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ORIGINAL ARTICLE

WILEY Congenital Heart Disease

Vasopressor magnitude predicts poor outcome in adults with congenital heart disease after cardiac surgery

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Abstract

Background: High levels of vasoactive inotrope support (VIS) after congenital heart surgery are predictive of morbidity in pediatric patients. We sought to discern if this relationship applies to adults with congenital heart disease (ACHD).

Methods: We retrospectively studied adult patients (≥18 years old) admitted to the intensive care unit after cardiac surgery for congenital heart disease from 2002 to 2013 at Mayo Clinic. Vasoactive medication dose values within 96 hours of admission were examined to determine the relationship between VIS score and poor outcome of early mortality, early morbidity, or complication related morbidity.

Results: Overall, 1040 ACHD patients had cardiac surgery during the study time frame; 243 (23.4%) met study inclusion criteria. Sixty-two patients (25%), experienced composite poor outcome [including eight deaths within 90 days of hospital discharge (3%)]. Thirty-eight patients (15%) endured complication related early morbidity. The maximum VIS (maxVIS) score area under the curve was 0.92 (95% CI: 0.86-0.98) for in-hospital mortality; and 0.82 (95% CI: 0.76-0.89) for combined poor clinical outcome. On univariate analysis, maxVIS score ≥3 was predictive of composite adverse outcome (OR: 14.2, 95% CI: 7.2-28.2; $P < 0.001$), prolonged ICU LOS ICU LOS (OR: 19.2; 95% CI: 8.7-42.1; $P < 0.0001$), prolonged mechanical ventilation (OR: 13.6; 95% CI: 4.4-41.8; $P < 0.0001$) and complication related morbidity (OR: 7.3; 95% CI: 3.4-15.5; $P < 0.0001$).

Conclusions: MaxVIS score strongly predicted adverse outcomes and can be used as a risk prediction tool to facilitate early intervention that may improve outcome and assist with clinical decision making for ACHD patients after cardiac surgery.

KEYWORDS
adult congenital heart disease, cardiac surgery, critical care, vasoactive

1 | INTRODUCTION

As a result of recent advances in surgical technique, more than 95% of children with congenital heart disease (CHD) will now survive into adulthood.[1,2] Estimates now place the adult congenital heart disease (ACHD) population around 1 to 1.3 million with a growth rate of 5% per year.[2] Despite improved survival, congenital heart surgery, and cardiopulmonary bypass can still lead to significant morbidity and

mortality.[3,4] ACHD patients often require ongoing intervention for their CHD throughout their lifetime for a variety of reasons that include repair of residual defects, valve and conduit replacement as the child grows, and electrophysiological interventions for arrhythmias.[1,5,6] A recent review by Holst et al demonstrated a high rate of repeat sternotomy in the ACHD patient population.[5] Reoperations can be associated with a higher risk of complications in these patients compared to the non-CHD cardiac surgical populations.[5,7-9] Although the challenges associated with ACHD reoperation are well recognized, more work is needed to identify specific perioperative risk factors that will facilitate development of risk stratification models to guide the care of these complex patients.[6,8] Currently, there are no cardiac scoring systems for assessing surgical risk in the ACHD patient population. Tools for predicting outcome following non-CHD adult cardiac surgery do exist,[10,11] but are not inclusive of ACHD specific risk factors.

The ideal CHD risk prediction tool would recognize the limitations of existing scoring systems and incorporate specific variables that are predictive of poor outcome in adult CHD surgical patients. Recently, the postoperative requirement for vasopressor and inotrope hemodynamic support has been validated as a strong predictor of morbidity and mortality following pediatric CHD surgery.[12] The vasoactive inotrope score (VIS) is a summation of the total dose of vasopressor and inotrope requirement at a single point in time. The maximum vasoactive inotrope score (maxVIS) calculated during the first 48 hours after surgery is a strong predictor of prolonged mechanical ventilation and intensive care unit (ICU) length of stay for infants <6 months[12] and <3 months of age.[13] The relationship between maxVIS and ACHD surgical outcomes has not been investigated.

We sought to evaluate the association between vasopressor/inotrope requirements and outcome after ACHD surgery, in order to identify whether the maxVIS score is a valid risk stratification tool for ACHD patients. We hypothesized that the maxVIS score would be a strong predictor of early death, prolonged mechanical ventilation, ICU length of stay, acute renal failure, stroke, pneumonia, or reoperation following ACHD surgery.

2 | MATERIALS AND METHODS

2.1 | Patient data collection

We performed a retrospective chart review of patients 18 years of age and older, who underwent cardiac surgery for repair of congenital heart defects at Mayo Clinic from November 2002 and September 2013. This study was approved by the Mayo Clinic Institutional Review Board.

The electronic medical record (EMR) was utilized to collect demographic data, ICU admission and discharge date, length of mechanical ventilation, and death status and date. Comorbidities were noted by chart review of the 5 years preceding the surgery.[14] In addition, patients were assigned a RACHS-1 (risk adjustment for congenital heart surgery) score based on their operative procedure as described by Jenkins et al[15,16]

The inotrope and vasopressor doses were collected at 15 minute intervals using automated data capture of the EMR system for the first 96 hours of CICU admission. The VIS was calculated using the equation described and validated in the pediatric population [VIS = Dopamine dose (μg/kg/min) + Dobutamine dose (μg/kg/min) + 100* Epinephrine dose (μg/kg/min) + 10*Milrinone dose (μg/kg/min) + 10,000*Vasopressin dose (U/kg/min) + 100* Norepinephrine dose (μg/kg/min)].[12] Day one Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment scores (SOFA) were calculated using previously describes methods.[17,18]

2.2 | Outcome measures

Primary end point of composite poor outcomes was evaluated and defined as either having early mortality or comorbid events during ICU stay following cardiac surgery (renal failure, reoperation for bleeding, sternal wound infection, stroke, pneumonia, prolonged ICU LOS, and prolonged postoperative mechanical ventilation.) Mortality data was determined from evaluating the EMR or searching the Social Security Death Registry. Early mortality was defined as in-hospital death or death within 90 days of hospital discharge. Determination of renal failure, reoperation for bleeding, sternal wound infection, stroke, and pneumonia were retrieved from the patient clinical chart. ICU LOS was calculated using ICU admission and discharge time stamps retrieved from the EMR system. Length of mechanical ventilation was determined from the time of ICU admission to the time of the extubation when ventilator measurements were discontinued in the medical record. The 75th percentile of ICU LOS was used to establish the cutoff value for defining prolonged ICU LOS. Prolonged mechanical ventilation was defined as ventilation ≥5 days based on previous research that had been published for the same patient population.[5] In addition, due to the small incidence of complication related outcomes, which includes renal failure, reoperation for bleeding, sternal wound infection, stroke and pneumonia, a second composite outcome variable, complication related outcome variable, defined as the occurrence of any of these morbidity outcomes was also assessed in the analysis.

2.3 | maxVIS score definition

The postoperative temporal characteristics of VIS dose values up to 96 hours were examined. The maximum VIS values at each 24-hours time interval during the first 48 hours after surgery were then calculated. The VIS numerical ranges were converted to integer score based on the temporal characteristics of VIS at each 24-hours period. Patients were assigned a maxVIS score based on the highest VIS score achieved during either the first or subsequent 24-hours period (Table 1).

TABLE 1 MaxVIS score classification

MaxVIS score	Maximum VIS in 0-24 h	Maximum VIS in 24-48 h
1	<10	<5
2	10-14	5-9
3	15-19	10-14
4	20-24	15-19
5	≥25	≥20

Abbreviation: VIS, vasoactive inotrope support.

2.4 | Statistical analysis

Baseline characteristics and clinical outcomes were described using medians with 25th and 75th percentiles for continuous variables, and frequencies and proportions for categorical variables. The area under the curve (AUC) with 95% confidence interval (CI) was calculated after adjusting for significant confounding variables in order to assess the performance of maxVIS model in discriminating poor clinical outcomes and comparing with standard scoring systems. The Hosmer-Lemeshow (H-L) test was used to assess the goodness of fit of the model for maxVIS alone. Chi-square probability and R value was determined to compare scoring systems and demonstrate strength of correlation with poor outcome. The observed and predicted log odds plots were created to ascertain whether the risk model predicted clinical outcomes correctly for VIS index. The odds ratio (OR) with 95% CIs was calculated after adjusting for significant covariates for each primary outcome variables to assess the association between adverse events and VIS values. Potential confounding variables, including year of surgery, age, RACHS-1 score, prior sternotomy status, aortic cross clamp time, circulatory arrest times, BMI, and diabetes status were assessed in the model. The year of surgery was included to adjust for changes in surgical procedures and patient care over time that may have affected mortality rate over the past 10 years. A backward elimination strategy with a statistical significance level of 5% was used to exclude statistically insignificant confounding covariates from the model. The analysis was performed on both composite and each individual outcome variable. Analysis of variance was performed to compare APACHE II, SOFA, and maxVIS scoring systems in the two outcome groups. All statistical tests were two-sided with α level set at 0.05 for statistical significance.

TABLE 2 Baseline patients characteristics

Variable	*n* (*n* = 247)
Age at surgery (y)	33 (18-83)
18-30	94 (38.1%)
31-50	106 (42.9%)
51-65	35 (14.2%)
≥65	12 (4.9%)
BMI (kg/m^2)	25 (15-44)
Underweight (<18.5)	15 (6.1%)
Normal (18.5-<25)	104 (42.1%)
Overweight (25-<30)	83 (33.6%)
Obese (≥30)	45 (18.2%)
Gender	
Male	102 (41.3%)
Female	145 (58.7%)
Ejection fraction (%)	55.36 ± 10.79
Hypertension	35 (14.1%)
Smoking	35 (14.1%)
Dyslipidemia	34 (13.7%)
Stroke	25 (10.1%)
Infective endocarditis	20 (8.1%)
Diabetes type 2	15 (6.1%)
Coronary artery disease	12 (4.8%)
Renal failure	5 (2.0%)
Prior sternotomies	
1	137 (55.5%)
2	71 (28.7%)
3	24 (9.7%)
4	13 (5.3%)
5	2 (0.8%)
RACHS-1 category	
1-3	229 (92.7%)
4-6	18 (7.3%)

Abbreviations: BMI, body mass index; RACHS-1, risk adjustment for congenital heart surgery.
Values expressed as number (*n*) and percentage, median (range), or mean ± 2SD.

3 | RESULTS

Between November 2002 and 2013, 1040 ACHD patients age 18 years and older were admitted to the CICU following cardiac surgery of whom 243 had complete demographic, clinical, and inotropic-vasoactive data available. Four patients had two separate admissions with admission dates ranging from 88 days to 1512 days apart. Each admission for these four patients was treated as an independent event and specific statistical technique was applied to adjust for intercorrelation within subjects. The demographic, baseline clinical, and operative data are shown in Tables 2 and 3. SOFA scores were calculated for all but 110 patients who had no bilirubin values measured prior to surgery. The day 1 SOFA score was 9.36 ± 2.54 and the APACHE II score was 17.52 ± 15.46.

The patient outcome results are summarized in Table 4. Sixty-two patients experienced composite adverse event (25%), including eight deaths within 90 days of hospital discharge (3%). Thirty-eight patients (15%) had at least one complication related morbidity event (renal failure, reoperation for bleeding, sternal wound infection,

TABLE 3 Operative and postoperative data

Variable	*n* (*n* = 247)
Cardiopulmonary bypass time (min)	108.31 ± 54.54
Aortic cross-clamp time (min)	52.76 ± 45.58
ICU LOS (d)	2 (1-77)
APACHE II score	17.52 ± 15.46[a]
Day 1 SOFA score	9.36 ± 2.54[b] *n* = 181
Length of mechanical ventilation (d)	1 (0-77)
Postoperative vasoactive medication utilization	
Milrinone	255 (100%)
Epinephrine	237 (92.9%)
Dopamine	39 (15.3%)
Vasopressin	35 (13.7%)
Operations	
Pulmonary valve repair/replacement	37%
Tricuspid valve repair/replacement	19%
Aortic valve repair/replacement	14%
Mitral valve repair/replacement	11%
Other	8%
Aortic aneurysm	5%
Atrial septal defect	4%
Ventricular septal defect	2%

Abbreviations: APACHE II, acute physiology and chronic health evaluation II score; ICU LOS, intensive care unit length of stay; SOFA, and sequential organ failure assessment score.
Values expressed as number (*n*) and percentage, median (range) or mean ± 2SD.
[a]*n* = 198.
[b]*n* = 181.

TABLE 4 Summary of poor clinical outcome

Clinical outcome variable	*n*
Combined poor clinical outcome	
Composite mortality and morbidity	62 (25%)
Complication-related morbidity[a]	38 (15%)
Primary outcome	
Mortality[b]	8 (3%)
Secondary outcome	
Prolonged ICU LOS	50 (20%)
Prolonged mechanical ventilation	22 (9%)
Pneumonia	21 (9%)
Renal failure	18 (7%)
Reoperation for bleeding	8 (3%)
Sternal wound infection	7 (3%)
Stroke	5 (2%)

Abbreviations: ICU, intensive care unit; LOS, length of stay.
Values expressed as total number (*n*) plus percentage.
[a]Complication-related morbidity includes any of the following morbidity events: renal failure, reoperation for bleeding, sternal wound infection, stroke, and pneumonia.
[b]Mortality is in-hospital death or death within 90 days of hospital discharge.

stroke, or pneumonia). All eight patients with early mortality also experienced at least one morbidity event. None of the potential confounding factors, RACHS categories with dichotomized values of 1-3 and 4-6, year of surgery, age group, prior sternotomy status, aortic cross clamp time, circulatory arrest times, BMI, and diabetes status were found significantly correlated with either the composite adverse event or each individual outcome variable.

3.1 | Vasoactive administration

Epinephrine was the most widely used vasopressor on ACHD patients (79.8%), and milrinone was the second most widely used vasopressor (70.4%). Only five patients (2%) received dobutamine, and seven patients (2.8%) received norepinephrine during the first 96-hours postoperative period.

3.2 | VIS characteristics

The pairwise comparisons of maxVIS values between the first and the second 12 hours within each 24-hours period are shown in Table 5. The maxVIS values were significant difference between the first 12-hours and the second 12-hours interval during the first 24-hours postoperative period (estimated marginal mean difference 1.8; $P = 0.0094$). No significant difference was found between the two 12-hours intervals during the subsequent 24-96 hours period. Since 100% patients received vasoactive support during the first 24-hours postoperative period, and the maximum VIS values during this period was used in the VIS prediction model, we concluded that it was appropriate to use a 24-hours interval in calculating VIS values without losing any significant clinical information.

The temporal characteristics of VIS values during the first 96-hours postoperative period of all patients by poor clinical outcome were presented in Figure 1. Overall VIS values are higher for those patients with at least one poor clinical outcome than those patients without any poor outcome. For both outcome groups, VIS values are higher during the first 24 hours than the subsequent postoperative period for patients with and without any poor outcome, and the values stay relatively stable after 48 hours. Moreover, the amount of vasoactive support ACHD patients received had much shorter duration on vasoactive support if they did not experience any poor outcome. After 48 hours, only 12% of those patients who did not have any poor outcome were still requiring vasoactive support, comparing to 79% patients who did experience at least one poor outcome.

3.3 | maxVIS model performance—discrimination and calibration

The performance characteristics of maxVIS prediction model for ACHD patients are shown in Table 6. The H-L test result and ROC area

suggest maxVIS has good calibration and reasonable discrimination consistently for both the composite outcome and each individual morbidity outcome. For the composite poor outcome, the AUC was 0.819 (95% CI: 0.755 to 0.883), and there is close agreement between predicted and observed poor outcome rate (H-L test, $P = 0.205$). Several complication-related events that included reoperation for bleeding (3%), sternal wound infection, and stroke (3%), had relatively wide 95% CI for the AUC. This finding along with nonsignificant P value was likely due to the small number of incidences of each event.

Mortality has the highest AUC value with narrow 95% CI (AUC = 0.916, 95% CI: 0.856 to 0.976). All eight adult patients who experienced either in-hospital death or death within 90 days of hospital discharge have maxVIS value ≥3.

TABLE 5 MaxVIS value pairwise comparison—adult CHD patients

Time interval	LS mean[a] (95% CI)	Mean difference	*P* value
0-24 h			
0-12 h	14.3 (12.9, 15.7)	1.8	0.0094
12-24 h	12.5 (11.1, 13.9)		
24-48 h			
24-36 h	10.1 (8.6, 11.5)	1.9	0.3606
36-48 h	8.2 (6.7, 9.7)		
48-72 h			
48-60 h	8.3 (6.8, 9.9)	0.9	0.9621
60-72 h	7.4 (5.8, 9.0)		
72-96 h			
72-84 h	6.5 (4.9, 8.2)	0.5	0.9889
84-96 h	6.0 (4.3, 7.7)		

Abbreviation: CI, confidence interval.
[a]LS mean, least square mean, is the estimated marginal mean value of maxVIS after controlling for poor clinical outcome.

3.4 | VIS index model risk prediction performance

Figure 2 presents the predicted risk of a composite poor clinical outcome using the VIS index. Overall the predicted risk of having a poor clinical outcome is very consistent with the observed risk for the complication related morbidity, prolonged ICU LOS, and prolonged mechanical support.

3.5 | maxVIS model strength of association with risk

Based on the sensitivity and specificity of maxVIS score shown in Table 7, maxVIS value of 3 was selected as the optimal cutoff value with a sensitivity of 72.6% and a specificity of 84.3% in predicting a poor clinical outcome. The outcomes of patients with maxVIS ≥3 (high maxVIS) were combined and compared with those patients with maxVIS <3 (high maxVIS).

The results of strength of association for selected outcomes are presented in Table 8. The association of maxVIS with early mortality, renal failure, reoperation for bleeding, sternal wound infection, stroke, and pneumonia was not estimated due to the small incidence of these outcomes. Overall high VIS (maxVIS ≥ 3) was strongly associated with adverse events (OR: 14.2; 95% CI: 7.2-28.2; $P < 0.0001$). Patients in the high VIS category were also more likely than those in the low VIS category to experience prolonged ICU LOS (OR: 19.2; 95% CI: 8.7-42.1; $P < 0.0001$), prolonged mechanical ventilation (OR: 13.6; 95% CI: 4.4-41.8; $P < 0.0001$) and complication related morbidity (OR: 7.3; 95% CI: 3.4-15.5; $P < 0.0001$). Table 9 demonstrates the comparison of outcome and performance characteristics of scoring systems for APACHE, SOFA, and maxVIS. Significant score increases were demonstrated in the poor outcome group ($P < 0.01$) and receiver operating curves demonstrated superior correlation with poor outcome of maxVIS compared to APACHE and SOFA.

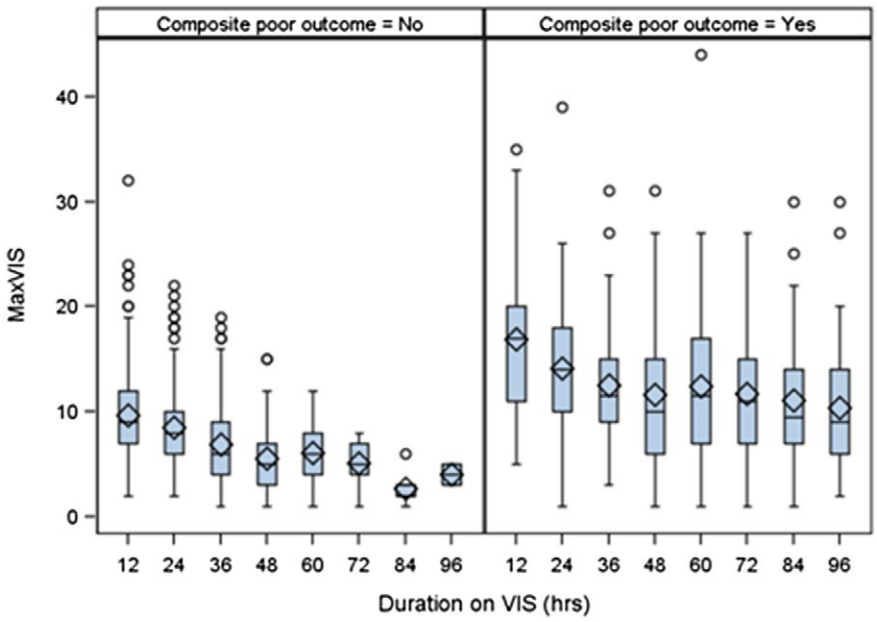

FIGURE 1 Box plot of maxVIS during the first 96-hours postoperative period by outcome—Adult CHD patients by outcome. The graphical presentation of VIS temporal pattern shows that maxVIS values are higher during the first 24 hours than the subsequent postoperative period for patients with and without any poor outcome, and the values stay relatively stable after 24 hours

TABLE 6 Performance characteristics of maxVIS

Clinical outcome variable	AUC	95% CI	H-L *P*-value
Combined clinical outcome			
Composite poor outcome	0.819	(0.755, 0.883)	0.205
Complication-related morbidity	0.761	(0.672, 0.850)	0.793
Primary outcome			
Mortality[a]	0.916	(0.856, 0.976)	0.529
Secondary outcome			
Prolonged ICU LOS	0.851	(0.790, 0.912)	0.064
Prolonged mechanical ventilation	0.835	(0.747, 0.924)	0.435
Renal failure	0.856	(0.790, 0.922)	0.133
Reoperation for bleeding	0.694	(0.462, 0.925)	0.175
Sternal wound infection	0.642	(0.488, 0.797)	0.088
Stroke	0.793	(0.641, 0.944)	0.552
Pneumonia	0.718	(0.595, 0.840)	0.830

Abbreviations: AUC, area under the curve; CI, confidence interval; H-L, Hosmer-Lemeshow test; ICU, intensive care unit; LOS, length of stay.
[a]Mortality is in-hospital death or death within 90 days of hospital discharge.

4 | DISCUSSION

This is the first study to evaluate the association between postoperative vasopressor support and clinical outcomes for the ACHD surgical patient. High dose vasopressor support following adult congenital cardiac surgery is highly predictive of poor outcome. The maxVIS score quantifies the maximum amount of vasopressor/inotrope support required by a patient during the first 96 postoperative hours. Our findings validate the maxVIS as a sensitive predictor of postoperative morbidity and mortality that can be used for risk stratification for the ACHD surgical population. We propose a VIS index risk prediction tool (Figure 3), that can be used to guide prognosis and management at any point in time in 96 hours postoperative ICU course. This simplified VIS index model outperforms the original maxVIS model for predicting early mortality and morbidity for ACHD patients. The VIS index strengthens the traditional inotrope score's ability to predict poor outcome by incorporating dose magnitude and duration of inotrope support into the equation and could be used as an illness severity score to lead to improved clinical care and guide therapeutic decision-making. MaxVIS may also have prognostic utility in counseling patients and families regarding their prognosis.

Currently, robust, well-validated risk prediction and stratification tools for ACHD surgery do not exist. Furthermore, pediatric CHD and adult non-CHD cardiac risk scores perform poorly when applied to the ACHD population. Our validation of the maxVIS for predicting poor outcome is an important step toward developing risk stratification tools that are specific to the unique challenges encountered

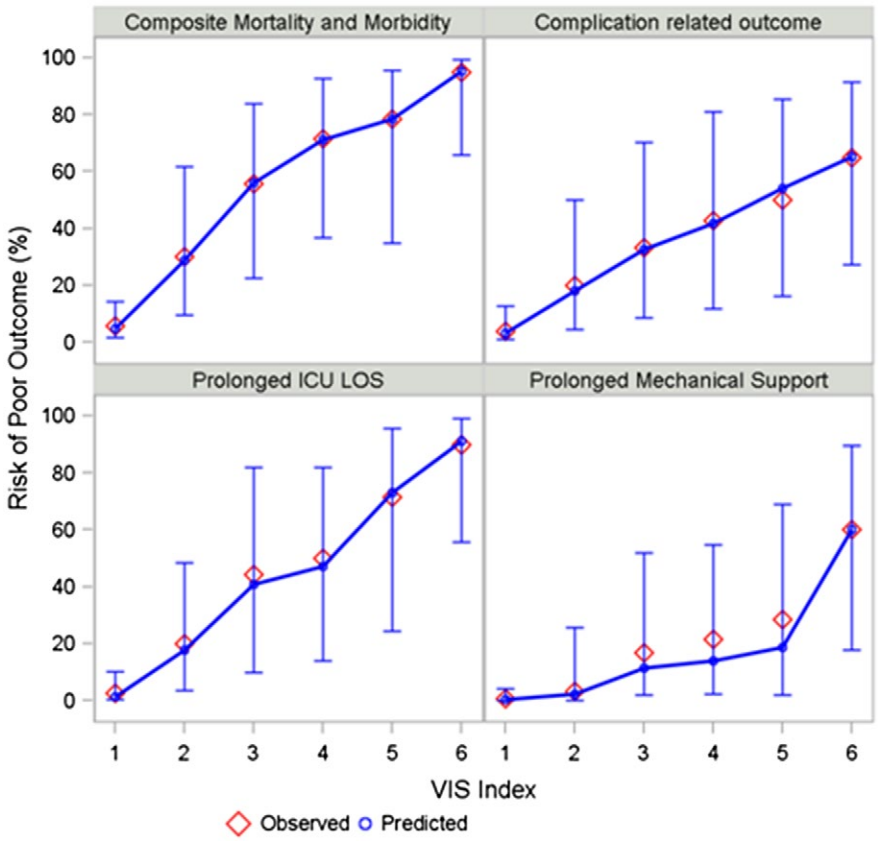

FIGURE 2 VIS index predicted risk of poor clinical outcome by variable. The relationship between the observed risk and the predicted risk based on the VIS index model is illustrated graphically. Overall the predicted risk of having a poor clinical outcome is very consistent with the observed risk for complication related morbidity, prolonged ICU LOS, and prolonged mechanical support

TABLE 7 Sensitivity and specificity of maxVIS in predicting poor clinical outcome

maxVIS	1	2	3	4	5
Sensitivity	100%	90.3%	72.6%	43.5%	21.0%
Specificity	0%	42.2%	84.3%	94.1%	99.5%

Abbreviation: VIS, vasoactive-inotropic score.

TABLE 8 Univariate analysis—maxVIS as a predictor of poor outcome

Clinical outcome variable	*n* (%)	OR	95% CI	*P*
Combined clinical outcome				
Composite poor outcome	62 (25.1%)	14.2	(7.2, 28.2)	<0.0001
Complication-related morbidity[a]	38 (15.4%)	7.3	(3.4, 15.5)	<0.0001
Primary outcome				
Mortality[b]	8 (3%)	N/A	N/A	N/A
Secondary outcome				
Prolonged ICU LOS	50 (20.2%)	19.2	(8.7, 42.1)	<0.0001
Prolonged mechanical ventilation	22 (8.9%)	13.6	(4.4, 41.8)	<0.001

Abbreviations: CI, confidence interval; ICU, intensive care unit; LOS, length of stay; OR, odds ratio.
[a]Complication-related morbidity includes any of the following morbidity events: renal failure, reoperation for bleeding, sternal wound infection, stroke, and pneumonia.
[b]Due to the small incidence of the event, odds ratio of mortality is not estimable.

TABLE 9 Scoring systems comparison—outcome and performance characteristics

Scoring system (0-24 h)	Poor clinical outcome: No (*n* = 185)	Poor clinical outcome: Yes (*n* = 62)	*P*
maxVIS	9.7 (4.53)	17.4 (7.72)	<0.001
APACHE II	12.1 (7.38)	22.1 (5.1)	<0.001
SOFA	7 (1-13)	11 (1-18)	<0.01
Composite poor outcome	AUC	*R*	*P*
maxVIS	0.819	0.541	<0.001
APACHE II	0.731	0.368	<0.001
SOFA	0.741	0.413	<0.001

Abbreviation: APACHE II, Acute Physiology and Chronic Health Evaluation II score; maxVIS, vasoactive-inotropic score; SOFA, Sequential Organ Failure Assessment score.
Values expressed as number (*n*) and percentage, median (range) or mean ± 2SD.

VIS index	Risk of Poor Outcome (%)	95% CI (%)
1	6	3 – 11
2	30	16 – 48
3	56	33 – 76
4	60	30 – 84
5	75	45 – 92
6	95	72 – 99

FIGURE 3 VIS Index Risk Prediction Tool. The VIS index risk model was consistent in predicting the risk of poor clinical outcomes for adult CHD patients. The color grids indicate the degree of risk with light green color indicating the lowest risk and maroon color indicating the highest risk of developing adverse outcomes following cardiac surgery

during the ACHD perioperative period. Scoring systems developed for the general cardiac surgical population can support prediction of anesthesia risk, surgical mortality, and even prolonged mechanical ventilation and hospital length of stay.[10,11,19] However, scoring systems like the European System for Cardiac Operative Risk Evaluation (Euro SCORE) were developed for coronary artery bypass patients, they have failed to adequately predict morbidity and mortality risk when applied to the ACHD patient.[20] The significant association between vasopressor requirements and poor outcome in the ACHD population is consistent with the findings of the original pediatric CHD VIS validation studies.[12,13] Since Wernovsky's conception of the inotrope score (IS) in 1995, vasopressor requirements following pediatric CHD surgery are commonly described with the IS or the newer version of this score, the VIS.[21] The VIS is simply the IS with the addition of milrinone, vasopressin, and norepinephrine to accommodate current clinical practice. The original pediatric VIS validation performed by M. Gaies et al was the first to demonstrate the highly significant association between the maximum vasopressor support required during the first 48 postoperative hours and poor outcome.[12] Three additional pediatric VIS validation studies have confirmed a consistent association between higher magnitude of vasopressor support and poor outcome.[4,13,22]

This is the first study to our knowledge to apply the pediatric VIS to the adult CHD population. Surprisingly few investigations have specifically evaluated the association between vasopressor support and risk for poor outcome after adult congenital cardiac surgery. A recent prospective study of 88 adult cardiac surgical patients included patients requiring surgery for CHD. All nonsurvivors required inotropes in this analysis, and patients who required more

than one inotrope had significantly longer hospital lengths of stay (linear regression, $P = 0.013$).[23] Vasopressor utilization has also been associated with a greater postoperative base deficit and increased ICU length of stay in the general cardiac surgical population.[24]

There are several limitations to our analysis that warrant consideration. First, our evaluation of the maxVIS is based on an ACHD patient population from a single institution. Therefore, even with the modest patient sample size, our results may not be representative or generalizable to all patient populations. Additionally, while we provide prognostication data on the role of VIS, there are no practical studies in the literature asserting the utility of VIS in improving patient outcomes. Utilization of our VIS index risk prediction tool could be used in such future study.

In conclusion, we report the first validation of the maxVIS score for predicting morbidity and mortality after cardiac surgery in the ACHD population. The maxVIS is a valid ACHD risk stratification tool that can facilitate early intervention that may improve outcome and assist with clinical decision making for ACHD patients after cardiac surgery.

AUTHOR CONTRIBUTIONS

Design of the study, data analysis/interpretation, statistics, drafting the article, critical revision of the article, and final approval of the article: JTP, SV, ACE.

Data analysis/interpretation, critical revision of the article, and final approval of the article: DOA, JK, KH, AWG, JAD, SSC.

REFERENCES

1. Warnes CA. The adult with congenital heart disease: born to be bad? *J Am Coll Cardiol*. 2005;46(1):1-8.
2. Moodie D. Adult congenital heart disease: past, present, and future. *Tex Heart Inst J*. 2011;38(6):705-706.
3. Aydin SI, Seiden HS, Blaufox AD, et al. Acute kidney injury after surgery for congenital heart disease. *Ann Thorac Surg*. 2012;94(5):1589-1595.
4. Butts RJ, Scheurer MA, Atz AM, et al. Comparison of maximum vasoactive inotropic score and low cardiac output syndrome as markers of early postoperative outcomes after neonatal cardiac surgery. *Pediatr Cardiol*. 2012;33(4):633-638.
5. Holst KA, Dearani JA, Burkhart HM, et al. Risk factors and early outcomes of multiple reoperations in adults with congenital heart disease. *Ann Thorac Surg*. 2011;92(1):122-130.
6. Somerville J. Management of adults with congenital heart disease: an increasing problem. *Annu Rev Med*. 1997;48:283-293.
7. Giamberti A, Chessa M, Abella R, et al. Morbidity and mortality risk factors in adults with congenital heart disease undergoing cardiac reoperations. *Ann Thorac Surg*. 2009;88(4):1284-1289.
8. John AS, Warnes CA. Clinical outcomes of adult survivors of pulmonary atresia with intact ventricular septum. *Int J Cardiol*. 2012;161(1):13-17.
9. Kirshbom PM, Myung RJ, Simsic JM, et al. One thousand repeat sternotomies for congenital cardiac surgery: risk factors for reentry injury. *Ann Thorac Surg*. 2009;88(1):158-161.
10. Dupuis JY, Wang F, Nathan H, Lam M, Grimes S, Bourke M. The cardiac anesthesia risk evaluation score: a clinically useful predictor of mortality and morbidity after cardiac surgery. *Anesthesiology*. 2001;94(2):194-204.
11. Tu JV, Jaglal SB, Naylor CD. Multicenter validation of a risk index for mortality, intensive care unit stay, and overall hospital length of stay after cardiac surgery. Steering committee of the provincial adult cardiac care network of Ontario. *Circulation*. 1995;91(3):677-684.
12. Gaies MG, Gurney JG, Yen AH, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. *Pediatr Crit Care Med*. 2010;11(2):234-238.
13. Davidson J, Tong S, Hancock H, Hauck A, da Cruz E, Kaufman J. Prospective validation of the vasoactive-inotropic score and correlation to short-term outcomes in neonates and infants after cardiothoracic surgery. *Intensive Care Med*. 2012;38(7):1184-1190.
14. Herasevich V, Pickering BW, Dong Y, Peters SG, Gajic O. Informatics infrastructure for syndrome surveillance, decision support, reporting, and modeling of critical illness. *Mayo Clin Proc*. 2010;85(3):247-254.
15. Jenkins KJ, Gauvreau K, Newburger JW, Spray TL, Moller JH, Iezzoni LI. Consensus-based method for risk adjustment for surgery for congenital heart disease. *J Thorac Cardiovasc Surg*. 2002;123(1):110-118.
16. Jenkins KJ, Gauvreau K. Center-specific differences in mortality: preliminary analyses using the risk adjustment in congenital heart surgery (rachs-1) method. *J Thorac Cardiovasc Surg*. 2002;124(1):97-104.
17. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. Apache ii: a severity of disease classification system. *Crit Care Med*. 1985;13(10):818-829.
18. Vincent JL, Moreno R, Takala J, et al. The sofa (sepsis-related organ failure assessment) score to describe organ dysfunction/failure. On behalf of the working group on sepsis-related problems of the European Society of Intensive Care Medicine. *Intensive Care Med*. 1996;22(7):707-710.
19. Doerr F, Badreldin AM, Heldwein MB, et al. A comparative study of four intensive care outcome prediction models in cardiac surgery patients. *J Cardiothorac Surg*. 2011;6:21.
20. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (euroscore). *Eur J Cardiothorac Surg*. 1999;16(1):9-13.
21. Wernovsky G, Wypij D, Jonas RA, et al. Postoperative course and hemodynamic profile after the arterial switch operation in neonates and infants. A comparison of low-flow cardiopulmonary bypass and circulatory arrest. *Circulation*. 1995;92(8):2226-2235.
22. Crow SS, Robinson JA, Burkhart HM, Dearani JA, Golden AW. Duration and magnitude of vasopressor support predicts poor outcome after infant cardiac operations. *Ann Thorac Surg*. 2014;98(2):655-661.
23. Bhukal I, Solanki SL, Ramaswamy S, Yaddanapudi LN, Jain A, Kumar P. Perioperative predictors of morbidity and mortality following cardiac surgery under cardiopulmonary bypass. *Saudi J Anaesth*. 2012;6(3):242-247.
24. Maillet JM, Le Besnerais P, Cantoni M, et al. Frequency, risk factors, and outcome of hyperlactatemia after cardiac surgery. *Chest*. 2003;123(5):1361-1366.

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