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24th hour vasoactive inotrope score is associated with poor outcome in adult cardiac surgery

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SUMMARY

OBJECTIVE: The aim of this study was to investigate the efficacy of vasoactive inotrope score at the 24th postoperative hour for mortality and morbidity in elective adult cardiac surgery.

METHODS: Consecutive patients who underwent elective adult coronary artery bypass and valve surgery in a single tertiary center for cardiac surgery between December 2021 and March 2022 were prospectively included. The vasoactive inotrope score was calculated with the dosage of inotropes that were continuing at the 24th postoperative hour. Poor outcome was defined as any event of perioperative mortality or morbidity.

RESULTS: The study included 287 patients, of whom 69 (24.0%) were on inotropes at the 24th postoperative hour. The vasoactive inotrope score was higher (21.6±22.5 vs. 0.94±2.7, p=0.001) in patients with poor outcome. One unit increase in the vasoactive inotrope score had an odds ratio of 1.24 (95% confidence interval: 1.14–1.35) for poor outcome. The receiver operating characteristic curve of vasoactive inotrope score for poor outcome had an area under the curve of 0.857.

CONCLUSION: Vasoactive inotrope score at the 24th hour can be a very valuable parameter for risk calculation in the early postoperative period.

KEYWORDS: Cardiac surgical procedures. Inotropic agents. Outcome assessment. In-hospital mortality.

INTRODUCTION

Cardiac surgical procedures are performed with increasing volumes and better outcomes[1]. Nevertheless, patients undergoing cardiac surgery are at risk of mortality and morbidity in the perioperative period. Prolonged intubation, extended intensive care unit (ICU) stay, acute renal injury, and cerebrovascular events are common major risks encountered following cardiac surgery[2,3].

During weaning from cardiopulmonary bypass (CPB) at the end of cardiac surgery and in the early postoperative period, inotropes are utilized to stabilize hemodynamics and improve cardiac function. Depending on the patient's preoperative comorbidities, the extent of Ischemia-reperfusion damage, and intraoperative variables, severe myocardial dysfunction can arise, leading to low cardiac output syndrome and end-organ malperfusion[4]. Inotropic and vasopressor agents are the first-line treatments for low cardiac output syndrome[5]. The dosing and number of these agents are managed according to the hemodynamic and metabolic requirements of the patient with higher doses denoting a worse condition[6].

Inotropic and vasopressor agents are associated with distinct complications, including vasoconstriction, arrhythmia, pulmonary, and hepatic complications. Patients who require high doses of inotropes are more prone to postoperative complications. The vasoactive inotropic score (VIS) is a score calculated from the doses of administered inotropic agents and reflects the level of total inotrope requirement of the patient, which allows for objective quantification of the level of inotropes required by a patient[7]. Although originally developed to include dopamine, dobutamine, and epinephrine, it was subsequently expanded to include more agents. VIS has been shown to be a marker of disease severity and a prognostic factor for mortality and morbidity. It was initially used in the pediatric age group for prognostic purposes but has also been used in adult cardiac surgery patients[8].

Several risk scoring systems have been developed for outcome prediction following cardiac surgery. The current European System for Cardiac Operative Risk Evaluation (EuroSCORE II) reflects the risk of a planned cardiac operation using patient factors and operation type. Although it provides very useful information, the operative and early postoperative periods are also important in the final state of the patient. No current risk score incorporates direct or indirect data that reflect intraoperative parameters[9]. The level of inotropes necessary in the early postoperative period may reflect both the patient's preoperative state and the intraoperative parameters. Therefore, we aimed to investigate the efficacy of VIS for predicting mortality and morbidity after elective adult cardiac surgery.

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METHODS

The study was designed as a single-center prospective study. Approvals were obtained from the hospital academic board and the local ethics committee (approval number HNHEAH-KAEK 2021/KK/291). The study was conducted in full compliance with the ethical principles of the Declaration of Helsinki. Consecutive patients who underwent elective adult cardiac surgery at our tertiary cardiac center between December 2021 and March 2022 were included in the study. Patients who required urgent surgery and who required extracorporeal membrane oxygenation (ECMO) during the weaning period or early postoperative period were excluded. Operations were performed by different surgical teams of the hospital following routine surgical protocols, and patients were treated in the ICU by a single anesthesiology team.

Demographic parameters, preoperative echocardiography results, EuroSCORE II calculations, and operative data including CPB and cross clamp (CC) times were recorded. VIS was calculated at the first 24th hour of the postoperative ICU stay. The time to extubation, renal injury, need for mechanical support with intra-aortic balloon pump (IABP), stroke, reoperation, and death were recorded. Renal injury was determined according to the RIFLE classification[10]. EuroSCORE II was calculated for each patient using the online calculator[11]. A cerebrovascular event was defined as a new-onset neurological deficit in the postoperative period, as evidenced by radiological imaging. Acute renal failure was defined as the need for renal replacement therapy in the intensive care unit. Extended ICU stay was defined as longer than 2 days of ICU stay. Reoperation for bleeding included all patients reoperated for excessive chest tube output in the postoperative period. A poor outcome was defined as any perioperative mortality or morbidity.

Calculation of vasoactive inotrope score

As a routine protocol of perioperative management in our institute, inotropes were started, targeting a mean arterial pressure of >65 mmHg. In patients with high pulmonary capillary wedge pressure and pulmonary artery pressure (PAP), milrinone was started at 0.2–0.4 μg/kg/min. An IABP was placed if a low cardiac output state was present despite maximum doses of inotropes with a systolic arterial pressure<100 mmHg, mean PAP>25 mmHg, central venous pressure>15 mmHg, and cardiac index <2.1 L/min/m^2.

Inotrope and vasopressor doses were recorded to calculate VIS with the following formula: dopamin (mcg/kg/min)+dobutamine (mcg/kg/min)+100×epinephrine (mcg/kg/min)+100×norepinephrine (mcg/kg/min)+10×milrinone (mcg/kg/min)+10,000×vasopressin (munits/kg/min). VIS calculation was performed with the dosage of inotropes continuing at the 24th postoperative hour[12].

Statistical analysis

IBM SPSS 22 software was used for statistical analysis. Continuous parameters are given as mean±standard deviation, while categorical parameters are given as numbers and percentages. The normal distribution of continuous parameters was assessed using the Shapiro-Wilk test. For group comparison, continuous variables with normal distribution were compared using the Student's t-test, continuous variables without normal distribution were compared using the Mann-Whitney U test, and categorical variables were compared using the chi-squared test. Factors significant in univariate analysis were carried onto multivariate analysis for the assessment of risk factors. Receiver operating characteristic (ROC) curves were constructed to compare the efficacy of VIS and EuroSCORE II in predicting poor outcome.

RESULTS

The records of 287 consecutive patients who met the inclusion criteria during the study period were evaluated. The mean age of the patients was 60.0±10.7, 199 (69.3%) were males, and 88 (30.7%) were females. The mean EuroSCORE II was 1.89±1.34. The baseline patient characteristics are presented in Table 1. In the 24th postoperative hour, vasoactive agents were necessary for 69 (24.0%) patients. The mean VIS on the first operative day was 3.82±11.26. The mortality rate among the study patients was 4.2%. The composite endpoint of poor outcome was observed in 40 (13.9%) patients. The observed morbidities are summarized in Table 1.

Patient factors were compared between patients with and without poor outcome (Table 2). Chronic obstructive pulmonary disease was more frequent, the mean preoperative ejection fraction was lower, and CPB and CC times were longer in patients with mortality (p=0.005, p=0.011, p=0.001, and p=0.013, respectively). Combined coronary artery bypass grafting (CABG) and valve procedures were more common among patients with poor outcome (p=0.005). VIS (p<0.001) and EuroSCORE II (p<0.001) were higher in patients with poor outcome. The factors that were significant between the groups were all represented by the EuroSCORE II. After controlling for EuroSCORE II and CPB time, VIS was found to be independently associated with poor outcome with an odds ratio (OR) of 1.24 (95% confidence interval [CI]: 1.14–1.35). The same analysis was repeated for isolated CABG, where VIS

Table 1. Summary of patient characteristics.

Variables	n (%)
Age	60.0±10.7
Gender	
Male	199 (69.3%)
Female	88 (30.7%)
EuroSCORE II	1.89±1.34
Diabetes mellitus	147 (51.2%)
Chronic obstructive pulmonary disease	34 (11.8%)
Left ventricular ejection fraction (%)	52.6±8.6
Left ventricular ejection fraction ≤50%	113 (39.4%)
Pulmonary artery pressure (mmHg)	26.2±12.4
Cardiopulmonary bypass time (min)	125.8±46.0
Cross clamp time (min)	80.3±33.8
Operation type	
CABG	203 (70.7%)
Valve	65 (22.6%)
CABG+valve	19 (6.6%)
VIS	3.82±11.3
Intra-aortic balloon pump use	15 (5.2%)
Poor outcome	40 (13.9%)
Mortality	12 (4.2%)
Prolonged intubation	10 (3.5%)
Prolonged ICU stay	22 (7.7%)
Acute renal failure	4 (1.4%)
Cerebrovascular event	8 (2.8%)
Reoperation for bleeding	9 (3.1%)

CABG: coronary artery bypass graft; EuroSCORE II: European System for Cardiac Operative Risk Evaluation II; ICU: intensive care unit; VIS: vasoactive inotrope score.

was independently associated with poor outcome with an OR of 1.21 (95%CI: 1.10–1.33). Individual morbidities of prolonged ICU stay, prolonged intubation, cerebrovascular events, and reoperation for bleeding were also significantly associated ($p<0.001$) with higher VIS means.

The efficacy of VIS was assessed and compared against EuroSCORE II using ROC analysis. Area under the curve (AUC) was greater for VIS (0.857) compared to EuroSCORE II (0.788). A value of 4.5 for VIS had a sensitivity of 77.5% and a specificity of 92.7% for poor outcome (Figure 1). The AUC of VIS for poor outcome in CABG-only patients was 0.814 and in valve-only patients was 0.870.

DISCUSSION

After weaning off CPB and the initial stabilization period in the ICU, the variety and dose of inotropes and vasopressors required represent both the extent of low cardiac output syndrome and myocardial dysfunction. Although acting to increase cardiac contractility and systemic perfusion, the use of inotropes and vasopressors has been associated with increased mortality and organ dysfunction. With more severe myocardial dysfunction and low cardiac output, higher doses of inotropic exposure will be necessary for the patient, with a high associated VIS[6,13].

The VIS quantifies the total dose of inotropes and effectively reflects the patient's risk of mortality and morbidity during their hospital stay. The VIS is a numerical score that

Table 2. Patients factors in patients with and without poor outcome.

	No poor outcome (n=247)	Poor outcome (n=40)	p-value
Age	59.7±10.6	62.0±10.7	0.203
Gender			0.167
Male	175 (70.9%)	24 (60.0%)	
Female	72 (29.1%)	16 (40.0%)	
EuroSCORE II	1.70±1.16	3.06±1.70	<0.001
Diabetes mellitus	128 (51.8%)	19 (47.5%)	0.612
Chronic obstructive pulmonary disease	22 (8.9%)	12 (30.0%)	0.001
Left ventricular ejection fraction (%)	53.2±8.0	49.0±10.8	0.022
Left ventricular ejection fraction ≤50%	91 (36.8%)	22 (55.0%)	0.029
Pulmonary arterial pressure (mmHg)	25.4±11.5	30.8±16.0	0.048
Cardiopulmonary bypass time (min)	120.1±40.2	161.0±62.0	<0.001
Cross clamp time (min)	77.7±32.0	95.8±40.1	0.002
VIS	0.94±2.7	21.6±22.5	<0.001
Operation type			0.005
CABG	181 (73.3%)	22 (55.0%)	
Valve	54 (21.9%)	11 (27.5%)	
CABG+valve	12 (4.9%)	7 (17.5%)	

CABG: coronary artery bypass graft; EuroSCORE II: European System for Cardiac Operative Risk Evaluation II; VIS: vasoactive inotrope score.

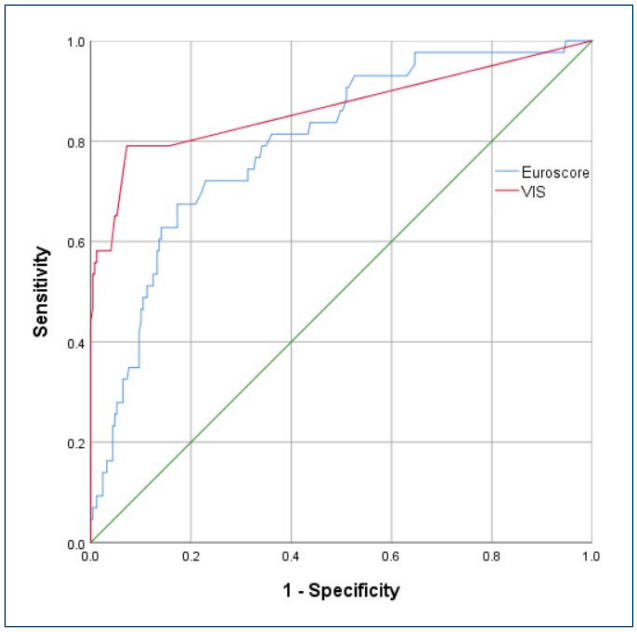

Figure 1. Receiver operating characteristic curves of European System for Cardiac Operative Risk Evaluation II and vasoactive inotropic score for poor outcome.

was first used in the pediatric patient group and was later studied in adult cardiac surgery[7,14,15]. Our results show that VIS is an effective indicator of poor outcome in adult cardiac surgery patients undergoing elective CABG and valve surgery. Studies on VIS have chosen different time points to determine the score and its relationship with outcomes. In a prospective multicenter study on pediatric patients below the age of 1 by Gaies et al., the maximum VIS value during the first postoperative 24 h was used[7], whereas in another study, the VIS at the end of surgery was used[14]. Koponen et al. calculated the maximal VIS (VISmax) during the first 24 h after surgery using the highest doses of vasoactive and inotropic drugs administered[15]. In another study, the highest VIS value was obtained from the data recorded in the first and next 24th hours after intensive care admission[16].

The optimal timing for the VIS value that best predicts patient outcomes is debatable. In this study, we calculated the VIS at the 24th postoperative hour. The very early postoperative period (i.e., the first 6 h) during the initial stabilization of the patient may be misleading due to mechanisms such as concurrent fluid and electrolyte imbalance, varying levels of systemic vascular resistance, and hypothermia, which influence the choice and dosage of anesthetics. Any persistent cardiac dysfunction that requires inotropic and vasopressor support at the 24th hour would be associated with a higher risk of poor outcome in the postoperative course. Future studies may compare the VIS at different time points in a single cohort to determine the best interval associated with outcomes.

The level of VIS above which there is increased risk differs with the study population. Gales et al. have found a VIS above 20 to be associated with poor outcomes[7]. In a study on patients operated on for infective endocarditis, a VIS>10 was accepted as a high value[17]. In another cardiac surgery study, a cutoff value of 5.5 for VIS had 0.83 sensitivity and 0.54 specificity[14]. High VIS values have been associated with morbidity in pediatric cardiac surgery patients, and the higher cutoff value for VIS in the pediatric population has been explained by the decreased beta-adrenergic receptors with lower ages[6]. Higher cutoff values at 10–15 have been reported in a different study[17]. In our study, a cutoff value of 4.5 had a sensitivity of 77.5% and a specificity of 92.7% for adult CABG and valve surgery patients.

Maximum VIS in the first 24 h has been demonstrated to be an independent predictor of renal failure[18]. In our cohort, a high VIS was associated with an increased occurrence of the composite endpoint of any comorbidity. Although the number of each specific comorbidity was low, a higher VIS could be demonstrated for the occurrence of each comorbidity. A high VIS was associated with a prolonged ICU stay, renal failure, cerebrovascular events, and reoperation for bleeding. Future studies can be designed to determine cutoff values for VIS above which the risk of these morbidities is increased.

The EuroSCORE II is a prevalent scoring system that incorporates preoperative patient data, preoperative cardiac parameters, and the type of planned operation to predict perioperative risk[19]. In our study, the VIS performed better than the EuroSCORE II for demonstrating the risk of poor outcome. The EuroSCORE II is a highly validated risk score that utilizes preoperative factors to suggest a risk profile for patients undergoing cardiac procedures[20]. On the contrary, patient factors and the type of planned operation play significant roles in the risks faced by the patient in the perioperative period. Furthermore, perioperative complications are affected by factors that become evident during the operation. These include the duration of CPB, CC, and myocardial contractility at the end of the operation. These factors are not included in preoperative risk calculations. The dosage of inotropes necessary in the postoperative period may reflect the operative factors that influence outcomes. This state is better quantified by the VIS, which may explain its better performance for poor outcomes.

Our study has certain limitations. This study was performed at a single center with a limited number of patients. Urgent cases and those that required an ECMO were excluded to form a homogenous patient group. With a larger patient group, the

predictive ability of the VIS for individual morbidities can be better evaluated. The use of inotropes may vary across institutions, which may limit the external validity of our results.

CONCLUSION

This study showed that a higher VIS is associated with an increased risk of poor outcome following elective cardiac surgery in adult patients. Our results emphasize that the VIS at the 24th hour can be a very valuable parameter for risk calculation in the early postoperative period. Further risk analysis studies can determine the ideal time for score calculation, the potential benefit of its use alongside traditional risk scores, and the ideal cutoff values for individual postoperative complications.

AUTHORS' CONTRIBUTIONS

EMTM: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft. **MB:** Formal Analysis, Investigation, Methodology, Visualization, Writing – review & editing. **MA:** Conceptualization, Data curation, Methodology, Writing – review & editing.

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