were acquired separately in an apneic period of 5 to 10 seconds. Manual segmentation quantified end-diastolic and systolic volumes of the functionally single ventricle using an in-house plug-in for OsiriX. Stroke volume and ejection fraction were calculated from the volumetric data. Atrioventricular valve regurgitation was calculated from flow and volumetric data.

Anatomic Assessment

Arterial and venous anatomy were assessed using gadolinium-enhanced MRA as previously described.[8] Two consecutive angiograms were acquired within a single 20- to 30-second period of apnea. The first angiogram provided systemic arterial anatomy, and the second angiogram

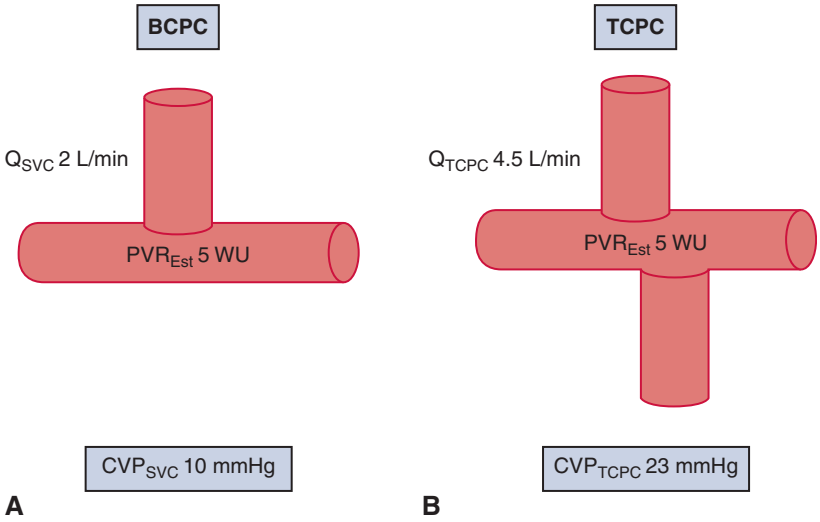


FIGURE 1. Diagrammatic presentation of methodology for calculating CVP_{TCPC}. This approach attempts to estimate the change in CVP should all systemic flow be directed to the pulmonary arteries after TCPC completion. A, At BCPC stage, SVC flow and CVP_{SVC} are measured to calculate an estimate of PVR that neglects distal atrial pressure. B, An estimate of the CVP_{TCPC} is calculated using the product of PVR and the assumed TCPC flow: aortic flow or SVC + IVC flow. In this way, the BCPC CVP is scaled in proportion to the anticipated flow in the TCPC circulation. *BCPC*, Bidirectional cavopulmonary connection; *SVC*, superior vena cava; *PVR*, pulmonary vascular resistance; *WU*, Wood units; *CVP*, central venous pressure; *TCPC*, total cavopulmonary connection.

provided second-pass contrast enhancement of venous and PA anatomy. Systemic venous decompressing collaterals from SVC territory to IVC territory were visualized using late-phase 3-dimensional MRA. These collaterals were graded by severity as previously described.[3]

Measurement of Central Venous Pressure During Preoperative Cardiac Magnetic Resonance

After CMR data acquisition, a right internal jugular venous line (Abbocath-T 22G; Venisystems, Lake Forest, Ill) was sited aseptically under ultrasound guidance.[9] The mean CVP (CVP_{BCPC}) was transduced after careful flushing and zeroing, under the same conditions as the CMR, at passive end expiration. After measurement, the cannula was removed and the site dressed.

Pressure-Flow Metrics

Pressure and flow data were used to calculate the following metrics (Figure 1 and Video 1):

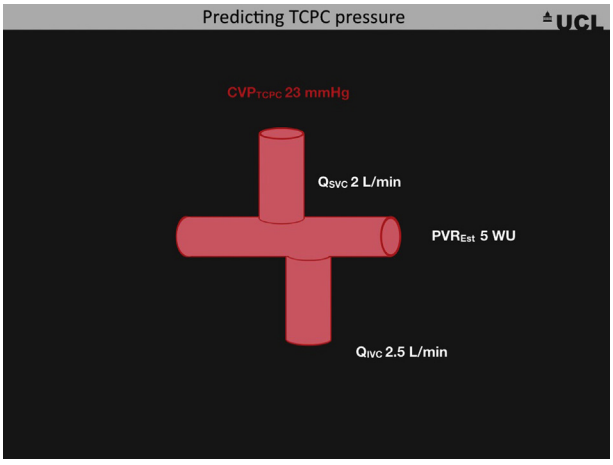
1. A simple estimate of PVR (PVR_{EST}) that neglects left atrial pressure, calculated by dividing CVP at time of BCPC by Q_p (SVC flow or SVC flow + native PA flow): $PVR_{EST} = CVP_{BCPC}/Q_P$
2. An estimate of CVP after completion of the TCPC (CVP_{TCPC}) assuming post-TCPC PA flow will equal aortic flow, Q_{Ao}: $CVP_{TCPC} = PVR_{EST} \times Q_{Ao}$

Sensitivity Analysis to Alternative Method of Measuring Systemic Flow

Estimated CVP_{TCPC} is calculated using aortic flow, which necessarily includes systemic to pulmonary collaterals (SPCs). We also performed a sensitivity analysis using CVP_{TCPC}, which excludes SPC flow (substituting aorta flow with SVC + IVC (or descending aorta) flow).

Predetermined Outcome Measures

Postoperative ICU electronic records were available for patients from 2012 onward (n = 70). In this group, the mean of hourly CVP in the 24 hours after TCPC (CVP_{ICU}) was recorded for comparison with preoperative CMR measures. Early outcome was evaluated in 2 ways: (1) length of hospital stay (measured from the day of TCPC surgery until the day of discharge from hospital to home); and (2) composite early outcome of need for emergency fenestration, emergency TCPC takedown, or early death (<30 days after TCPC). Medium-term outcome was evaluated as (1) death or transplantation at any time during follow-up.



VIDEO 1. Animation of methodology for estimating post-TCPC CVP. In this patient, CVP measured in the Glenn is 10 mm Hg and the SVC flow is 2 L/min. The estimated PVR, neglecting atrial pressure, is 5 mm $Hg.L^{-1}.min^{-1}$. The total flow through the TCPC circuit after completion is estimated as 4.5 L/min (aortic flow or SVC + descending aorta or IVC flow). The estimated TCPC pressure is given as the product of flow and resistance, 22.5 mm Hg. Video available at: https://www.jtcvs.org/article/S0022-5223(20)31742-6/fulltext.

TABLE 1. Patient demographics in the study cohort, n = 131

Parameter	Median (IQR) or No. (%)
Male	80 (61%)
Age at BCPC (y)	0.5 (0.3-1.0)
Age at CMR (y)	3.2 (2.8-3.8)
Age at TCPC (y)	3.8 (3.2-4.4)
Weight at CMR (kg)	13.7 (12.8-15.5)
SpO_2 at CMR (%)	85 (80-87)
Cardiac catheterization after CMR	6 (4.5%)
Hypoplastic left heart syndrome	48 (36%)
Damus–Kaye–Stansel	68 (52%)
Preserved native PA flow	17 (13%)
Isomerism of left or right atrial appendage	4 (3%)
Bilateral SVC	15 (11%)
End-diastolic volume (mL)	57 (47-64)
End-systolic volume (mL)	24 (19-29)
Cardiac output (L/min)	3.3 (2.9-3.9)
Ejection fraction (%)	56 (52-63)
AV valve regurgitant fraction (%)	5 (0-10)
Systemic-pulmonary flow proportion of pulmonary venous return (%)	32 (25-43)
Severity of decompressing venous collaterals	
Grade 1	72 (55%)
Grade 2	23 (18%)
Grade 3	36 (27%)
CVP (mm Hg)	11 (10-13)
PVR index: (CVP/total PA flow index)	5.2 (4.0-6.3)
Coarctation ratio (isthmus/diaphragm aorta)	1.0 (0.94-1.1)
Nakata index	208 (152-256)
McGoon ratio	2.0 (1.7-2.3)
Diameter of azygos (mm)	3.5 (2.8-4.3)
ICU LOS (d)	2 (0-4)
Hospital LOS (d)	13 (10-20)
ICU 24-h CVP (mm Hg)	15 (14-18)
Postoperative time of extubation (<24 h)	64 (91%)
Elective fenestration at TCPC	54 (41%)
Early Fontan failure	7 (5%)
Death	1 (14%)
TCPC takedown	1 (14%)
Emergency fenestration only	5 (71%)

IQR, Interquartile range; *BCPC*, bidirectional superior cavopulmonary connection; *CMR*, cardiovascular magnetic resonance; *TCPC*, total cavopulmonary connection; *SpO_2*, oxygen saturations; *PA*, pulmonary artery; *SVC*, superior vena cava; *AV*, atrioventricular; *CVP*, central venous pressure; *PVR*, pulmonary vascular resistance; *ICU*, intensive care unit; *LOS*, length of stay.

Statistics

STATA 13.1 (StataCorp LP, College Station, Tex) and GraphPad Prism 5f (San Diego, Calif) were used for statistical analysis and figures. Data were examined for normality, and where appropriate, non-normally distributed variables were log-transformed to ensure normal distribution before analysis. Descriptive statistics are expressed as mean (±95% confidence interval [CI]) when normally distributed and median (interquartile range [IQR]) when non-normally distributed, unless specified. Proportions are expressed as percentages. Data were examined for normality using the Shapiro–Wilk test, and where appropriate, non-normally distributed variables were transformed before analysis. Median regression analysis was used to assess the relationship between hospital stay and covariates.

We used logistic regression analysis to assess the relationship between EFF and clinical parameters. Multivariable logistic regression analysis was used to assess independent relationships (and control for confounding) between EFF and associated covariates. Covariates with a P less than .1 were eligible for inclusion in the multivariable model. Nonparametric receiver operating characteristic (ROC) analysis was performed. The area under the resulting ROC curve was computed using the trapezoidal rule. The area under the curve (AUC) was used to identify the threshold of CVP_{TCPC} with the greatest classification accuracy. The threshold was derived using the methodology of Liu and colleagues,[10] which optimizes the product of sensitivity and specificity. Kaplan–Meier survival analysis was used to assess the relationship between covariates and medium outcome.

RESULTS

Demographics

CMR and CVP (CVP_{BCPC}) data were obtained in 131 patients (80 male) before TCPC completion under general anesthesia. Patient characteristics for the study cohort are described in Table 1. There were no significant differences between the study cohort and the 16 excluded patients in terms of age, sex, cardiac morphology, cardiac output, ejection fraction, length of hospital stay, or EFF. Of the patients who had CMR, 6 of 131 underwent subsequent diagnostic or interventional catheterization to further investigate the hemodynamics before proceeding to TCPC. The decision to perform additional catheterization was made by the multidisciplinary team after discussion of clinical data, including CMR, echocardiography, and clinical status.

The median age at CMR was 3.2 years (IQR, 2.8-3.8 years) and age at TCPC completion 3.8 (IQR, 3.2-4.4 years), mean interval 6.7 months (standard deviation, 5.5 months). TCPC completion is performed in our institution using an extracardiac conduit, and the TCPC was electively fenestrated in 41% of patients. Median CVP_{TCPC} was 23.6 mm Hg (IQR, 18.1-28.4; range, 5.2-48). There were no differences in CVP_{TCPC} between patients who did or did not receive elective fenestration (23.0 vs 23.8 mm Hg, $P = .9$).

In the sample of 70 patients with electronic ICU records, 11% (8/70) underwent operation room extubation and 91%

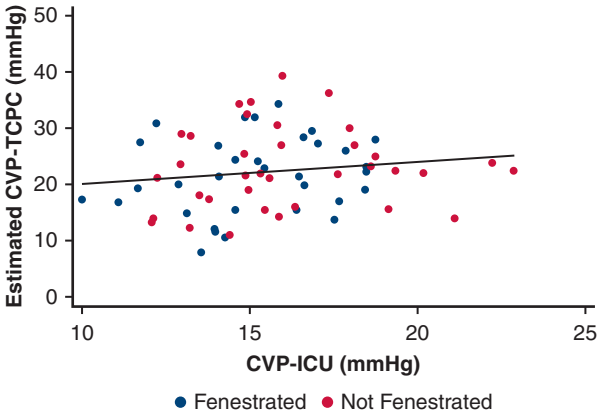


FIGURE 2. Scatter plot of CVP_{ICU} over 24 hours and estimated CVP_{TCPC}. Patients with fenestrated TCPC are shown in *blue* compared with nonfenestrated in *red*. *CVP*, Central venous pressure; *TCPC*, total cavopulmonary connection; *ICU*, intensive care unit.

(64/70) were extubated with 24 hours. The median time of extubation was 6 hours after admission to the ICU.

Relationship to Intensive Care Unit Pressure

Postoperative ICU electronic records were available in 70 patients. Estimated CVP_{TCPC} correlated significantly with CVP_{ICU} ($r = 0.26$, $P = .03$), particularly in patients without a fenestration (n = 33, $r = 0.45$, $P = .01$) (Figure 2). However, CVP_{TCPC} significantly overestimated CVP_{ICU} (15 ± 3 vs 22 ± 7 mm Hg). In patients with a time interval between CMR and ICU measurement less than 1 year (90%), the strength and significance of the correlation were higher ($r = 0.31$, $P = .01$).

Relationship to Clinical Parameters

There was no association between CVP_{TCPC} and patient age at CMR, age at BCPC, or sex. Patients with higher oxygen saturations at the time of CMR had lower estimated CVP_{TCPC} (beta -0.19, $P = .047$). CVP_{TCPC} was higher in patients with hypoplastic left heart syndrome (27 vs 22 mm Hg, $P < .005$), in whom there was a higher PVR_{Est} (6.1 vs 5.1 Wood units index, $P = .01$).

Outcome

Early Fontan failure. EFF occurred in 7 of 131 patients: emergency fenestration in 5 (1 of whom previously had an elective fenestration), emergency takedown in 1 (patient also had emergency fenestration), and death in 1 (patient also had emergency takedown) (Table 2).

CVP_{TCPC} was significantly associated with EFF (odds ratio [OR], 1.1; 95% CI, 1.01-1.21; $P = .03$). A threshold of CVP_{TCPC} 33 mm Hg or greater was found to have the highest specificity (90%) and sensitivity (57%) for identifying EFF (AUC = 0.73; 95% CI, 0.53-0.92; OR, 12.4; 95% CI, 2.5-62.3; $P = .002$) (Figure 3, *A*).

The relationship between CVP_{TCPC} and EFF was stronger in patients with a single SVC (n = 115, OR, 1.15; 95% CI, 1.03-1.28; $P = .01$). In this group, a CVP_{TCPC} threshold of 33 mm Hg or greater was also found to have the highest specificity (90%) and sensitivity (80%) for EFF (AUC = 0.85; 95% CI, 0.67-1.0; OR, 36.0; 95% CI, 3.7-35; $P = .002$) (Figure 3, *B*).

Except for the severity of systemic veno-venous collateral grade ($P = .04$), there was no other univariable associations between EFF and conventional preoperative CMR and demographic variables, including CVP_{BCPC}, ventricular volumes, ejection fraction, PVR_{EST}, hypoplastic left heart syndrome, azygos vein diameter, SPC flow, preoperative oxygen saturations, age at TCPC, age at BCPC, and sex (Table 3).

Medium-term outcome. During a mean follow-up of 6.8 years (standard deviation, 3.2 years), 4 patients died (1 at <30 days and 3 at >30 days) and 1 patient underwent cardiac transplantation. Seven patients were lost to follow-up. There were significant univariable associations between medium-term adverse outcomes and CVP_{TCPC} and veno-venous collateral grade (Table 3). CVP 33 mm Hg or greater was significantly associated with time to event, log-rank test ($P = .001$) (Figure 4). However, in our series, the covariate with strongest association with decreased transplant-free survival was the prior occurrence of EFF (OR, 164; 95% CI, 13.8-1943; $P < .005$).

Hospital stay. In the median regression analysis, hospital stay was associated with CVP_{ICU}, CVP_{TCPC} 33 mm Hg or greater, and the severity of offloading veno-venous collaterals. On multivariable analysis, only CVP_{TCPC} 33 mm Hg or greater was independently associated with hospital stay (Table 4).

Sensitivity Analyses

Alternative method of measuring systemic flow. Estimated CVP_{TCPC} calculated by excluding SPC flow was significantly lower than with SPC flow included 18 versus 24 mm Hg ($P < .05$). Calculated in this manner, there remained an equally significant association with EFF (OR, 1.2; 95% CI, 1.01-1.36; $P = .03$). However, there was no significant correlation with CVP_{ICU} for the group ($r = 0.1$, $P = .4$) and only a trend to correlation in patients without fenestration ($r = 0.35$, $P = .06$).

Patients who underwent cardiac catheterization. Given our practice of reserving cardiac catheterization as a second-line investigation, patients who underwent cardiac catheterization may have a different baseline risk of EFF. Excluding this group (n = 125) did not significantly change the association between CVP_{TCPC} and EFF (OR, 1.1; 95% CI, 1.03-1.25; $P = .01$).

DISCUSSION

With the evolution of surgical and perioperative management of the TCPC, biomarkers from previous eras

TABLE 2. Early and medium-term clinical outcome data for patients

Case	Follow-up (mo)	EF (%)	Estimated TCPC CVP	ICU CVP	CPB time	Elective fenestration	Emergency fenestration	Take-down	Early death	Late death	Late transplantation
1	0.9	51	36.0	-	159	Yes	No	Yes	Yes	-	-
2	9.5	63	39.9	-	78	No	Yes			Yes	
3	15.0	67	34.1	-	84	No	Yes			Yes	
4	65.8	52	27.2	-	97	Yes	No				Yes
5	88.4	58	36.3	17.4	115	No	Yes				
6	0.1	60	23.2	18.6	136	No	Yes	Yes			
7	3.8	51	22.0	20.2	97	No	Yes			Yes	
8	19.6	48	22.5	22.9	245*	Yes	Yes				

EF, Ejection fraction (%); *TCPC*, total cavopulmonary connection; *CVP*, central venous pressure; *ICU*, intensive care unit; *CPB*, cardiopulmonary bypass. *Additional procedures: atrial septectomy and closure of pulmonary valve.

may no longer prove robust. In this study, we have shown that a novel estimated pressure metric, CVP_{TCPC}, can be calculated from preoperative data and that it is associated with EFF and hospital stay, and moderately correlated with directly measured postoperative pressure from ICU (Figure 5).

Although EFF has decreased in incidence in published series, it is still an important clinical event.[4] In this study, we have used a conventional definition based on objective clinical events and investigated typical preoperative risk factors. CVP_{TCPC} may perform well as a predictive biomarker in our series because it is closely related to the hemodynamic hallmark of the condition high CVP.

Our analysis showed a reasonable correlation between measured CVP_{ICU} and estimated CVP_{TCPC}. However, there was a significant bias of approximately 7 mm Hg, and there are several possible causes for this discrepancy. One possible reason was that patients were mechanically ventilated for CMR but were predominately extubated and spontaneously breathing while in the ICU (median time of extubation was 6 hours after arrival to the ICU). It is well recognized that positive pressure ventilation increases PVR. Consequently, using PVR measured during CMR may result in overestimation of the CVP in spontaneously breathing patients post-TCPC. Studies have also shown that cardiac index is lower in TCPC versus Glenn cases, probably as a consequence of higher SaO_2 in the TCPC circulation.[11] Thus, using the pre-TCPC cardiac output in the estimation of CVP_{TCPC} could be another important cause of the observed positive bias. Causes of variation between CVP_{TCPC} and CVP_{ICU} (but not necessarily bias) include CVP-modifying therapies used in the ICU (intravenous fluids, sedation, inotropes, and diuretics), the time interval between CMR and the TCPC, and the fact that CVP_{TCPC} is a spot measurement in contrast to CVP_{ICU}, which is an average of measurements taken over an extended time frame. Although there is a bias, CVP_{TCPC} does predict EFF and is therefore a potentially useful clinical measure.

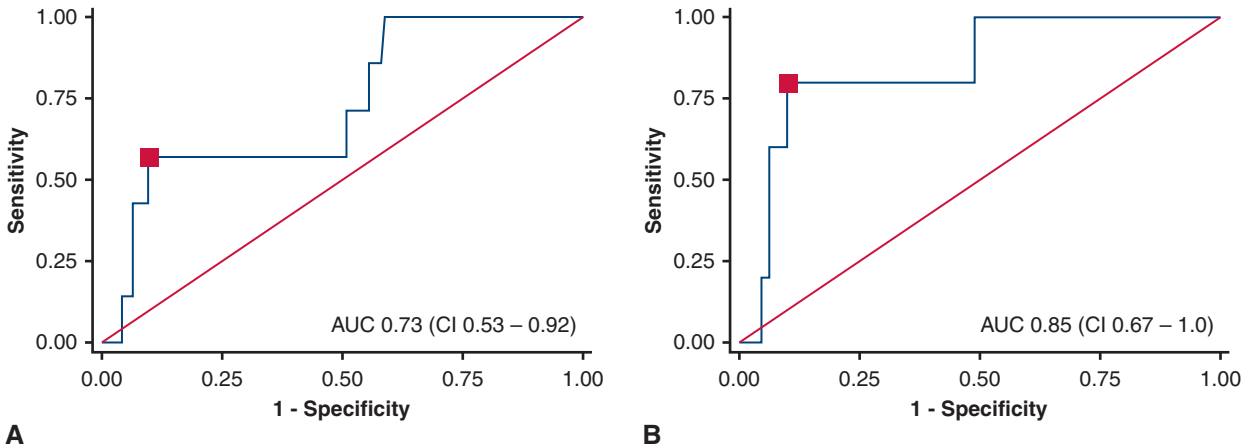


FIGURE 3. ROC for estimated CVP_{TCPC} and early TCPC failure. A, All patients, AUC 0.73 (CI, 0.53-0.92), sensitivity of 0.67 and specificity of 0.90 at cut-point 33 mm Hg (OR, 18.8, $P = .001$). B, Patients with single SVC, AUC 0.85 (CI, 0.67-1.0), sensitivity of 0.80 and specificity of 0.90 at cut-point 33 mm Hg (OR, 36; $P = .002$). Cut-points: *red squares*. *AUC*, Area under the curve; *CI*, confidence interval.

TABLE 3. Univariable analysis of association between clinical outcome and covariates

Variable	EFF		Death-transplantation	
	OR	Significance	OR	Significance
Estimated CVP_{TCPC} ≥33 mm Hg	12.4 (2.50-62.3)	**.002**	13.0 (1.99-95.3)	**.007**
Estimated CVP_{TCPC} (mm Hg)	1.10 (1.01-1.21)	**.03**	1.11 (1.01-1.24)	**.04**
CVP_{BCPC} (mm Hg)	1.18 (0.90-1.51)	.2	1.23 (0.91-1.66)	.2
Veno-venous collateral grade (1-3)	2.63 (1.02-6.78)	**.04**	6.15 (1.08-34.8)	**.04**
Ejection fraction (%)	1.00 (0.90-1.10)	.9	0.99 (0.88-1.12)	.9
End-diastolic volume index (mL/m^2)	1.01 (0.97-1.05)	.7	0.99 (0.95-1.04)	.8
PVR estimate ($WU.m^2$)	1.20 (0.88-1.62)	.2	1.26 (0.9-1.77)	.2
Azygos diameter (mm)	1.36 (0.79-2.36)	.3	1.55 (0.84-2.86)	.2
Hypoplastic left heart syndrome	0.83 (0.38-1.82)	.6	0.52 (0.18-1.45)	.2
Systemic-pulmonary collaterals (%)	22.7 (0.08-6421)	.3	6.38 (0.01-3572)	.6
Pre-TCPC SpO_2 (%)	0.96 (0.82-1.12)	.6	0.99 (0.83-1.19)	1.0
Age at BCPC (y)	0.88 (0.34-2.31)	.8	0.94 (0.32-2.71)	.9
Age at TCPC (y)	0.67 (0.29-1.55)	.3	1.13 (0.6-2.13)	.7
Sex (male)	1.63 (0.30-8.75)	.6	2.63 (0.29-24.2)	.4
Early Fontan failure	-	-	164 (13.8-1943)	**<.005**

Bold indicates statistically significant covariates. *EFF*, Early Fontan failure; *OR*, odds ratio; *CVP*, central venous pressure; *TCPC*, total cavopulmonary connection; *BCPC*, bidirectional superior cavopulmonary connection; *PVR*, pulmonary vascular resistance; *WU*, Wood units; *SpO_2*, oxygen saturations.

However, CVP_{TCPC} and CVP_{ICU} are not interchangeable, and this must be taken into account if CVP_{TCPC} were to be used clinically.

The fact that CVP_{TCPC} is associated with EFF, even when its constituent components (aortic flow and PVR) do not, suggests its importance as an integrator of deleterious hemodynamics. The stronger relationship between CVP_{TCPC} and clinical outcome in patients with single SVC is interesting and may be because accurate measurement of CVP_{BCPC} in patients with bilateral SVCs is more difficult because of asymmetric SVC size or PA narrowing between the bilateral Glenn anastomoses. Nevertheless, the diagnostic accuracy in the entire group remains satisfactory. In our sensitivity analysis, we used SVC and IVC or descending aorta flow as an alternative to aortic flow. We found that this approach had similar prognostic significance to using aortic flow, but the correlation with ICU pressure was reduced.

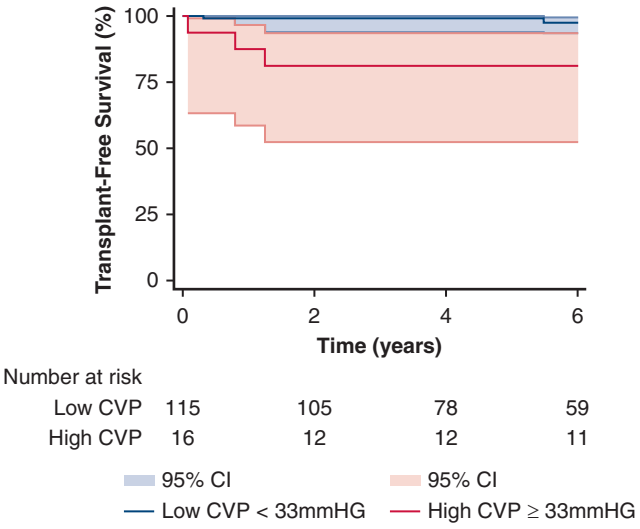


FIGURE 4. Kaplan–Meier survival curves plotting freedom from death or transplantation grouped according to high CVP_{TCPC} 33 mm Hg or greater (*red*) or low CVP_{TCPC} less than 33 mm Hg (*blue*). Log-rank test ($P = .001$). *CI*, Confidence interval; *CVP*, central venous pressure.

These data suggest that it may be possible to use CVP_{TCPC} to identify patients at increased risk of EFF. Such a metric could be used to improve perioperative and immediate postoperative care, for example, it could be used to better select patients who require elective fenestration. There is currently a lack of consensus regarding routine fenestration; although it may reduce postoperative CVP, it comes at the expense of increased systemic desaturation and a possible increased risk of systemic thromboembolism.[12-15] Thus, a metric that helps identify patients who could benefit from fenestration would be beneficial. However, significant further validation is required before CVP_{TCPC} could be used for this purpose.

Although not the primary aim of this study, there was an association between CVP_{TCPC} and death or transplantation in the medium term. This finding suggests that CVP_{TCPC} has some capacity to assess longer-term risk. However, this association appears to be mediated almost entirely via its association with EFF, because in our study, the majority of deaths occurred in patients with prior EFF.

TABLE 4. Univariable and multivariable median regression analyses between hospital stay and exploratory variables

Variable	Univariable		Multivariable	
	Coefficient	Significance	Coefficient	Significance
CVP_{ICU}	1.01	**.04**		
Estimated CVP_{TCPC}	0.15	.2		
Estimated $CVP_{TCPC} \geq 33$ mm Hg	12	**<.005**	13	**<.005**
CVP_{BCPC}	2×10^{-16}	1.0		
PVR_{EST}	0.24	.4		
Severity of decompressing venous collaterals	3.5	**.005**	2	.08
SPC flow	8.9	.1		
End-diastolic volume	−0.01	.8		
Ejection fraction	0	1.0		
Hypoplastic left heart syndrome	−1.5	.1		

Bold indicates statistically significant covariates. *CVP*, Central venous pressure; *ICU*, intensive care unit; *TCPC*, total cavopulmonary connection; *BCPC*, bidirectional superior cavopulmonary connection; *PVR*, pulmonary vascular resistance; *EST*, estimated; *SPC*, systemic to pulmonary collaterals.

Our group has previously shown the importance of qualitative assessment of decompressing veno-venous collaterals for early and late TCPC failure.[3] Collaterals facilitate decompression of the BCPC, allowing for normalization of CVP (which explains the lack of association between BCPC CVP and outcome); however,

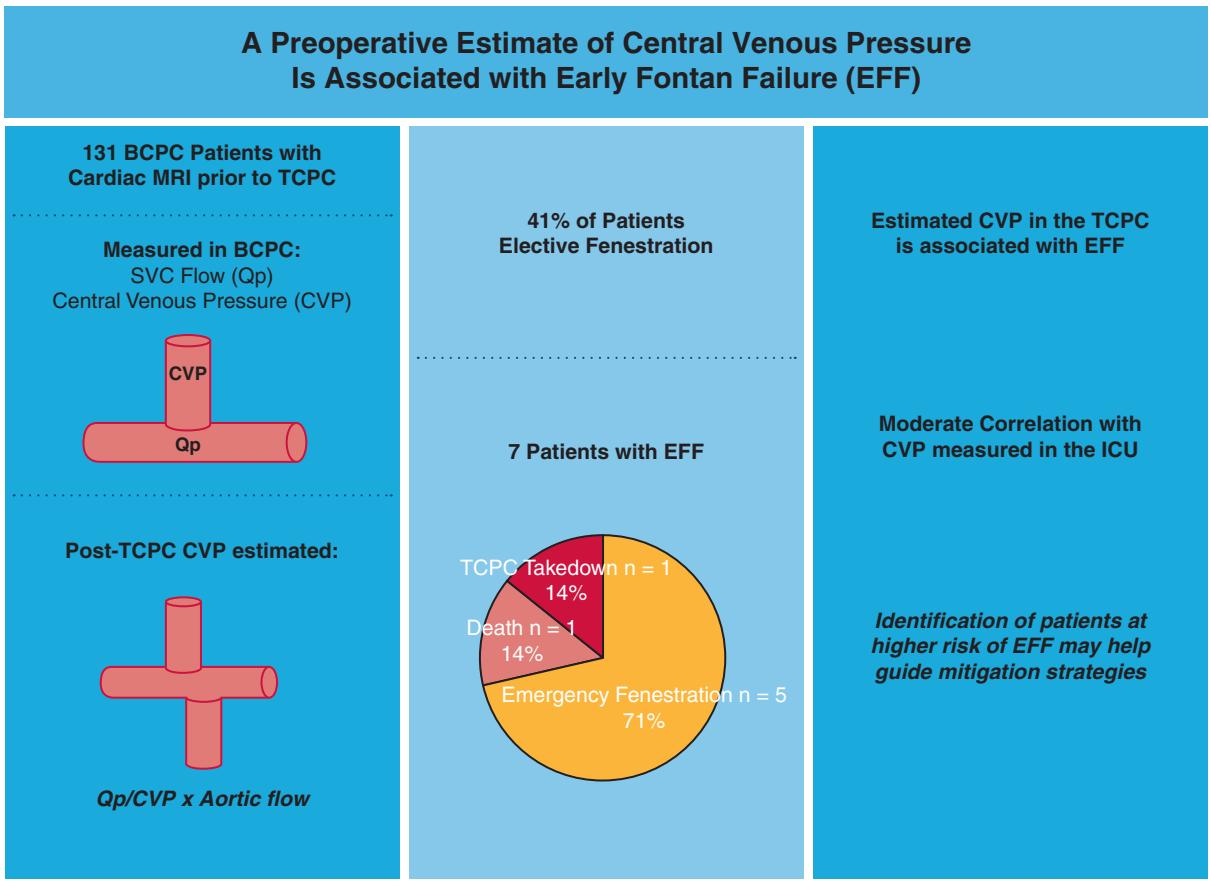


FIGURE 5. In this study, CMR was performed in patients with BCPC undergoing preoperative assessment for TCPC. Using routinely collected data: Qp, CVP, and aortic flow. We calculated a metric that attempts to estimate how much CVP would increase should the TCPC be completed if all systemic flow is directed to the lungs. Given that EFF is associated with high postoperative CVP, we investigated whether this metric was associated with EFF events and if it correlated to directly measured CVP in the TCPC during the ICU stay. Our study demonstrates an association between estimated TCPC pressure and EFF and a moderate correlation with CVP measured in the ICU. *BCPC*, Bidirectional cavopulmonary connection; *MRI*, magnetic resonance imaging; *TCPC*, total cavopulmonary connection; *SVC*, superior vena cava; *CVP*, central venous pressure; *EFF*, early Fontan failure; *ICU*, intensive care unit.

after TCPC completion, this route of decompression is no longer possible, and consequently PA pressure becomes elevated. The calculation of CVP_{TCPC} provides an actual estimate of the increase of pressure as a consequence of TCPC completion. Elevated CVP_{TCPC} and decompressing collaterals may identify patients with an adverse pulmonary vasculature; in such patients, it is possible that cardiac catheterization could be used to identify reversible causes (PA obstruction or elevated PVR) before TCPC completion.

Study Limitations

This is a retrospective study from a single center, which may limit generalization of the study findings insofar as our patient population and practice differ. However, our clinical practice will be broadly similar to many institutions. Nevertheless, one advantage of the retrospective design is that CVP_{TCPC} was not used during multidisciplinary meetings to guide decision making and therefore will not have influenced clinical outcomes, such as the rate of EFF, decision to defer TCPC, or fenestration.

Our method of preoperative clinical evaluation does not involve routine cardiac catheterization; therefore, we are not able to evaluate the relationship of elevated end-diastolic pressure (independently of CVP) in our dataset.

Given marked practice variation in preoperative assessment for TCPC completion, it is recommended that a prospective comparative study of CMR and cardiac catheterization be undertaken. In the absence of a direct comparison (ideally randomized controlled trial), we cannot exclude the possibility that performing a cardiac catheterization could provide comparable data to CMR.

CONCLUSIONS

CVP_{TCPC} is easily calculated at the time of pre-TCPC assessment by combining pressure and flow data. Although there is a significant bias between estimated and measured CVP, higher CVP_{TCPC} is associated with an increased risk of EFF events. Thus, this metric could be used to inform important clinical decisions, such as preemptive TCPC fenestration. However, further larger multicenter prospective studies are required to validate this metric, especially in centers that undertake routine TCPC fenestration.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: Fontan, central venous pressure, Fontan failure, TCPC, CMR