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RESEARCH REPORT

A Novel Preoperative Risk Score Incorporating Non-Invasive Hemodynamics to Predict Prolonged Mechanical Ventilation in Infants Undergoing VSD Repair

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ABSTRACT

Background: Infants with ventricular septal defect (VSD) and concurrent respiratory compromise exhibit significant heterogeneity in their recovery after surgical repair. Objective tools for preoperative risk stratification are lacking.

Aims: The primary aim of this study was to determine if preoperative hemodynamic data, acquired noninvasively using Electrical Cardiometry (EC), could predict prolonged mechanical ventilation (PMV) in infants undergoing VSD repair.

Methods: We conducted a retrospective study of 51 infants. EC monitoring (ICON) was performed from admission to the day before surgery. A composite risk score was developed using Principal Component Analysis (PCA) of clinical characteristics and EC-derived hemodynamic parameters. The predictive performance of this score for PMV (defined as ≥ 12 h) was assessed using correlation and receiver operating characteristic (ROC) curve analysis. Leave-One-Out Cross-Validation (LOOCV) was used to assess the model's stability.

Results: N-terminal pro-B-type natriuretic peptide (NT-proBNP) and the change in the Index of Contractility (ΔICON) were identified as key parameters correlating with clinical classifications of cardiac dysfunction ($r = 1.517$ and 1.470, OR = 4.560 and 4.350 respectively, $p < 0.05$). A PCA-derived composite score was identified as a potential predictor of PMV with $r = -0.522$ in correlation ($p < 0.001$) and AUC = 0.856 (SE = 0.857, SP = 0.773, LOOCV AUC = 0.830), outperforming individual clinical variables alone.

Conclusions: A composite risk score integrating individual data and EC hemodynamics monitoring can effectively identify infants at high risk for PMV following VSD repair. This approach may provide a valuable tool for perioperative management and resource allocation.

1 | Introduction

Congenital heart disease (CHD) is the most common congenital disability affecting infants, with ventricular septal defect (VSD) accounting for the highest prevalence among CHD types [1]. Early surgical repair is required to treat syndromes and though it reduces the morbidity hazard of cardiovascular events, long-term follow-up showed that isolated VSD is associated with a higher incidence of ventricular dysfunction in spite of the surgical closure [2]. The optimal timing of surgical repair in infants

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with VSD complicated by pneumonia or heart failure remains a significant clinical challenge, with patients exhibiting considerable heterogeneity in postoperative recovery. For the pediatric anesthesiologist and intensivist, the ability to accurately stratify risk prior to surgery is paramount for guiding preoperative optimization, anticipating intraoperative challenges, and planning postoperative care. However, clinicians currently lack objective, noninvasive tools to reliably predict which infants will have a prolonged or complicated course. This gap in monitoring capabilities can lead to adverse outcomes. Apart from the direct surgical damage to the cardiomyocytes, the cardiopulmonary bypass (CPB) further exacerbates pulmonary interstitial edema and systemic inflammatory response, which increases the incidence of complications such as arrhythmia, transudation, and low cardiac output syndrome (LCOS) and eventually leads to prolonged postoperative ventilation time, ICU stays, or even death [3, 4].

While goal-directed therapy (GDT) algorithms have shown promise in other settings, their implementation in infants is hampered by the limitations of existing hemodynamic monitoring techniques [5, 6]. Derived from Transthoracic Electrical Bioimpedance (TEB) technology, Electronic Cardiometry (EC) measures the changes in electrical impedance of aortic blood flow during the cardiac cycle to calculate cardiac output (CO) through four surface electrodes (Figure 1) [7]. The portable EC device, ICON, is the first and currently the only FDA-approved noninvasive device for CO monitoring in premature infants, neonates, or children. Multiple studies have demonstrated the accuracy of EC and its consistency with other CO measurements including pulmonary artery catheterization (PAC, the gold standard for CO estimation), thermodilution, echocardiography, and MRI in patients with [8–12]. EC excels in providing instantaneous hemodynamic trend analysis of CO, and the calculation is independent of clear visualization of heart structures [7]. EC monitoring pilot study of categorizing patients with septic shock by fluid responsiveness showed its promising potential in cardiac reverse assessment [13]. However, its utility in the preoperative setting for risk stratification has not been thoroughly investigated.

While traditional ventilatory parameters (e.g., oxygenation index, lung compliance) are critical indicators of respiratory status, the pulmonary compromise in VSD patients is primarily driven by hemodynamic burden. Therefore, we hypothesized that assessing preoperative hemodynamic reserve using noninvasive EC would provide an earlier and more direct predictor of postoperative outcomes than downstream respiratory mechanics. By conducting mathematical analysis on the hemodynamic profile and its association with short-term postoperative outcomes, we aimed to (1) validate EC-derived parameters against standard classifications of cardiac dysfunction and (2) develop a predictive model incorporating EC data to identify infants at high risk for prolonged mechanical ventilation (PMV).

2 | Materials and Methods

2.1 | Patients Management and Data Collection

This retrospective study included infants (under age one) who received VSD open-chest surgical repair via CPB from January 2017 to January 2023 in our hospital. Admission diagnosis confirmed as isolated nonrestricted VSD or mainly VSD complicated by Patent Foramen Ovale (PFO), Atrial Septal Defect (ASD), Patent Ductus Arteriosus (PDA), and/or Persistent Left Superior Vena Cava (PLSVC). Exclusion Criteria are as follows:

1. Complicated cyanotic congenital heart abnormalities or severe valvular regurgitation.
2. Severe extracardiac malformations, syndromic genetic disease or hemolytic disorders (e.g., G6PD deficiency).
3. Occurrence of severe noncardiac procedure-related complications that significantly impair the postoperative recovery.
4. Inapplicability of the ICON device: various types of arrhythmias or temporary pacemakers.

Preoperative routine management includes noninvasive pressure ventilation support, anti-infection, diuresis, and vasoactive agent administration. ICON devices (Osypka Medical GmbH, Germany, Figure 1) were used for CO measurement from the admission day (Baseline) to the day before surgery (Final). Surgical intervention is initiated immediately within a critical window of hemodynamic stability. This window is strictly defined by the confirmation of resolved infection (normothermia for ≥ 48 h and

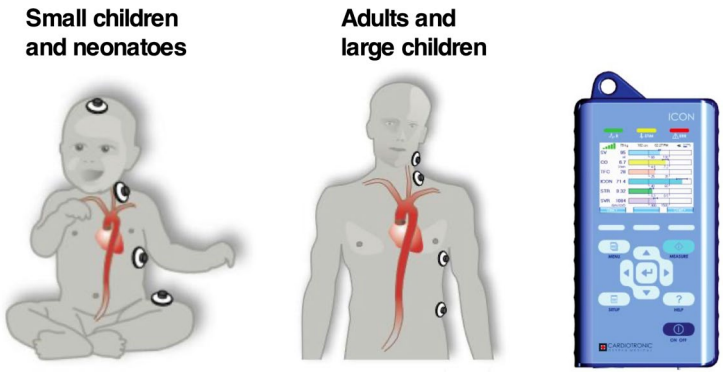

FIGURE 1 | Electronic cardiometry monitoring. Electrical cardiometry (EC) is a method of non-invasive technology for cardiac output measurement. This is available for infants or neonates used by ICON devices (Osypka Medical GmbH, Germany). Figure from ICON brochure shows the sensors placement (https://www.osypkamed.com/wp-content/uploads/2024/05/24.05.06-A4-ICON-EN_web.pdf).

improved inflammatory markers) and stabilized HF symptoms, verified by normalized heart rate and respiratory parameters for ≥ 24 h and the absence of acute decompensation on preoperative electrocardiography.

The improvement of cardiac function (cardiac function reserve) in patients during the preoperative medical treatments was calculated as follows:

$$\Delta CI = (\text{maximum CI} - \text{Baseline CI}) / \text{Baseline CI}^{*}100\%$$

$$\Delta ICON = (\text{maximum ICON} - \text{Baseline ICON}) / \text{Baseline ICON}^{*}100\%$$

2.1.1 | Definition of Mechanical Ventilation Duration

The duration of mechanical ventilation was defined as the time interval (in hours) from admission to the ICU post-surgery until the time of successful extubation. In this cohort, no patients underwent extubation in the operating room; all infants were transferred to the ICU incubated to ensure hemodynamic stability during the immediate postoperative transition. Postoperative management included assessment of fluid status: Routine ultrasound surveillance for ascites was not performed. Ascites was assessed via bedside ultrasound only when clinically indicated by signs such as abdominal distension or oliguria. For the purpose of this study, ascites was defined as the presence of clinically significant intraperitoneal fluid detected by ultrasound that required therapeutic intervention (e.g., enhanced diuretic therapy or peritoneal drainage). Peritoneal dialysis catheters were not routinely placed but were reserved for patients with severe fluid overload or renal compromise.

2.2 | Evaluation and Prediction

To ensure the physiological validity of the predictors used in our subsequent risk model, we first conducted a detailed hemodynamic assessment. This step was essential to confirm that the EC-derived parameters accurately reflect the underlying cardiac status before applying them as prognostic markers. For the preoperative evaluation stage, the severity of cardiac dysfunction measured by EC monitoring was analyzed and compared with left ventricular ejection fractions (LVEF) and N-terminal pro-B-type natriuretic peptide (NT-proBNP). As for the definition of the cardiac dysfunction groups, preoperative cardiac function was assessed using the Modified Ross Classification for pediatric heart failure [14]. Patients were categorized into two groups based on symptom severity:

- Mild Cardiac Dysfunction Group (MCDG): Defined as patients with Modified Ross Class I (asymptomatic) or Class II (mild tachypnea or diaphoresis with feeding).
- Severe Cardiac Dysfunction Group (SCDG): Defined as patients with Modified Ross Class III (marked tachypnea, prolonged feeding times with growth failure) or Class IV (symptoms such as retractions, grunting, or diaphoresis at rest).

The difference of hemodynamic profile as well as personal characteristics between the two groups was calculated, based on which we then figured out the key parameters for the cardiac dysfunction assessment. Principal Component Analysis (PCA) was used to identify the main characteristic variables of the data (principal components, PCs) and calculate a composite score to determine the combined effect of individual characteristics and hemodynamic profile. PCA is a statistical method that geometrically projects data onto lower dimensions to simplify the data while retaining trends and patterns.

2.2.1 | Outcome Definition

For the postoperative prediction model, the duration of mechanical ventilation was utilized as the primary indicator of short-term outcomes. Prolonged mechanical ventilation (PMV) was defined as a duration exceeding 12 h postoperatively. This threshold was selected to represent a significant deviation from the standard "fast-track" recovery pathway. Previous evidence suggests that postoperative morbidity and mortality rates do not significantly rise until intubation exceeds 12 h [15]. In our cohort, this cutoff was further validated by the distribution of ventilation times in the MSDG, where the median duration was approximately 14 h (Table 1), suggesting that 12 h serves as a clinically appropriate lower boundary to distinguish delayed recovery from the standard postoperative course. Consequently, the model was designed to analyze the association between the extracted PCs and PMV, thereby evaluating the predictive value of preoperative EC hemodynamic profiles for short-term recovery.

2.3 | Statistical Analysis

The suitability of the data for PCA was assessed by the Kaiser-Meyer-Olkin test and Bartlett's test. The factor loading matrix was examined to identify variables affecting the PCs. Finally, scores derived from PCs and a composite score were calculated. Normally distributed variables were presented as mean ± standard deviation and the non-normally distributed as median (P25, P75). Categorical variables were presented as percentages. Univariate analysis included *T*-tests or Mann–Whitney *U* tests to examine the differences between the two groups. Chi-square tests or Fisher's exact tests were used for categorical variables. Binary logistic regression was used for multivariate analysis. Spearman correlation analysis was used to determine the monotonic relationship between variables. Receiver operating characteristic (ROC) curves were constructed to calculate the area under the curve (AUC) and determine the optimal cutoff value. Statistical analysis was performed using SPSS version 26.0. The bar chart and heat map were processed by GraphPad Prism version 10.1. $p < 0.05$ was considered statistically significant. Given the constraints of the study cohort size ($n = 51$), we implemented Leave-One-Out Cross-Validation (LOOCV) to rigorously assess the model's stability and risk of overfitting. In this procedure, the model was iteratively trained on "n–1" samples and validated on the single remaining observation, repeating the process for the entire dataset. The validated AUC was calculated to provide an unbiased estimate of the model's predictive performance. All validation analyses were conducted using the pROC package in R software version 4.3.2.

TABLE 1 | Clinical characteristics.

Basic Characteristics	MCDG ($n=25$)	SCDG ($n=26$)	*N*	*p*
Gender				0.482
Male	11 (44.00%)	14 (53.85%)	25	
Female	14 (56.00%)	12 (46.15%)	26	
Respiratory system disease[a]				0.332
Yes	13 (52.00%)	17 (65.38%)	30	
No	12 (48.00%)	9 (34.62%)	21	
Age (months)	5 (3, 6)	3 (2, 5)	51	0.080
Height (cm)	62.40 ± 5.36	59.31 ± 6.95	51	0.082
Weight (kg)	6.50 (5.4, 7.5)	5.25 (4.2, 6.0)	51	0.008*
LVEF (%)	68.96 ± 4.74	69.15 ± 5.77	51	0.896
NT-proBNP (pg/mL)	1230.0 (455.8, 1817.5)	1739.0 (652.6, 4427.8)	51	0.023*
CPB (min)	81 (73.5, 100)	80 (73, 92)	51	0.685
ACC (min)	49 (40, 57.5)	47 (37, 55.5)	51	0.369
Postoperative complications				0.206
Yes	15 (60%)	11 (42.31%)	26	
No	10 (40%)	15 (57.69%)	25	
DMV (h)	14 (8, 46)	20 (9.5, 40.5)	51	0.438
Maximum VIS within postoperative 24 h	12.00 (9.00, 15.30)	12.98 (10.80, 16.70)	51	0.147
ICU Stays (days)	1 (1, 3)	2 (1, 4)	51	0.249
Postoperative Hospitalization Stays (days)	8 (7, 11)	10 (9, 12)	51	0.023*

Note: MCDG and SCDG indicates mild and severe cardiac dysfunction group respectively.
Abbreviations: ACC, arotic cross clamp; CPB, cardiopulmonary bypass; DMV, duration of mechanical ventilation; ICU, intensive care unit; LVEF, left ventricular ejection fractions; *N*, number of patients with data; NT-proBNP, N-terminal pro-B-type natriuretic peptide; VIS, vasopressor/inotropic score.
[a]Preoperative respiratory system diseases in this study cohort included upper respiratory tract infections, pneumonia, respiratory failure, congenital laryngomalacia, and bronchial hemangioma.
*$p<0.05$.

3 | Results

3.1 | Preoperative Cardiac Function

54 patients met the criteria and three cases were excluded because of data missing. A total of 51 cases proceeded to analysis with 25 (49%) male and 26 (51%) female. The age of all patients was 4 (2.5, 5) months, the weight was 5.76 ± 1.45 kg and the height was 60.82 ± 6.36 cm. Patients in SCDG had higher NT-proBNP (median 1230 vs. 1739 pg/mL, $p<0.05$) and lower weight (median 5.25 vs. 6.50 kg, $p<0.05$). There were no significant differences in gender, respiratory system diseases, age, height, and LVEF between the two groups (Table 1).

The preoperative hemodynamic profile measured by EC was described in Table 2 and Figure 2. At the first day of admission, patients in SCDG have lower baseline CI (median 4.0 vs. 4.70 L/min/m^2, $p<0.05$) when compared with MSDG (Figure 2a). During the preoperative adjustments, SCDG observed significantly higher ΔCI (median 19.68 vs. 2.30%, $p<0.05$), ΔICON (median 29.73 vs. 0.34%, $p<0.05$), and the maximum of TFC (median 44.50 vs. 36.00/kΩ, $p<0.05$) in Table 2. By the day before the surgery, SCDG patients' CI and ICON had increased significantly ($p<0.05$, Figure 2a,b). As for MCDG, there were no significant differences between their final and baseline CI or ICON, while their final TFC was significantly lower than the beginning ($p<0.05$, Figure 2c).

Cardiac classification significantly correlates with age, height, weight, NT-proBNP, baseline CI, ΔCI, ΔICON, and TFCmax (Figure 3, $p<0.05$). Among the EC indexes, the strongest correlation was observed between Ross Classification and ΔICON ($r=0.336$). TFCmax showed a significant correlation with NT-proBNP ($r=0.301$, $p<0.05$). ROC curve was performed to determine their cutoff values for the binary classification of cardiac dysfunction (Table 3). The cutoff value of ΔCI ≥ 2.4% is considered negligible for clinical monitoring purposes, thus ΔCI was excluded. The cutoff value of NT-proBNP ≥ 1500 pg/mL and ΔICON ≥ 25% were chosen according to the Youden Index (NT-proBNP = 1378, ΔICON = 25.6%). Multivariate analysis included weight, NT-proBNP, baseline CI, ΔICON, and TFCmax with the use of binary logistic stepwise regression (Table 4). NT-proBNP ≥ 1500 pg/mL and ΔICON ≥ 25% have significant associations with cardiac

TABLE 2 | Preoperative hemodynamic profile measured by EC.

Hemodynamic profile	MCDG ($n=25$)	SCDG ($n=26$)	p
HR (bpm)	139.28 ± 14.51	140.23 ± 13.30	0.808
Baseline CI (L/min/m^2)	4.70 (4.00, 5.20)	4.0 (3.73, 4.53)	0.043*
CImax (L/min/m^2)	5.44 ± 1.14	5.188 ± 0.971	0.426
Final CI (L/min/m^2)	4.60 (4.20, 4.90)	4.60 (4.08, 5.20)	0.813
ΔCI (%)	2.30 (0.00, 25.00)	19.68 (3.48, 36.88)	0.042*
Baseline ICON	137.31 ± 29.28	124.19 ± 32.60	0.137
ICONmax	152.87 ± 26.60	158.37 ± 27.16	0.469
Final ICON	158.40 (142.00, 165.90)	157.95 (137.05, 172.75)	0.611
ΔICON (%)	0.34 (0.00, 20.12)	29.73 (7.84, 46.80)	0.008*
Baseline TFC (/kΩ)	34.00 (29.00, 41.00)	32.50 (37.50, 45.75)	0.699
TFCmax (/kΩ)	36.00 (32.00, 43.00)	44.50 (34.50, 52.00)	0.039*
Final TFC (/kΩ)	30.00 (28.00, 33.00)	32.00 (28.00, 37.75)	0.532
STR	0.46 ± 0.08	0.45 ± 0.06	0.507

Note: MCDG and SCDG indicates mild and severe cardiac dysfunction group respectively.
Abbreviations: CI, cardiac index; CImax, the maximum of CI; HR, heart rate; ICON, index of contractility; ICONmax, the maximum of ICON; STR, systolic time ratio; TFC, thoracic fluid content; TFCmax, the maximum of TFC.
*$p<0.05$.

dysfunction ($r=1.517$ and 1.470, OR = 4.560 and 4.350 respectively, $p<0.05$).

3.2 | Postoperative Prediction

The total CPB duration was 81 (73, 97) minutes and 26 patients (50.98%) had complications after the surgery. Pleural effusion and ascites were the most common (occurred in 12 and 13 cases, respectively). Other complications included low cardiac output in 1 case, arrhythmia in 2 cases, and atelectasis in 5 cases. There was 1 rare case of abnormal coagulation function requiring thoracotomy for hemostasis. Except for extended hospitalization stays in SCDG (median 10 vs. 8 days, $p<0.05$), there were no significant differences in CPB and ACC time, occurrence of complications, DMV, ICU stays, and maximum VIS within the first postoperative 24 h between SCDG and MCDG (Table 1).

Based on the results of univariate and correlation analysis (Table 1 and Figure 3), we performed PCA on 10 variables: modified Ross Classification, age, weight, height, NT-proBNP, baseline CI, baseline ICON, ΔCI, ΔICON and TFCmax. The Kaiser-Meyer-Olkin measure was 0.669 > 0.6 and Bartlett's test yielded a significant result ($p<0.001$), indicating that the data met the prerequisite requirement for PCA. A total of three components were revealed with eigenvalues over 1, together accounting for 72.18% of the variance in the data. The loading coefficients table describes the contributions of each variable to each component (Table 5). Age, height, weight, Ross Classification, and NT-proBNP had significant correlations with the first component ($r=0.719$, 0.804, 0.709, −0.740 and −0.740, respectively). Baseline CI, Baseline ICON, ΔCI and ΔICON mainly contributed to the second component ($r=-0.517$, −0.785, 0.742 and 0.82, respectively) and TFCmax for the third component ($r=0.89$). The ultimate score of each PC and the overall composite score were calculated. Given the main contributions of variables, the scores derived from the first, second, and third PCs were named "individual score," "EC score," and "TFC score" respectively.

Correlation analysis (Table S1) revealed that the EC score had a significant negative correlation with DMV ($r=-0.470$, $p<0.05$) and ICU stays ($r=-0.417$, $p<0.05$). The composite score showed significant correlations with all the short-term prognostic indicators ($p<0.05$), and the strongest one lies in DMV ($r=-0.706$). Throughout the study period, no patients experienced extubation failure or required reintubation (0% incidence). Given the absence of these adverse events, our predictive modeling and outcome analysis were specifically directed toward identifying risk factors for delayed extubation (PMV). We divided the patients into two groups according to their DMV given the results of correlation analysis. Patients with postoperative ventilation time ≥ 12 h were in the PMV group. There were a total of 30 (58.82%) patients in the PMV group with longer CPB time, higher occurrence of complications, lower individual score, EC score, and composite score (Table 6, $p<0.05$). No significant differences were in ACC time and TFC score between the two groups.

To evaluate the clinical utility of the PCA derived scores, we performed binary logistic regression analysis (results details in Table S2). Two models were constructed to predict prolonged DMV, both adjusting for CPB time. In Model 1, the composite score was significantly associated with prolonged DMV (OR = 0.06, 95% CI: 0.011–0.331, $p=0.001$), whereas CPB time was not a significant predictor ($p=0.064$). In Model 2, both the Individual Score (OR = 0.200, 95% CI: 0.063–0.635, $p=0.006$) and the EC Score (OR = 0.284, 95% CI: 0.106–0.761, $p=0.012$) served as independent predictors of prolonged DMV. CPB time remained nonsignificant in both models.

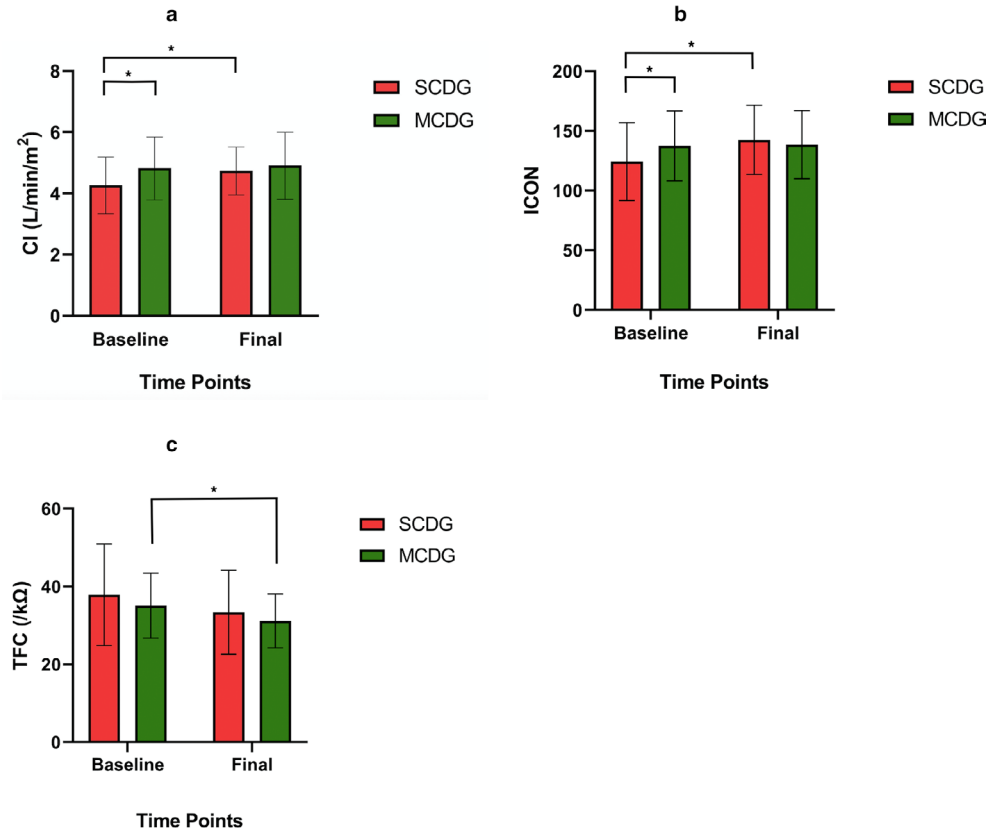

FIGURE 2 | Hemodynamic profile of the preoperative monitoring. MCDG and SCDG indicate mild and severe cardiac dysfunction groups respectively. (a) CI (cardiac index) comparison between MCDG and SCDG. (b) ICON (index of contractility) comparison between MCDG and SCDG. (c) TFC (thoracic fluid content) comparison between MCDG and SCDG. *$p < 0.05$.

The predictive performance of the derived scores was evaluated using ROC analysis (Figure 4). As detailed in Table 7, the composite score demonstrated the highest discriminative ability with an optimal cutoff value of 0.002, yielding a sensitivity of 0.857 and a specificity of 0.773. The original AUC was 0.856. To assess the stability of these cutoffs and performance metrics, LOOCV was performed. The composite score maintained a robust validated AUC of 0.830, confirming minimal overfitting. The individual score and EC score also showed consistent performance with validated AUC of 0.751 and 0.687, respectively.

4 | Discussion

Our study demonstrates that a data-driven approach, incorporating noninvasive hemodynamic monitoring with Electrical Cardiometry (EC), supplements clinical assessment and addresses the well-documented prognostic heterogeneity in this high-risk patient population. While the study indicated a high consistency between EC and echocardiography in critically ill pediatric patients [16], deviations existed and age was considered a confounding factor [17–19]. Median percentage error in the subject of children and adolescents reached an acceptable level (percentage error ≤ 30%) but is higher in neonates and infants (up to 45%) [20]. Reaserchers from European Society for Pediatric Research (ESPR) reaches agreement that while currently EC is not a substitute for echocardiography, it offers advantages in continuous monitoring and longitudinal changes from baseline of hemodynamic parameters [7]. Evaluating new technologies should prioritize their clinical utility as treatments incorporated with less accurate hemodynamic monitoring can also yield favorable patient outcomes. In this study, we observed a significant association between preoperative hemodynamic profiles and postoperative outcomes in VSD infants. Notably, our model successfully predicted PMV, which highlights the critical impact of underlying cardiac dysfunction on early recovery. The selection of the 12-h threshold for PMV is supported by both literature [15] and our cohort data. Analysis of the continuous variable, DMV, revealed significant correlations with both ICU length of stay and total postoperative hospital stay, confirming that ventilation time is a robust surrogate for overall recovery trajectory (Table S1). By aligning our cutoff with the median ventilation time of the uncomplicated group (MSDG, ~14 h, Table 1) and standard fast-track protocols, the chosen 12-h threshold seems to capture clinically significant delays rather than minor physiological variations.

4.1 | Cardiac Function Assessment

The ability to identify high-risk patients before they enter the operating room is of paramount importance. Our findings suggest that preoperative EC monitoring could inform critical clinical decisions regarding the timing of surgery, the intensity of preoperative optimization with vasoactive or diuretic agents, and the allocation of ICU resources. The finding that the change in hemodynamic parameters (specifically ΔICON) is more informative than absolute values aligns with modern concepts in

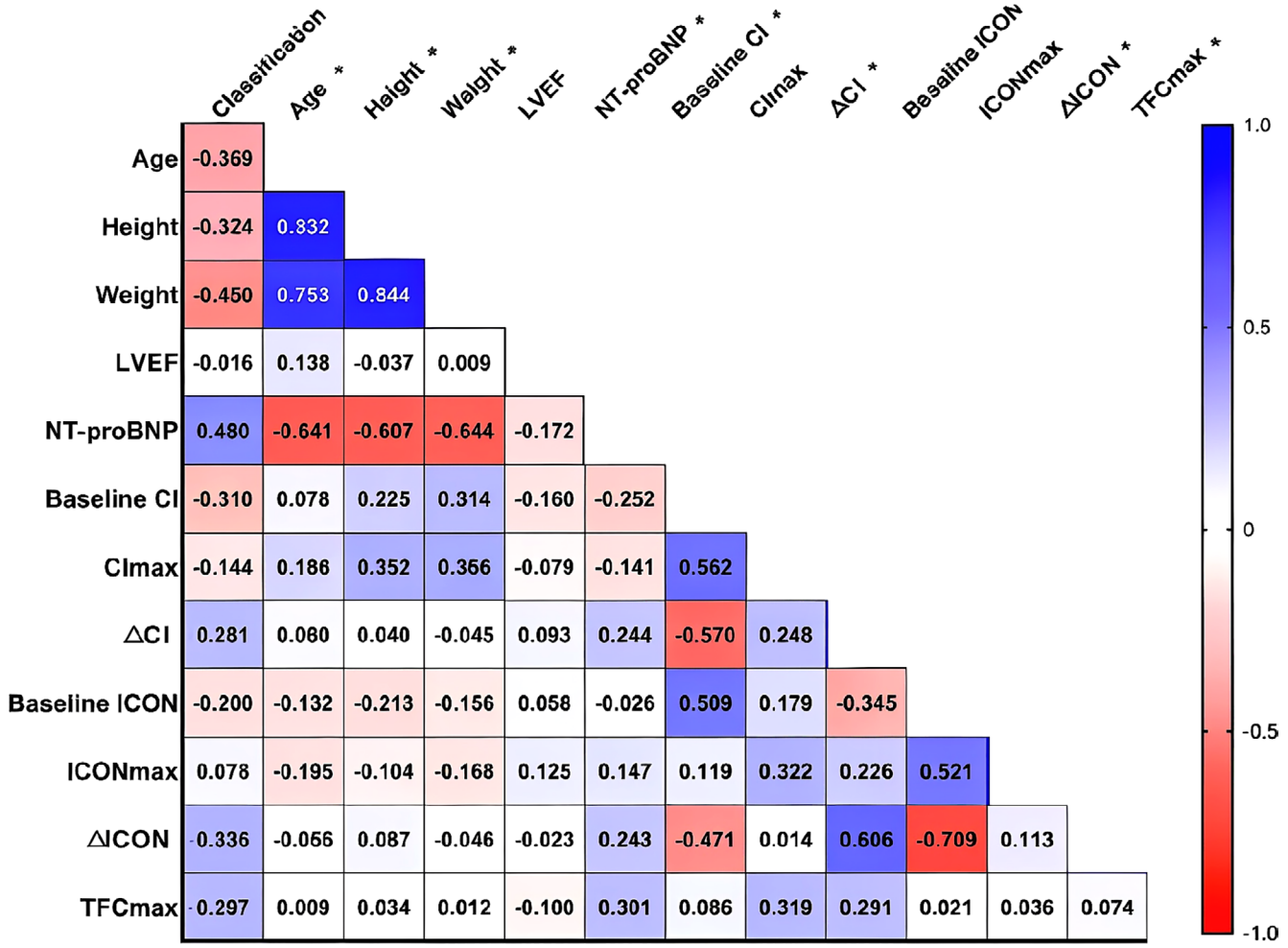

FIGURE 3 | Heat map of correlations between clinical characteristics and hemodynamic profile. CI, cardiac index; ICON, index of contractility; TFC, thoracic fluid content. Classification refers to modified Ross Classification. *Significant correlations between Classification and variables were marked ($p < 0.05$).

TABLE 3 | ROC Curves and the cutoff value.

Variable	AUC	SE	SP	Cutoff value
Weight (kg)	0.716	0.560	0.808	≤6.0
NT-proBNP (pg/mL)	0.686	0.654	0.720	≤1378
Baseline CI ($L/min/m^2$)	0.665	0.600	0.731	≤4.3
ΔCI (%)	0.663	0.808	0.520	≤2.40
ΔICON (%)	0.712	0.528	0.840	≤25.6
TFCmax (/kΩ)	0.668	0.423	0.960	≤45

Note: Cutoff values (e.g., Weight ≤6 kg) represent the optimal predictive thresholds derived from Receiver Operating Characteristic (ROC) curve analysis for identifying the risk of Prolonged Mechanical Ventilation (PMV).
Abbreviations: CI, cardiac index; ICON, index of contractility; TFCmax, the maximum of thoracic fluid content.

goal-directed therapy, where the trend and response to intervention are most critical.

CO is commonly used to assess cardiac reserve and determine tissue perfusion status, guiding adjustments in fluid management [7, 13, 21]. Our study observed that SCDG patients with severe cardiac dysfunction (HF over Class II by modified Ross classification) have lower baseline CI and it correlated negatively with the classification (Table 2 and Figure 3). These patients also showed significant improvements of CI and ICON by the surgery day when compared with the baseline. On the contrary, MCDG patients remained constant CI and ICON (Figure 2a,b). This revealed that preoperative treatments enhanced the CO of patients with HF and the effectiveness of the treatments could be tracked by using EC monitoring. ICON represents the myocardial contractility, which is the unique index derived from EC measurement. In our study, the maximum ratio of improvement of ICON to its baseline value (ΔICON) appeared to have a significant correlation with Ross Classification (Figure 3). ΔICON ≥25% had an acceptable AUC = 0.712 in ROC analysis and it's also an independent factor for cardiac function assessment (OR = 4.35, Table 4), which suggests that patients with severe cardiac dysfunction actively respond to preoperative treatments and their capability of cardiac contractility can be improved over 25%. Additionally, SCDG patients have both higher ΔCI and ΔICON than MSDG (Table 2). These results demonstrate that EC hemodynamic monitoring can provide instantaneous and informative feedback on the improvement of cardiac function, which is of great significance for the timely adjustment of treatment plans

TABLE 4 | Logistic regression analysis for evaluating cardiac function.

	Regression coefficient	Standard error	*Z*-value	*p*	OR	95% Confidence interval for OR
NT-proBNP ≥ 1500	1.517	0.641	2.368	0.018*	4.560	1.299–16.012
ΔICON ≥ 25%	1.470	0.677	2.173	0.030*	4.350	1.155–16.382
Intercept	−1.188	0.498	−2.387	0.017	0.305	0.115–0.809
$R^2 = 0.18$						

Abbreviations: ICON, index of contractility; NT-proBNP, N-terminal pro-B-type natriuretic peptide.
*$p < 0.05$.

TABLE 5 | Loading coefficients demonstrating correlations between the first, second, and third principal components for each variable.

	Individual score	EC score	TFC score	Common factor variance
Age	0.719	0.371	0.166	0.681
Height	0.804	0.393	0.15	0.824
Weight	0.791	0.46	0.228	0.889
Modified ross classification	−0.740	0.083	0.232	0.609
NT-proBNP	−0.740	0.082	0.384	0.702
Baseline CI	0.534	−0.517	0.251	0.615
ΔCI	−0.265	0.742	0.026	0.621
Baseline ICON	0.133	−0.785	0.161	0.659
ΔICON	−0.275	0.82	−0.177	0.779
TFCmax	−0.181	0.119	0.89	0.839

Note: In the later tables or charts, principal component 1 refer to individual score, principal component 2 refer to EC score and principal component refer to TFC score.
Abbreviations: CI, cardiac index; CImax, the maximum of CI; ICON, index of contractility; ICONmax, the maximum of ICON; NT-proBNP, N-terminal pro-B-type natriuretic peptide; STR, systolic time ratio; TFC, thoracic fluid content; TFCmax, the maximum of TFC.

based on the patient's condition. The association between the increase of ICON and cardiac classification further confirms the viewpoint of Biasis et al. [22] that monitoring changes or trends in cardiac output may be more meaningful than absolute values.

TFC refers to the total volume of fluid in the patient's thorax, including intracellular, interstitial, alveolar and pleural cavity fluid. Our study found significant differences in the maximum TFC values between SCDG and MSDG (Table 2), which aligns with the fact that high TFC indicates severe pulmonary interstitial oedema due to increased pulmonary flow from the shut [23]. In addition, the final TFC was significantly lower than the baseline value in the MCDG but not the SCDG (Figure 2c), indicating that worse diuretic response was associated with more advanced HF. The result that TFC also significantly correlated with NT-proBNP (Figure 3) is consistent with Sato et al. [24], who also used bioelectrical impedance analysis and found that oedema index correlated with BNP levels and patients with New York Heart Association (NYHA) III-IV of HF have higher oedema index. Moreover, patients with high TFC also manifest pulmonary congestion on chest X-ray [25], and studies found that the TFC can be used to predict the success of postoperative weaning and diagnose neonatal respiratory distress syndrome [23, 26]. While the cutoff value of peak TFC = 45/kΩ has an acceptable AUC = 0.668, it seems not an independent factor for evaluating cardiac dysfunction in our study (Table 4). Further study focusing on the potential utility of TFC needs to be done.

Collectively, these hemodynamic findings confirm that the identified variations in CI, ICON, and ICON are not merely statistical artifacts but represent genuine physiological impairments. Consequently, these validated variables were prioritized for inclusion in the multivariate prediction models for PMV described in the following section.

4.2 | Clinical Interpretation of Postoperative Outcomes

Regarding the controversy of the timing of surgical repair for left-to-right shunt CHD infants with HF, hypoxia or ongoing pneumonia, several studies conclude that these patients are not contraindicated for primary surgical repair [3, 27]. Though there was no increasing occurrence of postoperative mortality and major complications, prognostic heterogeneity was observed and these patients had longer ventilation time, ICU stays, and hospitalization stays [3]. Our findings largely align with the results of the previous study, with the exception of a notable variance observed solely in hospitalization stays between the mild and severe cardiac dysfunction cohorts. Therefore, our study underscores the enhanced short-term prognosis associated with

TABLE 6 | The difference of intraoperative indexes and each PCA-derived score in normal and prolonged DMV groups.

Basic characteristics	Not PMV ($n=21$)	PMV ($n=30$)	p
CPB (min)	45.48 ± 9.80	50.40 ± 13.68	0.164
ACC (min)	78.05 ± 11.6	90.37 ± 19.27	0.007*
Postoperative complications			0.003*
No	16 (76.19%)	10 (33.33%)	
Yes	5 (23.81%)	20 (66.67%)	
Baseline CI (L/min/m^2)	4.20 (3.90,4.88)	4.30 (3.90,5.320)	0.703
ΔCI	21.04 (0.60,37.48)	8.11 (0.00,0.25.58)	0.253
Baseline ICON	116.95 (104.98, 145.50)	133.5 (107.1159.1)	0.199
ΔICON	11.71 (1.90, 55.24)	18.78 (0.00,31.99)	0.209
Individual score	0.56 ± 0.82	−0.39 ± 0.93	0.000*
EC score	0.48 ± 1.05	−0.34 ± 0.83	0.003*
TFC score	−0.04 ± 0.81	0.03 ± 1.13	0.816
Composite score	0.43 ± 0.49	−0.30 ± 0.51	0.000*

Abbreviations: ACC, arotic cross clamp; CPB, cardiopulmonary bypass; ICON, index of contractility, also the name of the devices of Electronic Cardiometry; PMV, prolonged mechanical ventilation; TFC, thoracic fluid content.
*$p < 0.05$.

preoperative interventions. Especially for infants exhibiting HF symptoms alongside respiratory distress, proactive intervention strategies such as vasoactive medications, respiratory assistance, and comprehensive therapy bundles warrant consideration.

Research endeavors focused on refining preoperative management necessitate the implementation of quantified goal-directed therapy, wherein hemodynamic monitoring plays a pivotal role. Identification of key parameters such as pulse pressure variation, CI trending, and mean arterial pressure has been instrumental in reducing postoperative complications among surgical patients [28]. A pilot study also deployed noninvasive EC monitoring to steer fluid management in pediatric CHD patients with titrated vasoactive medication dosages guided by the real-time assessments of CI, stroke volume variation (SVV), and systemic vascular resistance index (SVRI) [29]. This methodology efficaciously curtailed fluid intake and mitigated the incidence of postoperative complications, thereby fostering enhancements in surgical outcomes.

PCA offers a powerful methodological advantage by distilling complex, multidimensional hemodynamic data into a single, clinically actionable predictor. Similar to recent applications in other congenital heart disease cohorts [30], PCA derived indices demonstrate significant prognostic value for adverse postoperative outcomes in CHD patients. This approach offers translational potential to refine risk stratification and guide personalized postoperative recovery strategies. Unlike traditional single-parameter analysis, the PCA derived EC score captures the holistic cardiac function, which explains its significant correlation with ventilation time in our cohort ($r = -0.47$, Table S1). This association validates the physiological premise that optimized hemodynamic delivery is a

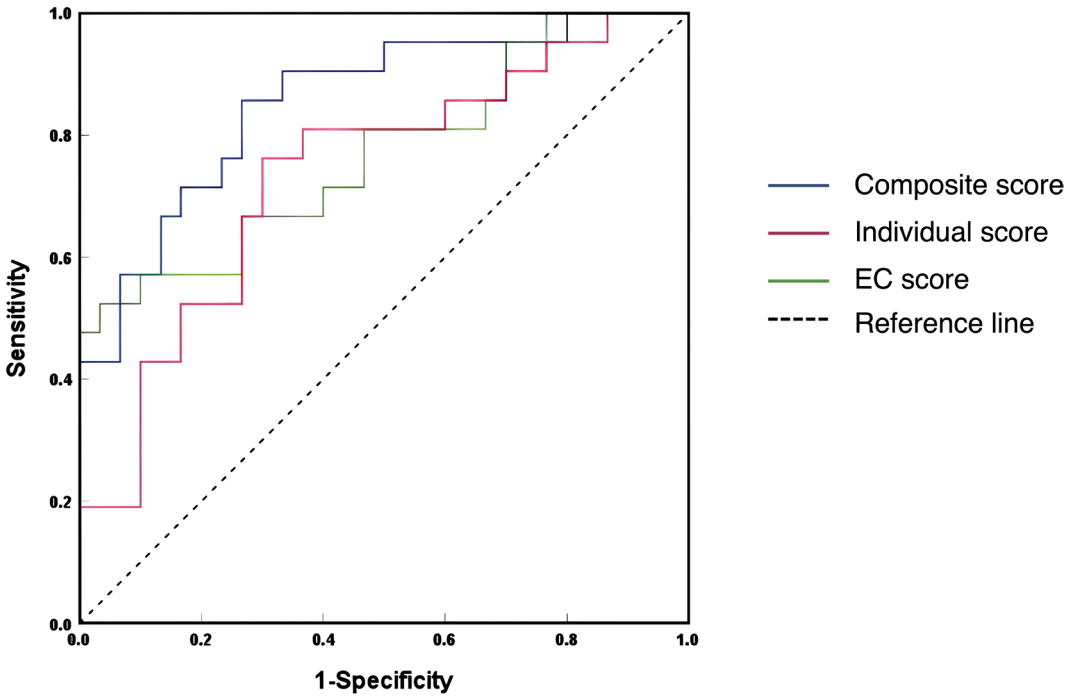

FIGURE 4 | ROC curve of PCA-derived scores for PMV. The curves illustrate the diagnostic performance of the composite score (blue), individual score (red), and EC score (green) in predicting PMV. Detailed performance metrics, including optimal cut-off values, sensitivities, specificities, and cross-validated AUCs, are presented in Table 7.

TABLE 7 | Predictive performance and internal validation of PCA derived scores for PMV.

Predictor	Cutoff	Sensitivity	Specificity	Original AUC	LOOCV validated AUC
Composite score	0.002	0.857	0.773	0.856	0.830
Individual score	0.659	0.524	0.967	0.770	0.751
EC score	−0.109	0.762	0.700	0.737	0.687

prerequisite for successful respiratory weaning. Consequently, focusing on ventilation duration is clinically pivotal: it acts as a sensitive indicator of postoperative recovery quality, where determining the risk of prolonged ventilation allows for early intervention to mitigate economic burdens and adverse sequelae [15, 31].

Though singular hemodynamic parameters exhibited no discernibly statistical meaning, the amalgamation of EC parameters into a principal component via PCA linear transformation revealed a significant association with outcomes (Table 6). In our study EC score emerged as an independent determinant of PMV (model 2 in Table S2) and ROC curve for predicting also presented acceptable diagnostic efficacy of EC score (AUC = 0.737, Table 7). Notably, the positive and substantial load coefficients of the EC score, particularly with the maximum increase in ΔICON and ΔCI (Table 5), underscore the significance of preoperative cardiac reserve in enhancing surgical outcomes. Sumbel et al. [18] used EC to monitor critically ill children and found that nadir and mean CO predicted ventilation days. However, our study supported the ESPR' view that the trajectory of hemodynamic changes or trends, not absolute value, serves as pivotal guidance for gauging the efficacy of interventions [7]. The identification of EC score as key predictors is physiologically grounded in the hemodynamic cost of weaning. The transition from mechanical ventilation to spontaneous breathing involves a shift from positive intrathoracic pressure to negative pressure, which significantly alters cardiac preload and afterload. Our selected preoperative features (ΔCI and ΔICON) serve as proxies for cardiac functional reserve, reflecting the patient's ability to tolerate these acute hemodynamic shifts. Thus, patients with compromised preoperative reserve are mechanically susceptible to failure during this critical transition. Clinically, this model represents a paradigm shift from reactive assessment to proactive optimization. While standard protocols (e.g., pulmonary mechanics) function as postoperative diagnostic checkpoints for immediate readiness, our model utilizes preoperative EC data to identify physiological vulnerabilities before surgical stress occurs. This approach transforms the clinical workflow: rather than merely waiting to assess the patient's condition at the moment of extubation, clinicians can capitalize on this preoperative window to initiate hemodynamic optimization, thereby ensuring high-risk patients are better prepared to meet standard extubation criteria.

However, hemodynamic status does not exist in isolation. Recognizing this, our study integrated intrinsic clinical characteristics—age, weight, height, NT-proBNP, and modified Ross Classification—to create an Individual Score derived from PCA. This score was also identified as an independent predictor of PMV (Table S2). Weight and age are widely acknowledged as determinants of surgical complications, duration of ventilation time, and hospitalization stays [32]. The association between the individual score (encompassed age, weight, and height) and surgical outcomes in our study underscores the pivotal role of infants' nutritional status in prognostic determinations [33]. Additionally, NT-proBNP, as a biochemical marker of myocardial impairment, retains its significance as a crucial metric in risk stratification [34, 35]. Regarding the intraoperative factors, our results did not consider CPB time as a significant risk factor, which also consists with some previous findings [36, 37]. This may be explained by the advancements in CPB techniques, such as refined ultrafiltration and the anti-inflammatory agents, which effectively mitigate interstitial edema and preserve pulmonary oxygenation, thereby decoupling CPB duration from ventilation outcomes [38, 39].

Ultimately, the integration of these dimensions proved superior. The composite score exhibited the strongest correlation ($r = -0.706$, Table S1) and the highest discriminative accuracy for predicting PMV (AUC = 0.856, Table 7). This discrepancy highlights a critical clinical insight: while separate variables mathematically explain variance, the integrated composite score offers superior risk stratification. By synthesizing static individual attributes with dynamic hemodynamic parameters, the composite approach captures a holistic patient profile, yielding a more comprehensive and precise prediction than any single dimension alone. This confirms the necessity of adopting patient-tailored strategies grounded in multidimensional data. A primary concern in studies with limited sample sizes is the risk of overfitting. We addressed this through rigorous internal validation. The LOOCV results confirmed that our core PCA derived scores maintain high predictive accuracy (validated AUC = 0.830 for the composite scores) even when subjected to strict cross-validation. This suggests that the identified hemodynamic and individual signatures represent genuine physiological signals rather than statistical noise. Furthermore, we are currently undertaking the next phase of this research project (unpublished), where the cohort has been expanded. Preliminary validation using machine learning algorithms (Random Forest and Decision Trees) on this expanded dataset has further corroborated the findings of the current study. Specifically, feature importance analysis confirmed that the preoperative binary variables (NT-proBNP and ΔICON in Table 4) and the PCA derived scores remain the most significant predictors of PMV.

This study also have several limitations. First, our study was strategically designed to focus exclusively on preoperative hemodynamic predictors. While this approach enables proactive risk stratification and early optimization before surgical stress occurs, it inherently immediate postoperative respiratory mechanics (e.g., airway resistance). Therefore, our model is intended to function as an early warning tool to complement, rather than replace, traditional postoperative extubation readiness trials.

Future models integrating these hemodynamic scores with standard respiratory indices may offer a more holistic predictive framework. Second, we acknowledge the constraints of the limited sample size and the single-center design restricted to VSD patients, which may affect generalizability to complex CHD. Finally, the clinical application of EC remains nascent, and potential variability in measurements compared to invasive standards must be considered. Additionally, the retrospective nature of this study precludes the establishment of definitive causal relationships. Consequently, prospective, multi-center validation is imperative to fully ascertain the clinical utility and accuracy of this noninvasive technology across diverse patient populations.

5 | Conclusion

In conclusion, preoperative monitoring with EC provides valuable data on cardiac function in infants with VSD. Predictive models incorporating these noninvasive hemodynamic indices effectively identify patients at high risk for PMV, which have the potential to become a valuable tool for the clinician in optimizing surgical timing and improving the postoperative outcomes.

Author Contributions

S.W. and M.L. contributed equally to this work and shared co-first authorship. They were responsible for conceptualization, methodology, formal analysis or drafting the initial manuscript. H.Z. and M.D. contributed equally to this work and shared co-corresponding authors. They were responsible for supervision and funding resources. B.M., Y.W., H.Z., and D.W. were responsible for investigation, data collection and curation, reviewing or editing the manuscript.

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Ethics Statement

This retrospective study was approved by the Ethics Committee of Capital Institute of Pediatrics (Approval number: SHERLL2023087) and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Consent

Written informed consent for the use and publication of their clinical data was obtained from the parents or legal guardians of all infant participants.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Table S1:** Correlations analysis for scores derived from principal components and prognostic outcomes. **Table S2:** Regression Models of PCA-derived score to predict the prolonged DMV.