North Clin Istanb 2020;7(4):329–334
doi: 10.14744/nci.2020.77775

Original Article PEDIATRICS

The effects of Vasoactive-Ventilation-Renal score on pediatric heart surgery

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ABSTRACT

OBJECTIVE: The effects of Vasoactive-Ventilation-Renal (VVR) score on the evaluation of pediatric heart surgery results were investigated in this study.

METHODS: This retrospective study included children younger than 18 years of age who were operated for congenital heart disease between was July 1st- December 31st 2018. Patients who needed ECMO support at the first postoperative 72 hours were not included in the study group. The postoperative initial, 24th and 48th-hour Vasoactive-Inotrope Score (VIS) and VVR scores of all patients were calculated in the intensive care unit (ICU). The effects of these scores on lengthy ICU duration (PCILOS, duration more than the upper 25th percentile) and to the hospital mortality (before 30 days) were evaluated.

RESULTS: There were 340 patients in this study. The median age was 12 months (1 day-18 years), and the median weight was 7 kg (2.5 -82 kg). 18% of the patients had single ventricle physiology. Total correction was performed in 88% of the patients. Median RACHS 1 score was 2 (1–6). PCILOS was>112 hours and total mortality was 4%. The 0th hour VVR ICU c index=0.73 (CI: 0.70–0.77), mortality c index=0.77 (CI: 0.69–0.85). VVR at 24th hour ICU c index=0.75 (CI: 0.71–0.79), mortality c index=0.86 (CI: 0.81–0.91). VVR at 48th-hour ICU c index=0.87 (CI: 0.82–0.92), mortality c index=0.92 (CI: 0.87–0.97). The VVR score at 48th-hour was a strong indicator for the prediction of both LICU duration (odds ratio [OR]: –1.44; p=0.001) and hospital mortality (OR: –1.28; p=0.001).

CONCLUSION: The postoperative VVR score can be a strong determinant for the prediction of early clinical results in congenital heart disease patients, which were considerably a heterogeneous group.

Keywords: Child; congenital heart surgery; mortality; vasoactive -ventilation- renal score

Cite this article as: *Ozturk E, Tanidir IC, Gunes M, Genc SB, Yildiz O, Onan IS, et al. The effects of Vasoactive-Ventilation-Renal score on pediatric heart surgery. North Clin Istanb 2020;7(4):329–334.*

Congenital heart diseases are a disease group that is composed of many different pathologies. These patients may be operated for total correction or palliative surgeries sometime in their lives. The age, body weight, preoperative clinical status, associated comorbidities of the patients and the need for cardiopulmonary bypass may directly affect the operation results and differences in mortality rates, ICU duration, and duration of hospitalization may appear correspondingly [1, 2].

There are different scoring systems for objective evaluation of morbidity and mortality of operated patients who are a member of heterogeneous and complex con-

Received: October 21, 2019 *Accepted:* January 14, 2020 *Online:* February 07, 2020

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genital heart disease group during their pediatric ICU stay [3–5]. The basic desired features of all these scoring systems are to build a reliable system that is available in common and decrease ICU costs, the efficient use of the sources, to be guiding in clinical decisions and practices and allow objective evaluation. However, the ideal scoring system is still a subject of debate [6].

RACHS-1 (Risk Adjustment in Congenital Heart Surgery), Aristotle Basic Complexity Score (ABC), Aristotle Comprehensive Complexity Score (ACC), are commonly used scoring systems mostly based on the difficulty of the surgery but do not contain adequate data about the clinical status at the ICU [7, 8]. Inotrope score (IS) and vasoactive-inotropic score (VIS) were the scoring systems mostly used in the evaluation of the outcome by the clinical status data in pediatric ICU, but their prediction was found modest [4, 6]. Lately, a postoperatively calculated vasoactive-ventilation-renal (VVR) score was claimed to be used as a strong predictor [9, 10].

Recently, the VVR score was started to be used in pediatric cardiac ICU postoperatively in our cardiac center. In this study, the effects of VVR score on the evaluation of pediatric heart surgery outcomes were investigated.

MATERIALS AND METHODS

This study was conducted in patients younger than 18 years who underwent CHS due to complex congenital heart defects between 1 July 2018 and 31 December 2018.

Cases requiring ECMO support within the first 72 hours, permanent pacemaker implantations, and those that were transferred to another unit for any reason were excluded from this study. This retrospective study was approved by the institutional ethics committee (ethical approval number: 2019/60) and was conducted in accordance with the principles of the Declaration of Helsinki.

The preoperative demographic data (gender, weight, and additional genetic syndromes), anatomical diagnosis, surgical data, clinical follow-up, and postoperative intensive care unit reports of the study group were evaluated. Preoperative, postoperative 24-hour and postoperative 48-hour blood urea and creatinin levels were recorded. Acute kidney injury (AKI) was classified using the AKI network staging system. Postoperative data of arterial blood gas parameters, including pH, partial pressure of carbon dioxide ($PaCO_2$), and the partial pressure of oxygen (PaO_2) at admission in PICU, 24 h and 48 h postoperatively, along with the corresponding ventilator settings, including peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), mean airway pressure, and respiratory rate (RR) in the volume-controlled mode of ventilation, were collected.

Doses of inotropic and vasopressor agents were also recorded at the time of each blood gas analysis. Postoperative serum creatinine was recorded at admission, 24 h, and 48 h postoperatively. VIS and VVR scores were calculated for all patients at the study time point. VIS was calculated using the formula; VIS=Dopamine dose (μg/kg/min) + Dobutamine dose (μg/kg/min) +100 × Epinephrine dose (μg/kg/min) +10 × Milrinone dose (μg/kg/min) +10000 × Vasopressin dose (μg/kg/min) +100 × Norepinephrine dose (μg/kg/min) [4]. Ventilation index (VI) was calculated using the formula: VI=RR × (PIP−PEEP) × $PaCO_2$/1000; Δ Cr was calculated by subtracting serum creatinine (in mg/dl) at the time of each measurement with preoperative serum creatinine and VVR using formula: VVR=VIS + VI + (Δ Cr × 10) [6]. For patients whose postoperative serum creatinine values were less than preoperative values, Δ Cr was taken as 0. For patients not requiring ventilator support at the time of measurement, VI was taken as 0.

Risk Adjustment in Congenital Heart Surgery (RACHS-1) [7], and Aristotle Comprehensive Complexity (ACC) score [8] were used to classify the procedures. The RACHS-1 system scale ranges from one to six. The ACC score level between one and four (level 1 [1.5 to 5.9]; level 2 [6.0 to 7.9]; level 3 [8.0 to 9.9] and level 4 [10.0 to 15.0]). The need for re-exploration for any reason, and rhythm abnormality within the first 72 h postsurgery was also recorded.

In this study, our two primary outcomes were operative mortality and pediatric cardiac intensive care unit length of stay (PCILOS). Operative mortality included all the deaths that occurred during the hospital stay when the operation was performed, and the deaths occurred after discharge within 30 days of the procedure. For further analysis of PCILOS, data were dichotomized as the upper (worst) 25th percentile versus lower (best) 75th percentile. PCILOS in the upper 25th percentile was considered prolonged pediatric cardiac intensive care unit length of stay.

Statistical Analysis

Data were analyzed using SPSS for Windows version 15.0 software (SPSS Inc., Chicago, IL, USA). Median with range was used to describe continuous data, whereas absolute count with percentage was used for categorical

data. Data were analyzed for correlation between the scores and outcomes using Spearman's rho.

Univariate analysis was performed for demographic and clinical characteristics of the patients to predict our two primary outcomes using Mann–Whitney U-test, Chi-square test, or Fisher's exact test as appropriate for individual variables. Significance variables were included in the multivariate logistic regression model, and the odds ratio (OR) was calculated. P<0.05 was considered significant.

Analysis of the discriminatory ability of VIS and VVR score (at 0, 24, and 48 h) methods were performed using the C statistic comparison with receiver operating characteristic (ROC) curves of the two methods. The best cut-off value for the VVR score was derived, having maximum accuracy and minimal weighted error.

RESULTS

This study included 340 cases that met the inclusion criteria. The median age of the patients was 12 months (1 day–18 years) and the median weight was 7 kg (2.5–82 kg). The most common diagnoses were ventricular septal defect (21.5%) and Fallot tetralogy (19%). Eighteen percent of the patients had single ventricular physiology. The median RACHS-1 score was 2 (1–6). The main characteristics of the cases are shown in Table 1.

Median ICU stay was 72 hours (16 hours–90 days). Prolonged ICU stay was found to be >112 hours. Total mortality was 4% (n=14).

The median VIS was 10 (0–40) and the median VVR score was 15 (0–60) at the beginning. At 24th hour, the median VIS was 5 (0–40) and the median VVR score was 10 (0–45). At 48th-hour, the median VIS was 0 (0–20) and the median VVR score was 2 (0–25). The VVR score was higher at each measurement point compared to the corresponding VIS. In the correlation analysis, the VVR score predicted the endpoints better than the VIS at each measurement point.

In particular, the 0 hour VVR prolonged ICU stay c index=0.73 (CI: 0.70–0.77), and the mortality c index=0.77 (CI: 0.69–0.85). 24 hour VVR prolonged ICU stay c index=0.75 (CI: 0.71–0.79), and the mortality c index=0.86 (CI: 0.81–0.91). 48th-hour VVR prolonged ICU stay c index=0.87 (CI: 0.82–0.92), and the mortality c index=0.92 (CI: 0.87–0.97). VVR 48th-hour score was the most powerful to show the mortality (0.92) and morbidity (0.87) (Table 2).

Table 1. Demographic characteristics of the patients undergoing cardiovascular surgery

Characteristics	n
Age, (month)	12 (0.01–216)
Male (%)	52
Weight, (kg)	7 (2.5–82)
Genetic syndrome	9.4
Surgery type	
Corrective	88
Palliation	12
Congenital heart disease	
Double ventricle	82
Single ventricle	18
RACHS-1 score	
<4	84.8
≥4	15.2
The Aristotle Score	
Level 1 1.5–5.9	10.0
Level 2 6.0–7.9	28.5
Level 3 8.0–9.9	25.7
Level 4 10.0–15	35.8
CPB (yes)	90
CPB time, (minute)	70 (0–515)

Values are median (range) or n (%). RACHS: Risk adjustment in congenital heart surgery; CPB: Cardiopulmonary bypass.

The results of the evaluation of the factors affecting prolonged intensive care unit stay are shown in Table 3. When the multivariate regression analysis of the factors with p<0.05 was done, age OR 0.8 (CI 95% 0.72–0.88 p=0.011), RACHS-1 score OR 2.1 (CI 95% 1.3–3.4 p=0.04), ACC level OR 0.6 (CI 95%) 0.4–0.9 p=0.02), the presence of postoperative arrhythmia OR 4.5 (CI 95% 2.4–6.6 p=0.001), and 48th-hour VVR score OR 1.44 (CI 95% 1.2–1.6 p=0.001) were found to be independent risk factors.

The results of the evaluation of the factors affecting mortality are shown in Table 4. When the multivariate regression analysis of factors with p<0.05 was done, RACHS-1 score>4 OR 4.5 (CI 95% 2–12) p=0.012, ACC level>3 OR 2.8 (CI 95% 0.8–9) p=0.02, AKI>2 OR 3.1 (CI 95% 1–9) p=0.03 and 48th-hour VVR score OR 1.28 (CI 95% 1.1–1.48 p=0.001) were found as independent risk factor.

VVR score at 48 h was further dichotomized in high and low to simplify its interpretation.

Table 2. Results regarding area under the ROC curve between the methods concerning the mortality and PCILOS outcomes

VVR score	Mortality*			PCILOS&		
	Spearman	Area under ROC curve	CI 95%	Spearman	Area under ROC curve	CI 95%
Admission	0.16	0.770	0.690–0.850	0.42	0.731	0.706–0.770
24th hour	0.24	0.860	0.810–0.910	0.55	0.750	0.710–0.790
48th hour	0.43	0.920	0.870–0.970	0.70	0.870	0.820–0.920

*: No significant difference was found between 24 and 48 h VVR (p>0.05) in predicting mortality, whereas both 24 (<0.05) and 48 h VVR (p=0.001) were significantly better than 0 h VVR; &: There is no difference between the groups when the groups are compared with each other (p>0.05). ROC: Receiver operating characteristic; PCILOS: Pediatric cardiac intensive care unit length of stay; VVR: Vasoactive-ventilation-renal; CI: Confidence interval.

Table 3. Factors affecting prolonged intensive care unit stay

Variables	pICU (+) n=71	pICU (-) n=269	p
Age/month	48.7±41.0	21.8±35.6	**0.003**
Sex/male	36	134	NS
Syndrome	20	12	**0.004**
RACHS ≥4	26	32	**0.001**
ACC level ≥3	37	61	**0.001**
AKI ≥2	16	21	**0.001**
Arrhytmia	22	10	**0.002**
VVR 48th hour	**12.6±9.3**	**2.4±3.5**	**0.001**

RACHS: Risk adjustment in congenital heart surgery; ACC: Aristotle comprehensive complexity score; AKI: Acute kidney injury; VVR: Vasoactive-ventilation-renal.

Table 4. Factors affecting mortality

Variables	Mortality (+) n=14	Mortality (-) n=326	p
Age/month	18±25.1	44±48.3	0.002
Sex/male	8	163	NS
Syndrome	5	27	NS
RACHS ≥4	9	56	0.001
ACC level ≥3	7	96	0.03
AKI ≥2	7	31	0.01
Arrhytmia	7	34	0.01
VVR 48th hour	**22.4±10.5**	**4.5±6.5**	**0.001**

RACHS: Risk adjustment in congenital heart surgery; ACC: Aristotle comprehensive complexity score; AKI: Acute kidney injury; VVR: Vasoactive-ventilation-renal.

When prolonged ICU stay cut-off was taken 6; the 48th-hour VVR score sensitivity was 82%, specificity was 78%. When hospital-mortality cut-off was taken 13, the 48-hour VVR score sensitivity was 91%, specificity was 87%.

DISCUSSION

In this study, the effects of VVR score on mortality and prolonged intensive care unit stay of pediatric patients with congenital heart disease were evaluated. We observed that the VVR score on the 48th-hour could strongly predict mortality and prolonged intensive care stay.

Congenital heart diseases are quite heterogeneous, including subgroups, such as cyanotic and acyanotic heart diseases. Mortality and morbidity rates may vary depending on the pathology and type of operation. To evaluate these rates and to ensure standardization of the intensive care unit, different scoring systems are used [7, 8]. Recently, it is stated that the hemodynamic evaluation of the heart is not sufficient for postoperative scoring systems and evaluating the other organ systems would be beneficial [6, 9, 11].

The VVR scoring system, which provides a combined evaluation of heart, lung and kidney functions were proposed by Miletic et al. [6]. They suggested that the VVR score is a powerful method for predicting cardiac surgery results in their study, including 222 congenital heart disease patients without residual mixing lesion and single ventricular physiology [6].

Subsequently, in another study involving patients with extremely complex diseases, such as patients with hypoplastic left heart syndrome undergoing the Norwood procedure, heterotaxy lesions, and patients with Fontan circulation requiring revision, they found that VVR score was much stronger than the initial studies

in predicting mortality and morbidity [10]. Alam et al. [9] stated that VVR was very useful in evaluating the results of congenital heart surgery based on a larger study, including 1097 patients, excluding patients admitted to ECMO. Similar to the studies of Alam and Miletic, we observed that the VVR score could strongly predict prolonged ICU stay and hospital mortality.

Approximately 25% of the patients who undergo cardiac surgery for palliation or correction develop low cardiac output syndrome. Patients with low cardiac output are at risk of mortality. Several strategies are being tried to reduce the potential threat of low cardiac output and to manage it appropriately. As the most important part of these strategies, different inotropic and vasoactive substances are routinely used after cardiac surgery [4, 5]. To assess the outcome of these inotropes, Gaies et al. [4] developed the vasoactive-inotropic score (VIS). In their population of infants undergoing cardiac surgery with cardiopulmonary bypass (CPB), higher maximum VIS in the first 48 hours after the operation was associated with increased odds of poor short term outcomes. Davidson et al. [12] suggested that the VIS score may be an independent risk factor for predicting clinical outcomes. However, it is a significant disadvantage that the percentage of prediction is low in hemodynamically stable patients with other organ system disorders that may affect mortality. On the other hand, Miletic demonstrated that VVR was more powerful than the VIS score in predicting the effects of kidney and lung function on outcomes for hemodynamically stable patients [6].

Alam et al. [9] found that median VVR scores were higher than concurrent median VIS scores. They found that VVR was significantly better than VIS in predicting clinical outcomes at all times. In their studies with 164 cases, Sherer et al. [3] reported that VVR predicted prolonged intensive care stay better than lactate and VIS values in the early postoperative period. Parameters significantly contribute to the postoperative results of patients.

In our study, the prediction rate of VVR was constantly found to be higher than VIS. This result proved the significant contribution of ventilation and renal parameters to the postoperative results of the patients. In addition to the VVR score, we also evaluated other factors affecting mortality and prolonged ICU stay. RACHS-1 score>4, ACC level>3 and AKI>2 were found to be effective factors on mortality, whereas RACHS-1 score>4, ACC level>3 and presence of postoperative arrhythmia were found to be effective factors prolonged ICU stay. These results were similar to the results reported previously [9, 13].

The VVR score is a bedside method and may be more useful than the new experimental biomarkers because of its low cost. However, the biggest disadvantage is that VVR is not verified with complex measurement methods, such as logistic organ dysfunction score, pediatric risk of mortality III score, and pediatric index of mortality II score [14, 15].

Limitations

The main limitation of this study is that this study reflects our clinical experience involving a limited number of patients from a single center. In addition, the inotropic use and mechanical ventilator support may show variation in daily practice depending on the absence of protocol.

In conclusion, although its limitations VVR score measurements, which can be easily calculated postoperatively in congenital heart diseases, maybe a strong predictor of clinical outcomes at an early time.

Ethics Committee Approval: This retrospective study was approved by the institutional ethics committee (ethical approval number: 2019/60) and was conducted in accordance with the principles of the Declaration of Helsinki.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions: Concept – EO, ICT, AG; Design – EO, ICT, AG; Supervision – EO, ICT, ISO, SH; Fundings – OY, ISO, SBG; Materials – OY, SBG, MG, ISO; Data collection and/or processing – OY, SBG, MG, ISO, SH; Analysis and/or interpretation – OY, SBG, MG, ISO; Literature review – SBG, MG, OY; Writing – EO, MG, AG; Critical review – ISO, SH, AG.

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