# Vasoactive-ventilation-renal (VVR) score: A potential tool for predicting early postoperative outcomes in adult mitral valve surgery

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## Abstract

**Background and Aims:** Vasoactive-ventilation-renal (VVR) score has been validated in predicting postoperative outcomes in pediatric cardiac surgery. The aim was to evaluate its potential in predicting early postoperative outcomes in adult patients undergoing mitral valve surgery.

**Material and Methods:** A single-center prospective observational study involved 100 patients undergoing mitral valve surgery. We evaluated preoperative variables (Ambler score), VVR, and vasoactive-inotropic score (VIS) on admission to the intensive care unit (ICU) and then at 12, 24, and 48 hrs postoperatively. Outcomes assessed were length of stay in ICU (LOS-ICU), length of hospital stay (LOHS), and mortality. The data were analyzed using multivariable logistic regression model, receiver operating characteristic (ROC) curves, and areas under curve (AUC).

**Conclusion:** Our study showed the potential utility of the VVR score as a powerful tool for predicting early outcomes after mitral valve surgery, with VVR at 48 hrs having superior predictive capability.

**Keywords:** Cardiac, intensive care, post-operative outcome, surgery

## Introduction

Mitral valve surgery is known to be associated with multiple organ dysfunction in the postoperative period, resulting in adverse outcomes.[1] The postoperative management of these patients focuses primarily on restoring cardiopulmonary homoeostasis and mitigating other endorgan damage associated with postoperative cardiopulmonary dysfunction.[2] There are many traditional general ICU scoring indices which have been used for prognostication of adult cardiac surgical patients; however, they are not cardiac-specific scores giving less weight to cardiac-specific parameters.[3]

Miletic KG *et al.*[4] introduced the concept of vasoactive-ventilation-renal (VVR) score for the stratification of postoperative outcomes in pediatric patients undergoing cardiac surgery. This incorporates cardiovascular, pulmonary, and renal system parameters. Its utility in predicting postoperative outcomes including the mortality has been extensively studied in the pediatric population.[5] To our knowledge, there is so far no study in the literature that evaluates the effectiveness of the VVR score in adult cardiac

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surgical patients. This study aims at evaluating the potential efficacy of VVR score in predicting early postoperative outcomes in adult patients undergoing mitral valve surgery.

## Material and Methods

A prospective observational single-center study was conducted for one-year duration. The study was approved by the institutional ethics committee (EC/Approval/17/C. Anae/13/06/2022). It included 100 consecutive patients aged >18 years who underwent elective or urgent mitral valve surgery during the study period. Informed and written consent was obtained from all the study participants.

Patients who required emergency surgery, requiring concomitant aortic valve surgery and coronary artery bypass grafting, on mechanical ventilator support or inotropic support, renal failure patients requiring hemodialysis and those requiring intra-aortic balloon pump (IABP) or extracorporeal membrane oxygenation (ECMO) support in the operating room or within the first 48 hrs of the postoperative period were excluded from the study.

After cardiac surgery, the patients were managed in the cardiac ICU. The volume resuscitation, inotropes and vasopressors were started and titrated as per the institutional protocol. Our criteria for weaning from the ventilator were mean arterial blood pressure (MAP): >65 mmHg; normothermia, SpO2>94% at 50% FiO2; adequate urine output (>1 ml/kg/hr); and chest drain <100 ml/hr. Once the above criteria were met, sedation was stopped and the patient was weaned from mechanical ventilation.

Data collection: The data were collected from the ICU database.

*Preoperative*: Age, sex, body mass index (BMI), preoperative serum creatinine, renal failure (serum creatinine >2 mg/dL), concomitant tricuspid valve repair, preoperative arrhythmias (atrial fibrillation/heart block/ventricular tachycardia), hypertension, diabetes and ventricular function (left ventricular ejection fraction), prior cardiac operation and surgical priority (elective or urgent), and Ambler scores were calculated accordingly.[6]

*Intraoperative*: The duration of the cardiopulmonary bypass (CPB) and the aortic cross clamp time were also noted.

*Postoperative*: Dose of inotropes and vasopressors requirement (dopamine, dobutamine, epinephrine, norepinephrine, milrinone, and vasopressin) and partial pressure of carbon dioxide (PaCO2) in arterial blood gas analysis after shifting to cardiac ICU (baseline- BL) and at 12 hrs, 24 hrs, and 48 hrs in the postoperative period. 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 observed and postoperative serum creatinine was recorded at the same study points.

The VVR score was calculated as follows: vasoactive-inotropic score (VIS) + ventilation index (VI) + ΔCr.[4]

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).[7]

VI = (ventilator respiratory rate) × (PIP - PEEP) × PaCO2/1000.

ΔCr = 10 × change in creatinine (preoperative serum creatinine was subtracted from each postoperative serum creatinine measurement).

VIS, VI, and ΔCr were calculated at each postoperative study time points. VIS and VI were recorded as zero for patients who did not receive inotropic and mechanical ventilation support. Patients whose postoperative serum creatinine measurements were less than or equal to baseline, ΔCr was assumed to be equal to 0. Need for re-exploration for any reason and need for hemodialysis in postoperative period were also noted.

Primary outcomes assessed were length of stay in ICU (LOS-ICU) and length of hospital stay (LOHS). The secondary outcome assessed was mortality.

### Statistical analysis

All statistical analysis was performed using SPSS 22 software (SPSS Inc., IBM Corp., Armonk, NY). Descriptive statistics are presented as median [inter-quartile range (IQR)] or mean (standard deviation, SD) for continuous variables, and as n (%) for categorical variables. Patient characteristics and clinical characteristics of outcome groups were compared by the *t*-test for continuous variables and Chi-square for categorical variables. The discriminative powers of the VVR score at different study time points in terms of outcomes were assessed by the area under the curve (AUC) of the receiver operating characteristics (ROC), which were compared using the DeLong method. The cut-off values of variables (above 25$^{th}$ percentile and below 75$^{th}$ percentile) use to maximize total accuracy and performed regression model. Logistic regression modeling was used to assess the association between predictive factors and the outcomes. Data are presented as odds ratios (ORs) and 95% confidence intervals (CIs). $P < 0.05$ was considered significant.

## Results

The demographic data of the patients, the preoperative variables including the Ambler score, the intraoperative variables, and the postoperative variables such as VVR score at different time intervals and outcome measures are summarized in Table 1.

**Table 1: Demographic preoperative, intraoperative, postoperative data**

| Variable | Number |
|---|---|
| Age (in yrs) (mean) | 48.6±14 |
| Female Sex | 54 (54%) |
| BMI <20 | 26 (26%) |
| Hypertension | 18 (18%) |
| Diabetes Mellitus | 22 (22%) |
| Preoperative AF | 52 (52%) |
| Preop Renal Disease | 8 (8%) |
| Urgent surgery | 11 (11%) |
| Prior operation | 9 (9%) |
| Ambler Score | 4±2.82 |
| CPB time | 51.4±20.2 |
| Aortic Cross clamp time | 68.2±26.3 |
| VVR at BL | 18 (10-39) |
| VVR at 12 hrs | 18.6 (3.8-47.20) |
| VVR at 24 hrs | 12.2 (0.6–49.2) |
| VVR at 48 hrs | 9.7 (1.2-54.67) |
| LOS -ICU (In Hours) | 49.05 (43.221) |
| LOHS (In Hours) | 116.39 (45.55) |
| Mortality | 5 (5%) |
| Need for HD postop | 6 (6%) |

*Data is Represented as Mean±SD, Number (Percentage) and Median (Range). AF=Atrial Fibrillation, CPB=Cardiopulmonary Bypass, VVR=Vasoactive Ventilation Renal Score, LOS ICU=Length of Stay in ICU, LOHS=Length of Stay in Hospital, HD=Hemodialysis*

We calculated the VVR at different study time points and then observed its correlation with the primary outcomes such as LOS-ICU and LOHS. In addition, we performed the receiver operating characteristic (ROC) analysis for the same. For all four study time points [e.g. admission to ICU (BL), at 12, 24, and 48 hrs), the VVR correlated well with the primary outcomes. The corresponding AUC curves are shown in Figure 1. Further, of the four VVR measurements, 48-h VVR (VVR48) had the highest AUC for both the primary outcome measures. The logistic regression analysis of VVR at different study points with primary outcomes is shown in Table 2. The VVR at 24 and 48 hrs showed statistically significant correlation with outcomes, of which the VVR at 48 hrs showed the best correlation (VVR 48 with LOS -ICU: coefficient 3.2, std error 0.9, OR 24.3, $P < 0.0007$; VVR 48 with LOHS: coefficient 3.7, std error 0.8, OR 42.4, $P < 0.0001$).

To further establish the role of VVR in predicting outcomes, we performed bivariate logistic regression modeling between VVR 48 (which had the highest AUC among VVR at different time points) and the corresponding VIS score at 48 hrs and results are shown in Table 3, which clearly showed that VVR at 48 hrs outperformed VIS at 48 hrs. The cut-off medians for LOS-ICU and LOHS were 33 and 96 hrs, respectively. The AUC for VVR at 48 hrs (LOS-ICU: 0.891, LOHS: 0.831) was also better than corresponding AUC for VIS at 48 hrs (LOS-ICU: 0.823, LOHS: 0.810) as shown in Figure 2. Logistic regression showed that VVR at 48 hrs was strongly associated with prolonged ICU stay (OR: 25.88, $P < 0.0001$), prolonged hospital stay (OR: 8.40, $P < 0.0009$) when compared to the corresponding VIS score at 48 hrs.

Mortality was observed in 5% of the patients; however, all the deaths were beyond 48 hrs (beyond the cutoff duration for ICU stay). None of them required ECMO or IABP support within 48 hrs of postoperative period. Six patients

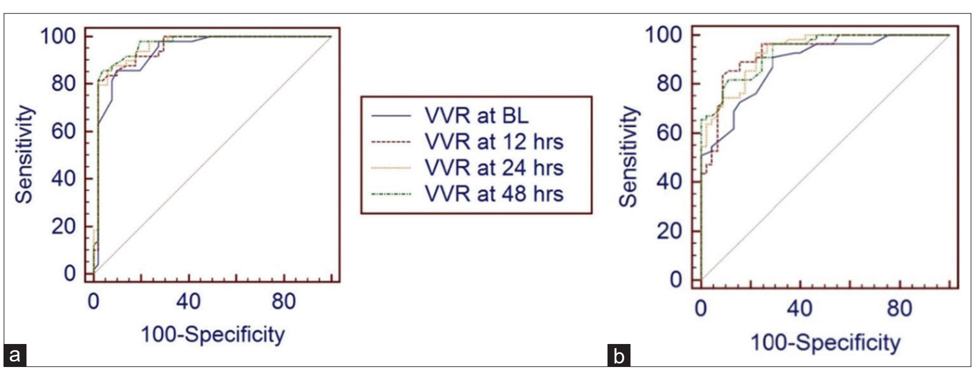


**Figure 1:** Showing receiver operating characteristic curve (ROC) curves of VVR at different time intervals: (a) – VVR at Different Time Intervals with ICU Stay (AUC at BL-0.934, at 12 hrs – 0.950, at 24 hrs- 0.957, At 48 hrs- 0.961. (b)– VVR at Different Time Intervals with Hospital Stay (AUC at BL- 0.884, at 12 hrs- 0.929, at 24 hrs- 0.932, at 48 hrs- 0.934

**Table 2: Logistic regression of VVR at different study point times for length of stay ICU (LOS-ICU) and length of hospital stay (LOHS)**

| Outcome | Variable | Coefficient | Std. error | *P* |
|---|---|---|---|---|
| LOS- ICU | VIS at 48 hrs | 2.19257 | 0.92340 | 0.0176 |
| | VVR at 48 hrs | 3.25370 | 0.72304 | <0.0001 |
| LOHS | VIS at 48 hrs | 1.91461 | 0.68348 | 0.0051 |
| | VVR at 48 hrs | 2.12887 | 0.63933 | 0.0009 |

**Table 3: Logistic regression of VVR at 48 hrs and VIS at 48 hrs**

| Outcome | Variable | Coefficient | Std. Error | *P* |
|---|---|---|---|---|
| LOS–ICU | VVR at BL | 0.23170 | 0.97657 | 0.8125 |
| | VVR at 12 hrs | 0.77406 | 1.04434 | 0.4586 |
| | VVR at 24 hrs | 2.54891 | 0.86173 | 0.0031 |
| | VVR at 48 hrs | 3.19161 | 0.94137 | 0.0007 |
| LOHS | VVR at BL | 0.68793 | 1.01444 | 0.4977 |
| | VVR at 12 hrs | 0.73975 | 1.09147 | 0.4979 |
| | VVR at 24 hrs | 3.06543 | 0.89940 | 0.0007 |
| | VVR at 48 hrs | 3.74739 | 0.84223 | <0.0001 |

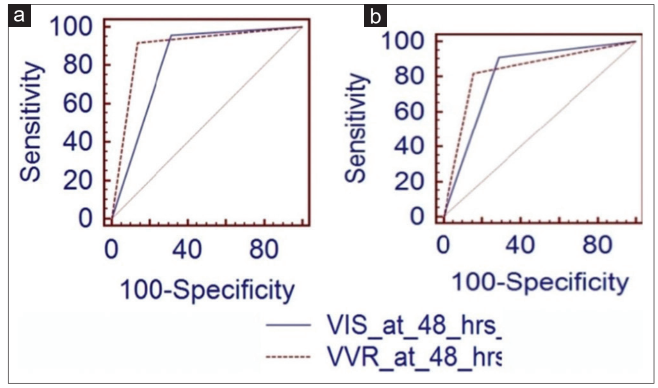


**Figure 2:** Showing ROC curves of VVR at 48 hrs and VIS (vasoactive inotropic score) at 48 hrs. (a) For ICU stay. (b) For hospital stay

required hemodialysis in the postoperative period, and none required surgical re-exploration for bleeding. The VVR score at various time points showed a good correlation with the mortality, with VVR at 48 hrs having a significant predictive capacity (std coefficient = 1.608 and $P < 0.0001$). The Ambler score was used to stratify the preoperative variables and then the correlation with the outcomes was observed. The Ambler score effectively predicted mortality as VVR at 48 hrs (Mean ± SD: 10.4 ± 2.88 vs 5.41 ± 2.78 in Mortality vs without Mortality, respectively; $P < 0.0001$), but did not show a statistically significant relation with primary outcomes (for LOS-ICU: coefficient = 0.095310, $P = 0.3095$; for LOHS coefficient 0.074598, $P = 0.2467$).

## Discussion

This prospective study showed that the VVR score is an independent predictor of outcomes in terms of LOS-ICU, LOHS, and mortality in adult patients undergoing mitral valve surgery. Furthermore, VVR at 48 hrs demonstrated a better predictive accuracy for all primary and secondary outcomes. Our analysis showed that the efficacy of VVR score in predicting postoperative outcomes in adult cardiac surgical patients is similar to the results of studies performed in pediatric cardiac surgical population.[4,5,8]

The VVR scores were more at baseline and 12 hrs, and then decreased during the next 48 hrs. The AUC of VVR at baseline and at 12 hrs was significantly lower than at 24 and 48 hrs to predict the outcomes. This could be because of the exposure to a new cardiac physiology owing to the dynamic changes in the ventilation and hemodynamic parameters following the separation from the CPB, thereby reflecting itself in the immediate postoperative period (on admission to ICU) and could be less likely related to the severity of organ dysfunction. Additionally, inclusion of serum creatinine in the score as a marker of kidney injury makes the negligible addition to the renal parameter at admission and at 12 hrs.

In our study, VVR at 48 hrs had the best AUC value among the study time points and showed a highly significant predictive capability of both primary outcomes and the mortality. Similar findings were observed in studies performed by Miletic KG *et al.*[4] and Shahzad Alam *et al.*[9] The 48 hrs VVR measurements can help us assess the sustained severity of the illness in the postoperative period, which could likely influence the outcome than transient organ dysfunction in immediate postoperative period.

Mitral valve surgery is an independent risk factor for acute kidney injury and pulmonary dysfunction in the postoperative period.[10,11] VIS was used in adult cardiac surgery as a predictor of postoperative outcomes and showed good correlation.[3] In our study, VVR at 48 hrs outperformed VIS at the same time in predicting outcomes. Our findings confirm that by adding measures of respiratory and renal dysfunction to the VIS is a better tool in predicting all outcomes. VVR could have definite advantage over VIS in those who may have considerable post-CPB lung and/or kidney injury with relatively preserved hemodynamic integrity.

To assess the effect of preoperative variables on outcomes, we have stratified patients using the Ambler score, which is a preoperative score to predict the mortality in patients undergoing mitral valve surgery.[6] We observed that the Ambler score could significantly predict mortality but none of our primary outcomes (LOS-ICU and LOHS). But, the VVR score better predicted all outcomes. This clearly shows that we need good post-cardiac surgery ICU scores like the

VVR score because many perioperative factors and events will add on to preoperative variables in predicting outcomes.

The VVR score includes multiorgan parameters and, therefore, could be a better predictor of outcomes in adults undergoing mitral valve surgery. Traditional scores such as SOFA, APACHE II, and others which were basically designed for the general ICU were used postoperatively in adult cardiac surgical population, but these are complex and some require newer experimental biomarkers.[12] Owing to its simplicity and ease of calculation, VVR can be used as a cost-effective prognostication tool on the bedside even in adult patients undergoing cardiac surgery.

### Limitations

It is a single-center, nonrandomized study involving patients only undergoing mitral valve surgery, therefore, further validation of VVR in all types of adult cardiac surgeries is recommended. We did not compare VVR with other evolving cardiac surgery-specific ICU scoring systems [e.g., cardiac surgery score (CASUS)],[13] so further studies comparing VVR with them are suggested. Finally, protocols to administer vasoactive medication and ventilator support, which are elements of VVR score, may vary according to physician interpretation and practice, making its utility difficult in the large multicenter studies.

## Conclusion

Our study showed the potential utility of the VVR score as a powerful tool in predicting early outcomes after mitral valve surgery, with VVR at 48 hrs having superior predictive capability.

### Data availability

The data that support the findings of this study are available from the corresponding author, [Nirav Parikh], upon reasonable request.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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