Original Article

When is the Ideal Time to Calculate the Vasoactive Inotropic Score as a Predictor of Mortality and Morbidity in Cardiac Surgery? A Retrospective Study

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ABSTRACT

Introduction: The aim of this study was to evaluate the prediction of vasoactive inotropic score (VIS) on early mortality and morbidity after coronary artery bypass grafting (CABG) and to determine the ideal time for score calculation.

Materials and Methods: The study included patients who underwent isolated on-pump CABG surgery between November 2021 and November 2022. Pre, intra, and postoperative data were obtained by retrospective chart review. The final VIS value in the operating room (VISintra) and the highest VIS value in the first 24 hours in the intensive care unit (VISmax) were calculated. The patients were divided into two groups; Group 1 who developed early postoperative morbidity and mortality and Group 2 who did not. And the data were analyzed by groups.

Results: A total of 221 patients with a mean age of 63.49 ± 9.96 years were evaluated and 73 (33%) were in Group 1. The cut-off value for VISintra was determined to be 6.20, VISmax was 6,05. VISintra and VISmax values were significantly higher in the poor outcome group. Multivariate analysis showed that only VISmax value was an independent variable on mortality-morbidity.

Conclusions: Our results imply that the vasoactive inotropic score is an easy and inexpensive score to calculate and can be used as a specific scoring system to predict poor early outcomes in CABG patients. According to statistical analyses, the most predictive time among VIS measurements was VISmax, the highest value calculated in the ICU in the first 24 hours postoperatively.

Keywords: Cardiac surgery, coronary artery bypass grafting, morbidity, mortality

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INTRODUCTION

There are some preoperative scoring systems developed to predict postoperative mortality and morbidity in Coronary Artery Bypass Grafting (CABG) operations, with the European System for Cardiac Operative Risk Evaluation Score II (Euroscore II) being one of the most widely used.[1] It has been reported in some studies that the vasoactive inotropic score (VIS), which has been used in recent years, is as effective as the Euroscore II.[2-10]

Studies that were made at first in congenital cardiac surgery and later in adult cardiac surgery have reported significant results on the predictor of mortality and morbidity of VIS, which is reported to reflect the sum of the doses of inotropic agents given to patients in cases of acute cardiovascular failure.[2-6] The calculation time of VIS is reported as different times in different studies in the literature, and it is reported that the results of all VIS measurements performed independently of the calculation

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time are significant in terms of predicting mortality and morbidity.[7-13] However, to the best of our knowledge, there is no clear information in the literature on the ideal measurement time that should be used for VIS calculation.

In our study, we aimed to evaluate the predictive value of both intraoperative and postoperative VIS measurement for early mortality and morbidity in patients undergoing CABG operation and to determine which one is more appropriate to use as the calculation time.

MATERIALS AND METHODS

Our study was conducted with patients who underwent isolated elective on-pump CABG at a tertiary hospital between November 2021 and November 2022. This clinical study was approved by Ordu University faculty of medicine ethics committee with decision number 2022/267 and conducted in accordance with the ethical principles of the Helsinki Declaration. Patients over the age of 20 who underwent elective isolated on-pump CABG surgery in our hospital were managed by the same surgical and anesthesia teams, and study data available were included in our retrospective study. Patients who underwent emergency CABG surgery, off-pump CABG, concurrent cardiac or major vascular surgery with CABG surgeries, patients who had an open heart surgery other than CABG, patients who had previously undergone open heart surgery, and patients who had used an intraoperative intra-aortic balloon pump (IABP) or an extracorporeal membrane oxygenator (ECMO) were excluded from the study. The following data for the patients included in the study were reviewed on the hospital automation system and hospital file archives and recorded:

Preoperative data; such as preoperative baseline clinical features, comorbidities, the presence of myocardial infarction (MI) in the preoperative period, COVID-19 history, laboratory parameters, preoperative ejection fraction (EF) values, and preoperative Euroscore-II values.

Intraoperative data; such as the number of coronary artery bypass grafts, aortic cross-clamp (ACC) duration, cardiopulmonary bypass duration (CPB), and at the end of the surgery VIS (VISintra) values.

Postoperative data; significant complications such as extubation time, mortality in the early postoperative period (first 30 days), cerebrovascular accident (CVA), atrial fibrillation (AF), acute kidney failure (ARF), mediastinitis, intensive care unit (ICU) stay, postoperative hospital stays of the patients and the highest VIS value in the first 24 hours (VISmax).

Prolonged extubation time; extubation that can be performed after the seven hours postoperatively, prolonged ICU stay; postoperative ICU stay of three days or more, and early period undesirable events were considered undesirable events that occurred in the first 30 days.

A total of 221 patients included in the study were examined and compared in two groups based on mortality and morbidity: Group 1: patients who developed early postoperative mortality and morbidity and Group 2: patients who did not.

Coronary artery bypass surgery procedure: CABG surgeries were generally performed with standard median sternotomy under general anesthesia. CABG accompanied by CPB was performed in all patients. Myocardial protection was provided by antegrade cold blood cardioplegia from the aortic root and intermittent retrograde cold blood cardioplegia from the coronary sinus, and all patients underwent complete revascularization. At the end of the operation, the patients were taken to the cardiac surgery intensive care unit and immediately monitored and followed for 24 hours with a standard D2 lead. They were extubated when they were awake and spontaneously breathing and when there was no abnormality in their blood gas parameters or hemodynamic status. A blood transfusion was applied to the patients when necessary (if the hematocrit level was <24–25%).

The VISintra value was calculated in the postoperative period when the patient's clinical data were most stable, and the VISmax was calculated with the highest inotropic agent values within the first 24 hours in the intensive care unit. For the VIS calculation, Gaies' formula was used "Dopamine dose ($\mu g\ kg^{-1}\ min^{-1}$) + Dobutamine dose ($\mu g\ kg^{-1}\ min^{-1}$) +100 × epinephrine dose ($\mu g\ kg^{-1}\ min^{-1}$) +100 × Norepinephrine dose ($\mu g\ kg^{-1}\ min^{-1}$) +10.000 × Vasopressin dose ($U\ kg^{-1}\ min^{-1}$) +10 × Milrinone dose ($\mu g\ kg^{-1}\ min^{-1}$)" (2).

Statistical analysis

The statistical analyses were performed using the SPSS v23.0 (IBM, New York, USA). Normality analyses of quantitative data were performed with the Kolmogorov–Smirnov test. The Mann–Whitney U test was used to compare data that did not show a normal distribution. Qualitative data were compared using the Pearson-Chi Square test. A ROC analysis was performed to determine the cut-off value for predicting morbidity and mortality. ROC analysis results were presented with AUC, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. Univariant and

multivariant logistic regression analyses were performed to determine the factors predicting morbidity-mortality. The data were presented as mean (95% CI) and n (%). Statistical significance was accepted as $P < 0.05$.

RESULTS

221 patients who underwent elective on-pump CABG surgery were included in the study. The mean age of the patients was 63.49 ± 9,96 (37-87), and 168 (76.1%) patients were male. There were 73 (33%) patients in Group 1 and 148 (67%) patients in Group 2. The number of patients with mortality was found to be 25 (11.3%). The characteristics and operative data of the patients are shown in Table 1.

Among the demographic characteristics, ASA 3, preop Atrial fibrillation (AF), Age, Euroscore II, CPB duration, extubation time, intensive care unit length of stay, VISintra, and VISmax values were found to be significant in the poor outcome group [Table 1].

The most common morbidities in Group 1 were found to be postoperative AF with 65.8% (48 patients), ARF (31.5%), mediastinitis (9.6%), and CVA (8.2%), respectively. Early mortality was found to be 34.5% [Table 2].

A ROC analysis was performed to determine the predictive cut-off values of morbidity and mortality of VISintra and VISmax. When the cutoff value for VISintra was determined to be 6.20, the sensitivity was calculated to be 70% (53.47–83.44) and the specificity to be 70.45% (54.8–83.24). When the cut-off value for VIS max was determined to be 6.05, the sensitivity was calculated to be 63% (46.94–77.88) and the specificity was 76.74% (61.37–88.24). The AUC value was calculated to be 70% in both [Table 3, Figure 1]. Univariant and multivariant logistic regression analyses were performed for the ratio of predicting morbidity-mortality among the data that were statistically significant in the analyses [Table 4]. Although all the data were significant on their own, no significant results were obtained in the multivariant analysis except for VIS Max. The analyses showed that the VIS max was an independent variable on mortality-morbidity. The OR value of VIS max was determined to be 1.148 (1.027–1.283).

DISCUSSION

It is reported that VIS was first defined as a predictor for mortality and morbidity in a study conducted by Gaies *et al*. in 2010[2] focusing on congenital cardiac surgery and that this hypothesis was supported by using the VIS score

Table 1: Clinical characteristics of study patients and groups

	Group 1 (*n*: 148)	Group 2 (*n*: 73)	*P*
Demographics			
Male Gender	117 (79,1%)	51 (69,9%)	0,132
Age (years)	61,9 (60,3-63,5)	66,7 (64,6-68,9)	<0,001*
BMI	27,4 (26,8-28,1)	27,8 (26,8-28,8)	0,509
ASA			
2	3 (2)	1 (1,4)	0,015*
3	145 (98)	68 (93,2)	
4	0 (0)	4 (5,5)	
Euroscore-II	1,3 (1,1-1,4)	1,6 (1,4-1,7)	0,001*
Preoperative EF (%)	54,4 (52,9-56)	53,1 (51-55,2)	0,197
Comorbidities			
History of MI	69 (46,6)	36 (49,3)	0,706
COPD	7 (4,7)	6 (8,2)	0,300
AF	7 (4,7)	11 (15,1)	0,008*
Diabetes mellitus	57 (38,5)	37 (50,7)	0,085
History of Covid-19 disease	34 (23)	11 (15,1)	0,170
Hypertension	84 (56,8)	44 (60,3)	0,618
Intraoperative data			
Mean distal anastomosis number	3,7 (3,6-3,9)	3,8 (3,7-4)	0,366
ACCtime (minutes)	82,5 (78,3-86,6)	88,5 (82,3-94,8)	0,080
CPB time (minutes)	117,9 (112,7-123,1)	139,8 (129-150,6)	<0,001*
VISintra	2,7 (1,4-4)	19,3 (11,2-27,3)	<0,001*
Postoperative data			
Mean extubation time (hours)	7,5 (6,6-8,4)	35,8 (17,5-54,1)	<0,001*
Mean ICU stay (days)	2,5 (2,4-2,7)	3,5 (2,8-4,2)	0,042*
Mean hospital stay (days)	9,1 (8,5-9,6)	10,8 (9,3-12,3)	0,096
VIS-max	2 (1,2-2,7)	24,6 (14,6-34,7)	<0,001*

BMI: Body Mass Index, ASA: American Society of Anesthesia, Euroscore: European System for Cardiac Operative Risk Evaluation Score EF: Ejection Fraction, MI: Myocardial Infarction, COPD: Chronic obstructive pulmonary disease, AF: Atrial Fibrillation, ACC: Aortic cross-clamp, CBP: Cardiopulmonary bypass, VISintra: Intraoperative Vasoactive Inotropic Score, VISmax: Vasoactive Inotropic Score in ICU, ICU: Intensive Care Unit, n: number, *P**<0,05

in adults for the first time by Yamazaki *et al*., in 2018.[7] In studies examining the VIS values of cardiovascular surgery patients, it is stated that VIS measurements were made at different times and the results were similar, and VIS was found to be very significant as a predictor in terms of mortality and morbidity.[7-11] It is reported that Gaies used the highest VIS value in the first 48 hours of the postoperative ICU process in their studies,[4] while Koponen *et al*.[9] calculated the VIS value with the highest drug doses given during the first 24 hours of the postoperative ICU process, which is the predictor value for 30-day and 1-year mortality. In their study, Yamazaki *et al*.[7] and Baysal *et al*.[8] stated that they calculated the VIS value at the end of the operation, which is the most stable intraoperative period, and described this measurement time as the period when the factors affecting the use of inotropic agents were minimized. Mete *et al*.,[11] on the other hand, measured the VIS value in the first 24 hours postoperative and considered this time as the period when misleading effects such as the effect of anesthetic drugs on patients, the current fluid-electrolyte imbalance, systemic vascular resistance, and hypothermia disappeared. When we review the literature, our study is the first in which measurements were performed in two different time periods in a single cohort, and the highest VIS value was calculated both in the most stable intraoperative period and in the first 24 hours in the intensive care unit. Statistically, both VISintra ($P < 0.01$) and VIS max ($P < 0.01$) were significant in predicting mortality and morbidity. In the results of the ROC analyses performed in our study, the predictability of the VISintra

Table 2: Postoperative unfavorable outcome

Postoperative unfavorable outcome	*n*: 73 (%)
Postoperative acute renal failure	23 (31,5)
Postoperative atrial fibrillation	48 (65,8)
Postoperative cerebral infarction or hemorrhage	6 (8,2)
Mediastinitis	7 (9,6)
30 days of mortality	25 (34,2)

n: number

Table 3: Receiver operating characteristic (ROC) analyses for VISintra and VISmax

	VISintra	VISmax
AUC	0,726 (0,615-0,837)	0,731 (0,618-0,843)
Cutoff	6,20	6,05
P-value	<0,001*	<0,001*
Sensitivity	70 (53,47-83,44)	63,41 (46,94-77,88)
Specificity	70,45 (54,8-83,24)	76,74 (61,37-88,24)
Positive predictive value	68,29 (56,66-78,02)	72,22 (59,02-82,44)
Negative predictive value	72,09 (60,79-81,15)	68,75 (58,74-77,27)
Accuracy	70,24 (59,27-79,73)	70,24 (59,27-79,73)

*$P<0.05$

Table 4: Univariant-multivariant regression analysis between independent variables with significant results

	Univariant		Multivariant	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	1,053 (1,022-1,086)	0,001*	1,026 (0,989-1,064)	0,169
Atrial Fibrillation	3,574 (1,323-9,652)	0,012*	2,768 (0,894-8,565)	0,077
Euroscore II	1,672 (1,13-2,472)	0,010*	1,094 (0,708-1,691)	0,685
CPB time	1,015 (1,007-1,023)	<0,001*	1,008 (0,998-1,018)	0,101
Extubation time	1,094 (1,027-1,164)	0,005*	1,025 (0,974-1,078)	0,341
ICU stay time	1,328 (1,101-1,601)	0,003*	1,132 (0,88-1,455)	0,335
VISintra	1,053 (1,024-1,082)	<0,001*	0,918 (0,836-1,007)	0,071
VISmax	1,079 (1,035-1,126)	<0,001*	1,148 (1,027-1,283)	0,015*

*$P<0.05$

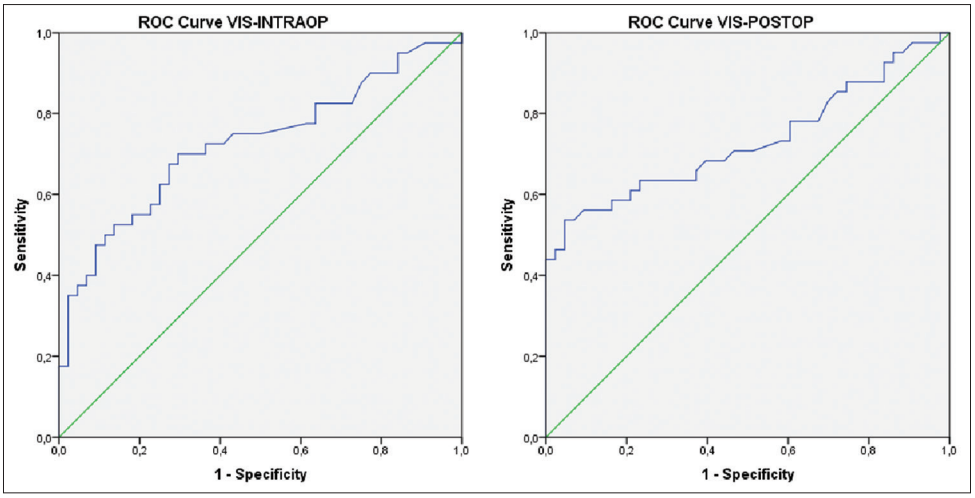

Figure 1: Receiver operating characteritics curves of VISintra and VISmax for poor outcome

and VIS max cut-off values of mortality and morbidity was found to be significant compared to other parameters evaluated in our study ($P < 0.01$). The cut-off value for VISintra was 6.20, and the cut-off value for VIS-max was 6.05. In some studies in the literature, cut-off values are reported to be between 15 and 20 in pediatric cardiac surgery and between 4.5 and 5.5 in adult cardiac surgery, and the difference in the values in the pediatric population is explained by decreased beta adrenergic receptors.[7,8,11]

As reported in the literature, advanced age and the presence of preoperative AF, high Euroscore-II value, long CPB duration, prolonged extubation time, and prolonged intensive care unit stay were also determined as independent parameters that predicted postoperative adverse events and mortality in our study. Although all the variables were observed to be univariantly effective based on the results of the logistic regression analysis performed in our study, only the VIS-max values were found to be statistically significant when multivariant analysis was performed ($P = 0.015$), and it was observed that the most appropriate time for calculating VIS was VIS-max according to the analyses performed. According to the results of our study, mortality and morbidity rates increase 1.148 times with each 1 unit increase in VIS-max value (OR value: 1.148 and *P*: 0.015).

Koponen *et al*.[9] reported that they evaluated SAPS II, APACHE II, and SOFA scores together with VIS-max in the ICU after cardiac surgery and that VIS-max showed predictive and distinctive ability for 1-year mortality, which is equivalent to SOFA score, and better than SAPS II and APACHE II. They state that the reason why VIS-max is more specific is that scores such as SOFA, SAPS, and APACHE were developed for patients with multiorgan failure in intensive care units and are not specific for cardiac patients.[9] In a large cohort of intensive care unit patients studied by Pölkki *et al*.,[13] VIS-max outperformed cvSOFA (cardiovascular SOFA) in predicting poor outcome in patients with cardiovascular failure. Therefore, they report that the cardiovascular component in the SOFA score should be replaced by VIS-max. Euroscore-II is a scoring system that is still in use in predicting mortality and morbidity, and it consists of the preoperative conditions of the patients and cardiac factors, and its probability of being affected by the parameters related to the surgery is low.[1,14,15] In studies, it has been reported that the VIS scoring system, which is calculated with the doses of vasoactive inotropic agents, is as effective as Euroscore-II or more significantly effective in predicting poor results, and that it is possible to be affected by the parameters related to the surgery.[1,2,7,8,15] Morbidity and mortality may develop in cases where a vasoinotropic agent is not used at all in CABG surgery. Therefore, we think that Euroscore-II and VIS measurements can be used together to determine mortality and morbidity.

Our study has limitations, such as being a single-center retrospective study and having a relatively limited number of patients. Due to the limited number of patients, the mortality and morbidity groups were taken together, and statistical analysis of the VIS relationship with each poor outcome could not be performed. According to the results of our study, although the predictability of VIS values for early postoperative morbidity and mortality is statistically significant, we think that multicenter studies with a higher number of patients are necessary.

CONCLUSION

In conclusion, in light of the results of our study, we think that VIS is a very easy and inexpensive score to calculate both at the end of the operation and during the intensive care unit stay. We believe that it is more specific than all other scoring systems in predicting the poor early outcomes of CABG patients. Also, according to our study results; both VIS timings were found to be statistically significant to predict mortality-morbidity. However, based on the results of the multivariant regression analysis, we think that the "VIS max" value, which is the highest VIS value calculated during the postoperative 24 hours, is the most appropriate time to calculate the VIS for routine use.

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Conflicts of interest
There are no conflicts of interest.

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