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Preoperative B-type natriuretic peptide levels are associated with outcome after total cavopulmonary connection (Fontan)

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Abstract

Objective—To determine the association between preoperative B-type natriuretic peptide (BNP) levels and outcome following TCPC.

Background—Surgical palliation of univentricular cardiac defects requires a series of staged operations, ending in a TCPC. Although outcomes have improved, there remains an unpredictable risk of early TCPC takedown. The prediction of adverse postoperative outcomes is imprecise, despite an extensive preoperative evaluation.

Methods—We prospectively enrolled 50 patients undergoing TCPC. We collected preoperative clinical data, preoperative plasma BNP levels, and postoperative outcomes including the incidence of an adverse outcome within one year of surgery (defined as death, TCPC takedown or the need for cardiac transplantation).

Results—Mean ± SD age was 4.7 ± 2.1 years. Median (IQR) preoperative BNP levels were higher in patients who required TCPC takedown and early postoperative mechanical cardiac support (n=3; 55 (42, 121)) compared with a good outcome (n=47; 11 (5,17)) ($p<0.05$). In fact, a

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preoperative BNP ≥ 40 pg/mL was highly associated with the need for TCPC take down (sensitivity = 100%, specificity = 93%; p<0.05), yielding a PPV of 50% and an NPV of 100%. Higher preoperative BNP levels were also associated with longer ICU length of stay, longer hospital length of stay and increased incidence of low cardiac output syndrome (p<0.05).

Conclusions—Preoperative BNP blood levels are uniquely associated with the need for mechanical support early after TCPC and TCPC take down, and thus may provide important information in addition to the standard preoperative assessment.

Introduction

The total cavopulmonary connection (TCPC) is the surgical procedure of choice for suitable patients with a variety of univentricular or non-septable hearts. After the TCPC there is no subpulmonary ventricle between the systemic venous return and the pulmonary circulation. The disadvantages of this circulation include ventricular contractility-afterload mismatch, absence of right ventricular to pulmonary artery coupling and systemic venous return, which is dependent on gravity and respiratory driven forces. This circulation lacks adaptability and often fails in the setting of increased pulmonary vascular resistance (PVR), valvular dysfunction, or decreased ventricular performance [1–5]. Although mortality after TCPC is low with careful patient selection, the accurate prediction of adverse postoperative outcomes is difficult, and there remains an unpredictable risk of early and late TCPC takedown.

B-type natriuretic peptide (BNP) is a 32-amino acid polypeptide hormone secreted by the myocardium in response to various stimuli that has natriuretic, diuretic, and vasoactive properties [6,7]. Recent studies demonstrated that perioperative changes in BNP levels may predict postoperative morbidity and mortality after surgery for the repair or palliation of congenital cardiac defects [8–12]. However, the potential utility of pre-operative BNP levels as predictors of post-operative outcomes in patients undergoing a TCPC has not been investigated previously.

We hypothesized that preoperative BNP levels would be associated with unexpected outcomes after TCPC in patients otherwise deemed to be suitable operative candidates on the basis of standard preoperative clinical, echocardiographic and hemodynamic assessments. Therefore, the objectives of this study were: (1) to determine preoperative BNP levels in children undergoing TCPC, and (2) to investigate the association between preoperative BNP levels and postoperative outcomes.

Methods

Design and subjects

We conducted a prospective cohort study in the pediatric cardiac intensive care unit (PCICU) at the University of California, San Francisco Children's Hospital between 07/2005 to 07/2006, 04/2008-07/2010, and 06/2011-7/2012 (n= 45) and the PCICU at Lucille Packard Children's Hospital between 01/2012-06/2012 (n=6). During these time periods, parents of all eligible patients were approached for informed consent and study enrollment. Eligible subjects included all children < 18 years undergoing TCPC. The preoperative anesthesia management, intraoperative surgical strategy, and subsequent

PCICU management followed standard institutional practices. In general, a pre-operative decision to utilize a fenestration was based upon the following criteria that would characterize the patient as “higher risk”: depressed ventricular function, modestly increased PVR, pulmonary parenchymal disease and/or lung hypoplasia, and the need to perform additional procedures that would require a prolonged CPB time. A peri-operative decision to perform a fenestration was made for an elevated Fontan pressure and/or poor hemodynamics upon emergence from CPB. The surgical and medical teams involved in the management of the patients were blinded to the BNP values.

Informed consent from the patients’ parents or guardians was obtained before enrollment in the study. The University of California, San Francisco and the Lucille Packard Children’s Hospital review boards approved the study.

Predictor variables

We collected all available preoperative clinical data including: patient demographics and preoperative hemodynamic data obtained at the time of cardiac catheterization, including the ratio of pulmonary blood to systemic blood flow (Qp/Qs), PVR, mean pulmonary artery pressure (mPAP), cardiac index (CI), presence or absence of atrioventricular (A-V) valvular regurgitation, and systemic ventricular end-diastolic pressure (SVEDP), and echocardiographic reports of ventricular function and AV valve regurgitation.

Blood samples were obtained from a venous or arterial catheter < 24 hours preoperatively. The samples were placed immediately on ice in chilled ethylenediamine tetraacetic acid-treated tubes. Whole blood was used immediately to measure BNP levels using a commercially available fluorescence immunoassay (Triage Meter Plus, Biosite Diagnostic, San Diego, CA). The measurable range of BNP on this device is between 5 and 5000 pg/mL. The estimated coefficient of variation for the assay is 9.2% to 11.4%.

Outcome variables

The primary end point was TCPC failure within one year of surgery. TCPC failure was defined as death, or the need for TCPC takedown or cardiac transplantation. Secondary end points were the (1) duration of mechanical ventilation, (2) ICU length of stay (LOS), (3) hospital LOS, and (4) development of low cardiac output syndrome (LCOS) within 48 hours after surgery. The definition of LCOS was derived from criteria published by Hoffman and colleagues which included a combination of changes in clinical signs and biochemical indicators. Specifically, LCOS criteria includes tachycardia, oliguria, poor perfusion, cardiac arrest, or metabolic acidosis, and the need for interventions aimed at augmenting cardiac output, such as increased pharmacologic support relative to the baseline and cardiac pacing [13].

Postoperative clinical and hemodynamic data were collected daily by an observer blinded to the BNP results, included the following: mean systemic arterial pressure, common atrial pressure, and heart rate upon admission to the ICU, postoperative ICU and hospital LOS, time to chest tube removal and chest tube output (CTO), pleural effusions on chest Xray, biochemical evidence of chylothorax, occurrence of LCOS and duration of mechanical ventilation. Postoperative biochemical data collected included hematocrit, arterial and venous blood gases, serum lactate, blood urea nitrogen, and creatinine upon admission to the ICU.

Data collection and management

Study data were collected prospectively and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at UCSF [14]. REDCap is a secure, web-based application designed to support data capture for research studies, providing: 1) an interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Statistical analysis

We analyzed group differences using the t-test for parametric data and the Wilcoxin rank-sum test for non-parametric data. We used simple and multivariate logistic regression to explore correlations between the continuous predictor variable (BNP) and the binary outcome variables (good/adverse outcome and incidence of LCOS). Next, we fit linear regression models to study correlations between the continuous predictor variable (BNP) and the continuous clinical outcome variables (ICU LOS, hospital LOS and duration of mechanical ventilation). However, considering the general rule of thumb in formal regression methods is to use only one covariate per every ten outcomes, the rarity of the outcome being studied (n = 3) made meaningful interpretation of our exploratory models unreasonable [15].

Statistical analyses were performed using STATA 12, with differences considered significant when two-sided *p* values were <0.05.

Results

Subjects

We enrolled 50 patients undergoing TCPC. All patients had an extracardiac conduit placed between the inferior vena cava and the pulmonary artery, 26 of which were fenestrated. All patients had a cardiac catheterization performed within 3 months before surgery. The patients' demographics, cardiac lesions and preoperative hemodynamic data are shown in Table 1.

Outcomes

Primary end points—Three patients (6%) had an adverse outcome. The preoperative diagnoses, surgical details and specific postoperative events classifying the adverse outcomes are shown in Table 2. All three patients with adverse outcome underwent additional procedures at the time of Fontan (Table 2). Seven (15%) patients with good outcome underwent additional procedures at the time of Fontan. These procedures included: pulmonary artery reconstruction (n=4); repair of right ventricular outflow tract aneurysm (n=1); repair of atrioventricular valve (n=1); and, coronary artery bypass graft with left internal mammary artery to left anterior descending coronary artery (n=1).

No enrolled patients died or required cardiac transplantation during the study period. Patients with an adverse postoperative outcome were older and weighed more (Table 3). The presence/absence of AV valve regurgitation and preoperative hemodynamic indices did not differ between patients undergoing TCPC with and without an adverse outcome (Table 3). Use of aortic crossclamping was not significantly associated with preoperative BNP levels. Upon return to the PCICU following surgery, first recorded heart rate, common atrial pressure, serum creatinine and serum lactate were higher in TCPC patients with adverse outcomes while arterial oxygen saturations were lower (Table 3).

Secondary end points—The median (IQR) duration of mechanical ventilation was 8 (7, 12) hours in patients who underwent TCPC. Eight patients (16%) developed LCOS within the first 48 hours after surgery. The median (IQR) ICU LOS and hospital LOS were 5 (4, 9) days and 14 (10, 22) days, respectively. Age, gender and preoperative hemodynamic data obtained from cardiac catheterizations were not associated with any secondary outcomes. Patients with adverse outcomes had a higher incidence of LCOS and longer ICU LOS (Table 3).

Preoperative BNP Levels and Outcomes—Preoperative BNP levels were greater in patients who required TCPC takedown than in patients with a good outcome (Figure 1, Table 3). Preoperative BNP levels were not associated with duration of mechanical ventilation. Preoperative BNP levels correlated with incidence of LCOS and ICU LOS. There was a trend toward longer hospital LOS with higher preoperative BNP levels ($p = 0.079$). There was no association between preoperative BNP levels and age or gender. Preoperative BNP levels did not correlate with preoperative Qp/Qs, PVR, mPAP, CI, SVEDP, mean arterial pressure, heart rate, arterial oxygen saturation, presence/absence of AV valve regurgitation or postoperative serum lactate.

We used receiver operating characteristic curves to evaluate the association between various cutoff values of preoperative BNP and adverse outcome and incidence of LCOS. A preoperative BNP cutoff value of 40 pg/mL was highly associated with adverse outcome, giving a sensitivity of 100% and a specificity of 93% (area under the curve: 0.96, 95% CI 0.91–1.0) (Figure 2). These results yield a positive predictive value (PPV) of 50% and a negative predictive value (NPV) of 100%. Because a preoperative BNP level ≥ 40 pg/mL was strongly associated with adverse outcome, we dichotomized patients by BNP levels of < 40 pg/mL or ≥ 40 pg/mL. The characteristics of patients with a preoperative BNP level < 40 pg/mL and ≥ 40 pg/mL are shown in Table 4. Patients with a preoperative BNP level ≥ 40 pg/mL had a greater incidence of LCOS and a longer ICU and hospital LOS than patients with a preoperative BNP level < 40 pg/mL (Table 4). Among the 47 patients with good outcomes, no differences were identified between the 3 patients with a preoperative BNP ≥ 40 and those 44 with a preoperative BNP < 40 (data not shown).

One patient enrolled was excluded from the analysis after an intraoperative decision was made to not proceed with the TCPC, because of the concern for severe AV valve regurgitation that was underestimated during the pre-operative evaluation. Interestingly, this patient had a pre-operative BNP level of 120 pg/ml.

Discussion

Outcomes following TCPC have improved markedly since 1971, when the Fontan procedure was first described [16]. However, the incidence of early mortality after TCPC remains between 3–8%. Likewise, long-term mortality is estimated to be as high as 10, 14, and 18% at 5, 10 and 15 years, respectively [2,3,17–19]. Contemporary risk factors for early and late adverse outcomes after Fontan type operations include impaired preoperative ventricular function, increased pulmonary artery pressures, and a common AV valve [3,18,19]. In a pilot study, we found that preoperative BNP levels were higher in patients with adverse outcome following TCPC than in patients with good outcomes, and that standard preoperative data were not significantly different between these two groups [9]. Therefore, in the current study we expanded our initial study to test the hypothesis that preoperative BNP blood levels are associated with early adverse outcome following TCPC. We found that a BNP level >40 pg/ml was highly associated with the need for early postoperative ECLS and/or TCPC takedown. Importantly, we have shown that, in low risk patients selected to undergo TCPC based on favorable preoperative hemodynamic assessments, BNP levels better discriminate outcome post TCPC than preoperative cardiac catheterization measurements. This is a meaningful finding since the exact preoperative hemodynamics that predict TCPC takedown remain elusive, and suggest that measurement of BNP blood levels may be important in the preoperative evaluation [20].

BNP is a hormone released by the myocardium that has natriuretic, diuretic and vasoactive properties [6,7]. Produced predominantly in ventricular tissue, BNP has emerged as a powerful biomarker of impaired myocardial performance, and has become an established aid in the diagnosis, prognosis, and treatment of a variety of cardiovascular disease states [8,10–12]. Its use in congenital heart disease is emerging, and recent studies demonstrate that perioperative BNP changes may predict outcomes in an age and lesion-specific fashion, including partial cavopulmonary connections for single ventricular heart disease [9]. However, previous studies in congenital heart disease did not demonstrate associations between outcomes and preoperative levels, only perioperative changes [8–12,21]. In our previous study examining perioperative BNP levels in patients undergoing partial cavopulmonary connections and TCPC, we found that preoperative BNP levels were higher in 2 patients with poor outcome following TCPC compared with 9 patients with good outcome after TCPC. With a five-fold higher sample size, the present study confirms this preliminary finding and to our knowledge is the first to robustly demonstrate the association between a single preoperative BNP value and postoperative outcome in patients undergoing surgery for congenital heart disease.

Although our findings demonstrate the association between an increased preoperative BNP level and poor postoperative outcome in patients undergoing TCPC, the potential mechanisms, particularly at a relatively low cut-off value (40 mg/dl), are unclear. The regulation of the production and release of BNP is not entirely understood, as it depends on multiple, often opposing, factors [10,11,22,23]. Factors known to increase BNP expression and release include increased ventricular wall stress (pressure and volume), hypoxia, increased central blood volume, and neuroendocrine mechanisms [7]. Interestingly, in patients with single ventricular physiology, Law et al demonstrated an elevation in BNP levels in patients with ventricular failure, independent of cavopulmonary failure [24]. We speculate that in the preoperative TCPC setting, BNP values may reflect important clinical parameters in ventricular performance not captured by our current routine evaluations. This requires further investigation.

Potential alterations in BNP expression, release, and clearance in the setting of abnormal cardiac development are unknown. Our results demonstrate that a relatively low preoperative BNP cutoff level (> 40 pg/ml) is associated with adverse outcome after TCPC. This is significantly lower than the cutoff levels first established for the diagnosis of congestive heart failure in adults [25,26], but is concordant with two previously published studies which showed that a threshold value of >30–45 pg/ml showed both sensitivity and specificity for predicting heart failure in children with a single cardiac ventricle. Importantly, this cutoff level is also greater than published values in similarly aged normal children (5.1 to 12.1 pg/ml) [27,28]. Further, our relatively low BNP cutoff level fits with the results of the Pediatric Heart Network Fontan cross-sectional study that demonstrated normal BNP levels in the majority of ambulatory Fontan patients (median time from Fontan 8.2 years), but higher BNP levels in patients with pre-Fontan systolic dysfunction and in patients with late post-Fontan complications[21].

There are several limitations to this investigation that warrant discussion. Most notable is the relatively small sample size, which was associated with a heterogenous group of anatomic lesions and the use of both fenestrated and non-fenestrated surgical techniques. The small sample size makes it difficult to conclude that BNP is a true predictor of adverse outcome following TCPC. However, there is a clear association between increased preoperative BNP levels and adverse postoperative outcome in this unique population. Further, this precludes our ability to demonstrate potential interactions between preoperative BNP levels and outcomes in subjects with specific cardiac lesions after the TCPC. In addition, all three patients experiencing adverse outcome underwent additional procedures at the time of the Fontan compared to 15% of the good outcome group. While there were no significant differences in duration of cardiopulmonary bypass time or aortic crossclamp time as a result, it is challenging to determine if these additional procedures played a role in the observed outcomes. Lastly, our study was undertaken only in children considered eligible for a TCPC. Since we have no data on higher risk patients (i.e. those excluded from TCPC following standard assessment), the associations demonstrated between preoperative BNP and outcomes are only applicable to Fontan patients with favorable preoperative hemodynamics.

We are confident that, due to the robust nature of the data, the results are not due to type I error. However, a small possibility of this always exists in pilot studies with small sample sizes such as this. In addition, the enrolled patients were from two high-volume pediatric cardiothoracic surgery centers, with the obligate subtle differences in surgical approach/ technique and postoperative management. Importantly, the strength of the association between postoperative outcome and a BNP cutoff level >40 pg/ml was sustained despite a small sample size from two centers, suggesting it is a robust measurement.

In conclusion, we found that preoperative BNP levels are strongly associated with the need for ECLS and TCPC takedown in the early postoperative period after TCPC. Specifically, we found that a value of >40 pg/ml was a highly sensitive and specific in its' association with TCPC take down within 12 months of surgery, the need for ECLS and prolonged ICU and hospital LOS. Large multi-centered studies are needed to definitively establish the predictive value of BNP blood levels in the management of patients following TCPC and to overcome the limitations of the present study. However, our current results suggest that preoperative BNP levels have potential to uniquely predict early outcome after TCPC, and thus, after validation in a larger TCPC population, should be considered for inclusion in the standard assessment of candidates for a Fontan type operation.

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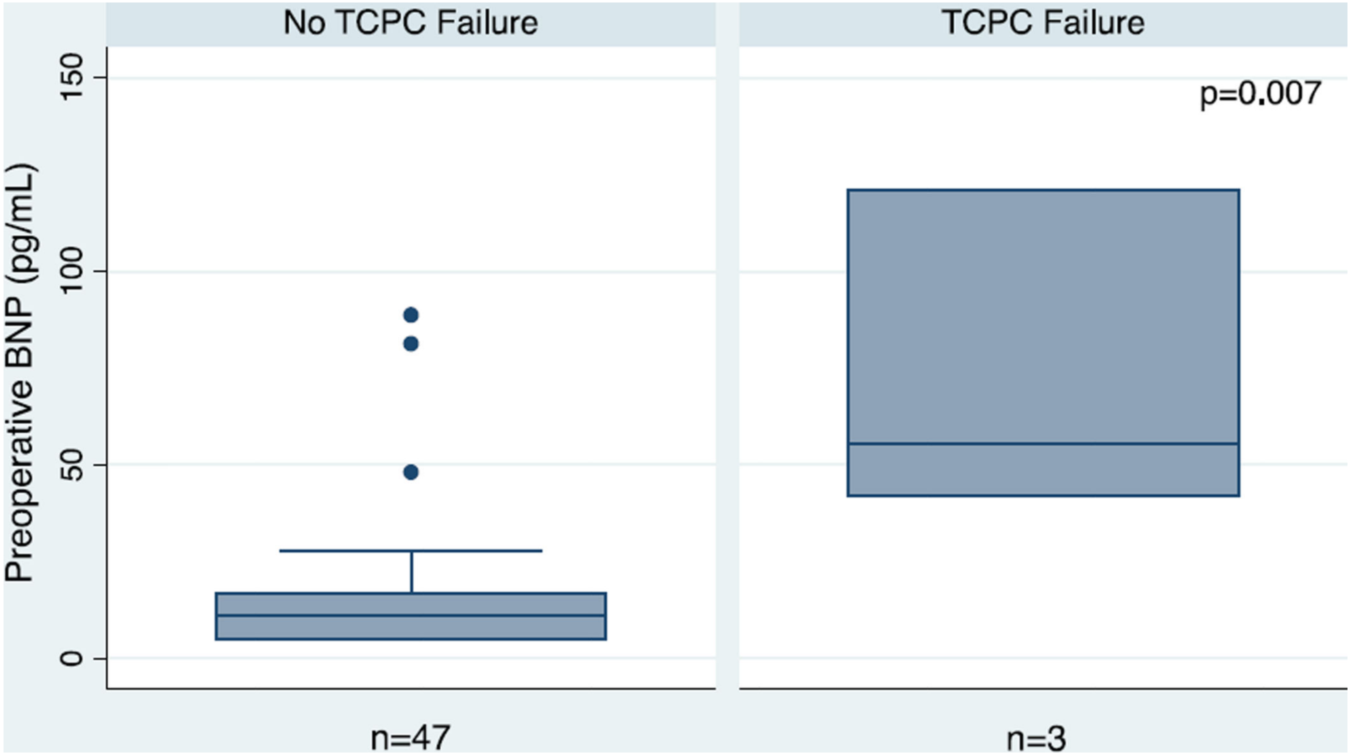

FIGURE 1. Preoperative BNP levels are higher in patients with adverse outcome in the early postoperative period following TCPC

Comparisons of preoperative BNP levels between patients with a good outcome (n = 47) and an adverse outcome (n = 3) after TCPC. Horizontal lines represent median values and interquartile ranges are represented with shaded boxes. An adverse outcome is defined as a failed TCPC requiring an intervention within 12 months of the original procedure.

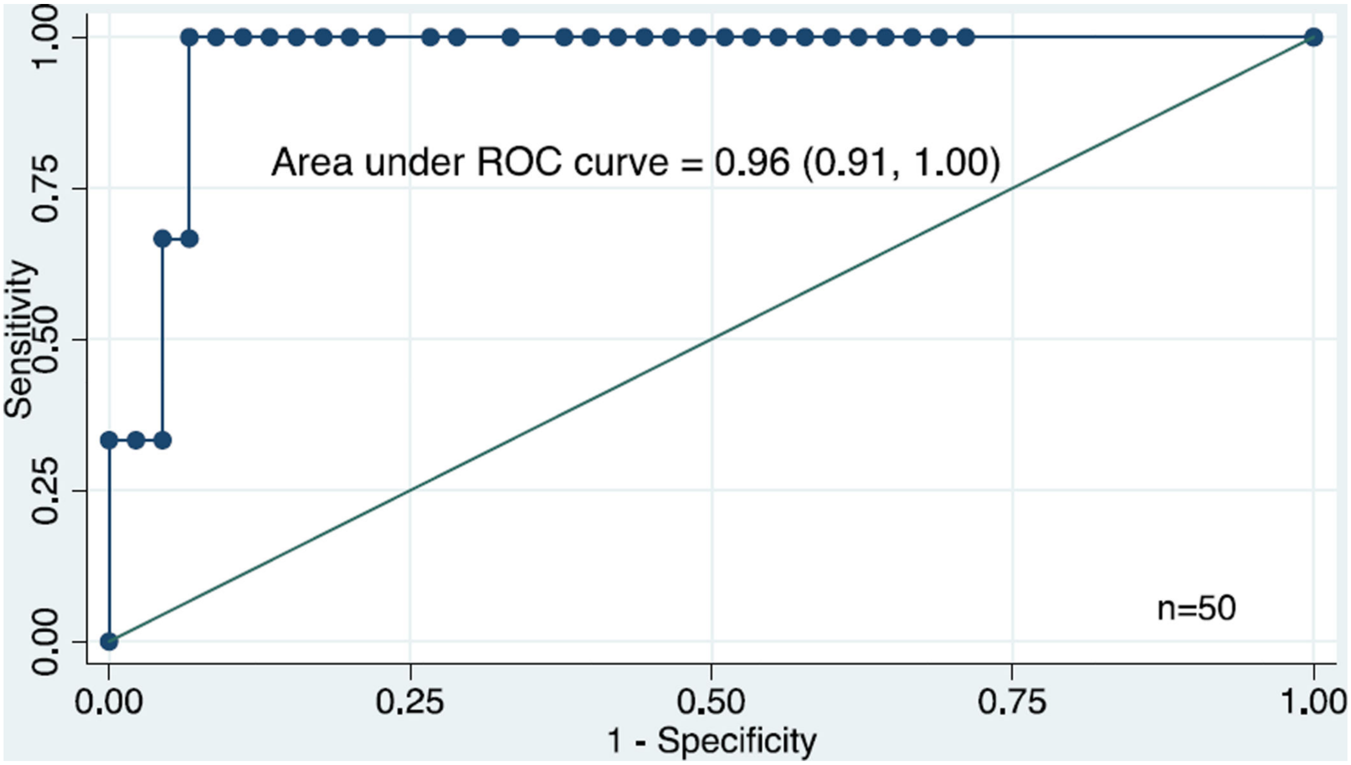

FIGURE 2. A preoperative BNP level ≥ 40 pg/ml is highly associated with adverse outcome following TCPC (Sensitivity = 100%; Specificity = 93%)

A preoperative BNP cutoff value of 40 pg/mL had a sensitivity of 100% and a specificity of 93% for predicting an adverse outcome (area under the curve: 0.96, 95% CI 0.91–1.0).

Table 1

Preoperative characteristics

Age (years)	4.7 ± 2.1
Weight (kilograms)	16.1 ± 6.0
Male, n (%)	30 (60)
Type of cardiac lesion, n (%)	
HLHS	23 (46)
Tricuspid atresia	7 (14)
DORV	7 (14)
Unbalanced AVSD	6 (12)
PA-IVS	4 (8)
DILV	1 (2)
TGA-VSD-PS	1 (2)
Ebstein's anomaly-HRV	1 (2)
Preoperative hemodynamic data	
Heart rate (bpm)	103 ± 15
Mean arterial pressure (mm Hg)	77 ± 12
Arterial oxygen saturation (%)	83 ± 6
Qp:Qs	0.73 ± 0.26
PVR (Wood's units)	2.0 ± 0.9
mPAP (mm Hg)	11 ± 3
CI (L/min/m2)	3.5 ± 1.2
SVEDP (mm Hg)	8 ± 4

Qp/Qs: ratio of pulmonary blood flow over systemic blood flow; PVR, pulmonary vascular resistance; mPAP, mean pulmonary artery pressure; CI, cardiac index; SVEDP, systemic ventricular end-diastolic pressure; HLHS, hypoplastic left heart syndrome; DORV, double outlet right ventricle; DILV, double inlet left ventricle; PA-IVS, pulmonary atresia-intact ventricular septum; TGA, transposition of great arteries; VSD, ventricular septal defect; HRV, hypoplastic right ventricle; PS, pulmonary stenosis; AVSD, atrioventricular septal defect. Data are presented as mean ± standard deviation.

Table 2

Diagnoses and specific postoperative events of patients with an adverse outcome

Patient	Surgery	Diagnosis	Outcome
1	TCPC - extracardiac, fenestrated; and, L pulmonary arteryplasty	HLHS	Fontan circulation taken down after return to the OR on POD 1 because of failed Fontan circulation. Unable to separate from CPB; placed on ECLS.
2	TCPC - extracardiac, fenestrated; and, R atrial maze, R atrial reduction, oversew of pulmonary valve	Ebstein’s anomaly-HRV	Fontan circulation taken down in the OR because of failed Fontan circulation, unable to separate from CPB; another MBTS was added in the same operation.
3	TCPC - extracardiac, fenestrated; and, focalization of hepatic veins	Unbalanced AVSD	Fontan circulation taken down 11 mo after operation because of poor hemodynamics requiring prolonged and frequent PCICU hospitalizations and the ultimate development of PLE; also had ECLS during the postoperative course of TCPC because of profound LCOS at PODs 2–5.

TCPC, total cavopulmonary connection; POD, postoperative day; HLHS, hypoplastic left heart syndrome; HRV, hypoplastic right ventricle; AVSD, atrioventricular septal defect; OR, operating room; CPB, cardiopulmonary bypass; PLE, protein-losing enteropathy; ECLS, extracorporeal life support; LCOS, low cardiac output syndrome.

Table 3

Characteristics of patients undergoing total cavopulmonary anastomosis with a good postoperative outcome or an adverse outcome

	Good outcome	**Adverse outcome**	***P***
N (%)	47 (94)	3 (6)	
Age (years)	4.5 ± 1.9	7.2 ± 4.1	**0.028**
Weight (kilograms)	15.7 ± 5.3	23.0 ± 12.2	**0.039**
Male, n (%)	27 (57)	3 (100)	0.151
Preoperative BNP level (pg/mL)	11 (5,17)	55 (42, 55, 121)	**0.007**
Use of CPB, n (%)	34 (72)	3 (100)	0.299
Duration of CPB (minutes)	54 (42, 86)	80 (63, 80, 96)	0.260
Use of aortic cross-clamp, n (%)	6 (13)	2 (67)	**0.013**
Duration of aortic cross-clamp (minutes)	31 (19, 42)	44 (44, 44)	0.480
Fenestration, n (%)	23 (49)	3 (100)	0.096
Extracardiac conduit, n (%)	47 (100)	3 (100)	
Glenn before Fontan, n (%)	43 (91)	3 (100)	0.797
Preoperative hemodynamic and laboratory data			
Mean arterial pressure (mm Hg)	77 ± 12	78 ± 5	0.809
Arterial oxygen saturation (%)	83 ± 6	83 ± 4	0.839
AV valve regurgitation , n (%)	19 (40)	2 (67)	0.382
Qp:Qs	0.72 ± 0.26	0.80 ± 0.30	0.623
PVR (Wood’s units)	2.0 ± 1.0	2.1 ± 0.6	0.779
mPAP (mm Hg)	11 ± 3	10 ± 3	0.607
CI (L/min/m2)	3.5 ± 1.2	2.8 ± 0.3	0.322
SVEDP (mm Hg)	8 ± 4	9 ± 2	0.848
Serum creatinine (mg/dL)	0.42 ± 0.08	0.55 ± 0.21	**0.048**
Creatinine clearance	99 ± 24	114 ± 45	0.336
Initial postoperative data upon return to PCICU			
Heart rate (bpm)	119 ± 18	152 ± 11	**0.002**
Arterial oxygen saturation (%)	92 ± 8	81 ± 13	**0.023**
Mean arterial pressure (mm Hg)	75 ± 11	70 ± 15	0.446
Common atrial pressure (mm Hg)	7 ± 4	15 ± 5	**0.005**
Serum creatinine (mg/dL)	0.52 ± 0.24	1.1 ± 0.32	**0.001**
Creatinine clearance	83 ± 23	51 ± 23	**0.022**
Serum lactate (mmol/L)	2.8 ± 1.8	5.6 ± 2.5	**0.016**
Outcomes			
LCOS, n (%)	5 (11)	3 (100)	**0.000**
ICU length of stay (days)	5 (4, 8)	11 (8, 11, 56)	**0.037**
Hospital length of stay (days)	14 (10, 21)	36 (14, 36, 64)	0.079

	Good outcome	**Adverse outcome**	***P***
Duration of mechanical ventilation (hours)	9 (7, 12)	7 (7, 7, 24)	0.850
Duration of chest tubes (days)	8 (5, 14)	9 (8, 9, 19)	0.414

BNP, B-type natriuretic peptide; CPB, cardiopulmonary bypass; AV, atrioventricular valve; Qp/Qs, ratio of pulmonary blood flow over systemic blood flow; PVR, pulmonary vascular resistance; mPAP, mean pulmonary artery pressure; CI, cardiac index; SVEDP, systemic ventricular end-diastolic pressure; LCOS, low cardiac output syndrome; ICU, intensive care unit. For the good outcome group (n=47), data are presented as mean ± standard deviation and median (interquartile range). For the adverse outcome group (n=3), data are presented as mean ± standard deviation and median (individual values). Creatinine clearance was estimated using the Shull formula.

Table 4

Characteristics of patients undergoing total cavopulmonary anastomosis with a preoperative BNP level < or ≥ 40 pg/mL

	Preoperative BNP level < 40 pg/mL	**Preoperative BNP level ≥ 40 pg/mL**	***P***
N (%)	44 (88)	6 (12)	
Age (years)	4.6 ± 2.0	5.0 ± 2.9	0.618
Weight (kilograms)	15.8 ± 5.6	18.0 ± 7.9	0.333
Male, n (%)	25 (57)	5 (83)	0.086
Use of CPB, n (%)	31 (70)	6 (100)	0.118
Duration of CPB (minutes)	55 (42, 90)	63 (52, 96)	0.423
Use of aortic cross-clamp, n (%)	6 (14)	2 (33)	0.225
Duration of aortic cross-clamp (minutes)	31 (19, 42)	44 (44, 44)	0.480
Fenestration, n (%)	22 (50)	4 (67)	0.486
Extracardiac conduit, n (%)	44 (100)	6 (100)	
Glenn before Fontan, n (%)	40 (91)	6 (100)	0.707
Preoperative hemodynamic and laboratory data			
Mean arterial pressure (mm Hg)	77 ± 13	76 ± 8	0.854
AV valve regurgitation, n (%)	16 (36)	5 (83)	0.982
Arterial oxygen saturation (%)*	84 ± 6	82 ± 6	0.502
Qp:Qs	0.71 ± 0.26	0.84 ± 0.27	0.191
PVR (Wood's units)	2.0 ± 0.9	2.1 ± 1.4	0.618
mPAP (mm Hg)	11 ± 3	11 ± 2	0.812
CI (L/min/m2)	3.5 ± 1.2	3.0 ± 0.4	0.281
SVEDP (mm Hg)	8 ± 4	9 ± 1	0.556
Serum creatinine (mg/dL)	0.42 ± 0.08	0.47 ± 0.15	0.278
Creatinine clearance	98 ± 24	112 ± 31	0.231
Initial postoperative data upon return to PCICU			
Heart rate (bpm)	119 ± 18	134 ± 21	**0.041**
Arterial oxygen saturation (%)	92 ± 8	87 ± 11	0.133
Mean arterial pressure (mm Hg)	75 ± 10	73 ± 17	0.708
Common atrial pressure (mm Hg)	7 ± 4	12 ± 5	**0.019**
Serum creatinine (mg/dL)	0.50 ± 0.16	0.83 ± 0.50	**0.001**
Creatinine clearance	83 ± 23	69 ± 27	0.202
Serum lactate (mmol/L)	2.8 ± 1.9	3.9 ± 2.0	0.126
Outcomes			
Adverse outcome, n (%)	0	3 (50)	**0.000**
LCOS, n (%)	2 (5)	6 (100)	**0.000**
ICU length of stay (days)	5 (4, 8)	8 (6, 18)	**0.020**

	Preoperative BNP level < 40 pg/mL	Preoperative BNP level ≥ 40 pg/mL	*P*
Hospital length of stay (days)	12 (10, 19)	22 (15, 34)	**0.020**
Duration of mechanical ventilation (hours)	9 (7, 12)	7 (7, 17)	0.286
Duration of chest tubes (days)	8 (5, 13)	10 (7, 17)	0.392

BNP, B-type natriuretic peptide; CPB, cardiopulmonary bypass; AV, atrioventricular valve; Qp/Qs, ratio of pulmonary blood flow over systemic blood flow; PVR, pulmonary vascular resistance; mPAP, mean pulmonary artery pressure; CI, cardiac index; SVEDP, systemic ventricular end-diastolic pressure; LCOS, low cardiac output syndrome; ICU, intensive care unit. Data are presented as mean ± standard deviation and median (interquartile range). Creatinine clearance was estimated using the Shull formula.

* Post-operative arterial saturations were significantly higher among the non-fenestrated Fontans compared to those with fenestrations: 94 ± 8 vs. 88 ± 8, p = 0.016.