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Research Article

Evaluation of Predictors of High Vasoactive Ionotropic Score Following Mitral Valve Replacement Surgery

Dr. Bhagyashree Bhalerao[1], Dr. Vedika Agrawal[1], Dr. Shrikant Ghuge[1]

[1]Department of anaesthesia, Lokmanya Tilak municipal medical college and general hospital, Sion, Mumbai, 400022, India

ABSTRACT

This study was performed in patients undergoing mitral valve replacement surgery to know the effectiveness of predictors of high VIS (Vasoactive Inotropic Score), leading to increased requirements of inotropic supports post operatively, prolonged mechanical ventilation and ICU stay with increased morbidity and mortality. This prospective observational study was carried in cardiac operation theatre in a tertiary care hospital. 60 patients undergoing MVR were included under the study. Patient and surgical factors pre operatively and requirement of VIS post operatively, with any morbidity or mortality were studied. We found that mean age >60 years, female gender were associated with high VIS. Preoperative factors such as comorbidities (COPD, Hypertension, DM), EF between30-50%, severe pulmonary hypertension, severity of MS, hepatic and renal dysfunction have predictive value. Also, the intraoperative factors such as mean CPB time, mean aortic clamp time and duration of ventilation can predict the requirement of high VIS. Patients who require high VIS during mitral valve replacement surgery were at risk for prolonged mechanical ventilation and an extended ICU stay. Hence, through our study, we concluded that patients with the above mentioned predictors should be treated with caution.

Key Words: *Vasoactive inotropic score, Mitral valve replacement surgery, predictive factors*

***Corresponding Author**
Dr. Shakuntala Basantwani
Department of anaesthesia, Lokmanya Tilak municipal medical college and general hospital, Sion, Mumbai, 400022, India

INTRODUCTION

Mitral valve replacement surgery is usually performed in patients with mitral stenosis. Pathophysiological changes associated with severity of mitral valve disease like right ventricular dysfunction, pulmonary artery hypertension, left atrial enlargement, hepatic and renal dysfunction may be found in the preoperative period [1, 2]. Also due to the presence of coexisting pathologies like diabetes, hypertension, chronic renal disease, hypothyroidism, these patients are at increased risk for developing poor myocardial contractility leading to deterioration in ventricular function which may continue in the postoperative period [3-5]. Left ventricular dysfunction, which is common after valve replacement surgeries using cardiopulmonary bypass (CPB), and is often treated with ionotropic drugs to maintain adequate hemodynamic status [6, 7]. Positive ionotropic drugs are frequently initiated to improve post bypass ventricular function and to restore adequate end organ perfusion [8]. High ionotropic score may be required in such "high-risk" patients who can be easily identified preoperatively [7].

Patient and surgical factors that are present preoperatively are assessed for their predictive value for postoperative complications. Risk factors that are found to be significant are assigned a specific weight in the overall summation of risk [9]. The VIS is one such scale which is used to predict morbidity and mortality following cardiac surgery. The VIS is a numerical scale showing the amount of vasoactive and ionotropic score calculated using a simple formula [8].

The duration of surgery, CPB time, aortic cross-clamping time, and reperfusion time all influence the need for high VIS.

Vasoactive-Inotropic Score (VIS) was developed as successor of Ionotropic Score (IS). Ionotropic Score (IS) = Dopamine dose(mcg/kg/min) + Dobutamine dose(mcg/kg/min) + 100× Epinephrine dose(mcg/kg/min)
Vasoactive-Inotropic Score (VIS) = IS+10 × Milrinone dose(mcg/kg/min) + 100 × norepinephrine dose(mcg/kg/min) + 10000 × vasopressin dose(mcg/kg/min)

Inotropic Score (IS) = dopamine dose (μg/kg/min)
+ dobutamine dose (μg/kg/min)
+ 100 × epinephrine dose (μg/kg/min)

Vasoactive-Inotropic Score (VIS) =
IS + 10 × PDE inhibitor (milrinone or olprinone) dose (μg/kg/min)
+ 100 × norepinephrine dose (μg/kg/min)
+ 10000 × vasopressin dose (U/kg/min)

The amount of cardiovascular support required following cardiac surgery using cardiopulmonary bypass can be calculated using vasoactive-ionotropic score (VIS). The maximum VIS value within 24 h after ICU admission has been assessed as a good predictor of unfavourable outcomes [10, 11]. However, some studies have suggested a possible association between high VIS and prolong stay in intensive care unit (ICU), prolonged mechanical ventilation (PMV), poor long-term prognosis, and increased morbidity and mortality [12].

Hence, through this study, we want to assess preoperative and intraoperative predictors in patients undergoing mitral valve replacement surgery leading to requirement of high VIS.

MATERIAL AND METHODS

This was a Prospective, Observational Study done at a Cardiovascular Thoracic Surgery Operation Theatre of Tertiary care Hospital between October 2019 to October 2021. Consecutive convenient consenting sampling method. Consecutive patients over 18 years of age were included in the study. Whereas, Patients with concomitant coronary artery disease, Patients with other valvular diseases like aortic stenosis, aortic regurgitation or mitral regurgitation, Not willing to participate in the study was excluded from the study. Patients, in whom surgical plan was changed, were withdrawn from the study. All patients undergoing mitral valve surgery from October 2019 to 2021 (by Complete Enumeration Method).

Patients were explained in detail the study procedure to fullest extent possible in language best understood. Subsequently, a written informed consent was taken from each patient prior to enrolment into the study. Each subject's original consent form signed and dated by the subject / by the subject's legally acceptable representative was retained by the investigator.

A standard institutional protocol for routine pre-anaesthetic check-up were followed. Informed consent for the study were obtained from all the patients. In the operating room standard monitors like 5 lead ECG, pulse oximeter, NIBP was applied. All routine cardiovascular medications were continued until the morning of surgery. Demographic data i.e. Age, Sex, Body Mass Index (BMI), New York Heart Association (NYHA), American Society of Anaesthesiologists (ASA) (Labelled as group A factors) grading prior to surgical procedure was recorded. Patients having concomitant diseases Labelled as group B i.e. hypertension, diabetes, chronic obstructive pulmonary disease, hypothyroidism was noted. Any patients undergoing emergency surgery or having history of previous surgery was noted. Preoperative Haemoglobin (Hb), Serum Creatinine, Liver Function Test (LFT) (total Bilirubin, SGOT, SGPT) Labelled as group C were noted. Transthoracic Echocardiographic results (Labelled as group D) i.e. Mitral valve area, Left Ventricular Ejection Fraction, Left Atrial size, severity of pulmonary hypertension and right ventricular function was recorded. Premedication, anaesthesia induction and intubation were carried out as per routine operation theatre (OT) protocol. All surgical procedures were conducted under General Anaesthesia with midline sternotomy approach with Cardio Pulmonary Bypass (CPB) using heparin. The duration of Cardio Pulmonary Bypass (CPB) and cross clamp time Labelled as group E was noted. On pump Haematocrit was noted. If Haematocrit was less than 21, blood was added. After completion of surgery aortic cross clamp was released and patient was weaned from Cardio Pulmonary Bypass (CPB) using positive ionotropic agents. Ionotropic support required for weaning the patient from CPB were noted and recorded. The signs of low cardiac output i-e systolic blood pressure of < 90 mm of Hg, MAP<65 mm of Hg, Urine output of < 0.5 ml/kg/hour, were recorded and ionotropic support was adjusted accordingly to improve cardiac output. Patients were transferred to post surgical intensive care unit and Ionotropic score was noted at 6 hours, 12 hours, 18 hours, 24 hours, 30 hours, 36 hours, 42 hours and 48 hours after surgery. The duration of ionotropic score, length of intensive care unit stay was also recorded.

OBSERVED PARAMETERS

Demographic data: Age, Sex, Body Mass Index (BMI), New York Heart Association (NYHA) class, American Society of Anaesthesiologists (ASA) grading (Group A).

Clinical: Hypertension, Diabetes, Chronic obstructive pulmonary disease, Hypothyroidism (Group B).

Laboratory Findings: Haemoglobin, Renal Function Test: Blood Urea Nitrogen, Serum creatinine, Liver Function Test: Total Bilirubin, SGOT, SGPT, Thyroid Function Test: T3, T4, TSH Values (Group C).

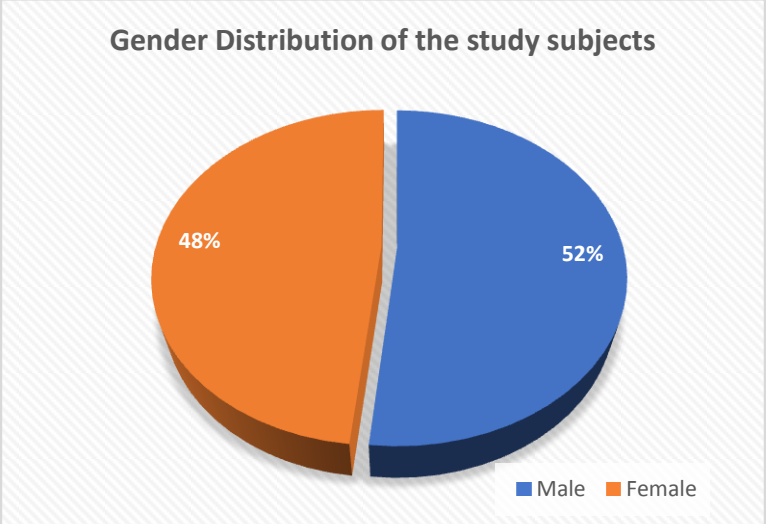
Echocardiographic results: Mitral valve area, Left ventricular Ejection Fraction, Left Atrial size, Severity of pulmonary hypertension, Severity of mitral regurgitation (Group D)

On pump factors: Duration of Cardio Pulmonary Bypass, Duration of cross clamp, Blood added / not added (Group E).

OBSERVATION AND RESULT

A total of 60 eligible patients fulfilling the inclusion/exclusion criteria were taken in our study. Statistical Analysis was carried out using SPSS version 20.0 software, Excel and Open-epi. Descriptive statistics were presented as median [inter-quartile range (IQR)] or mean (standard deviation) for continuous variables. Logistic regression modelling was used to assess association between predictive factors and the primary outcome.

Graph 1: Gender distribution of the study subjects (n=60)



Graph 1 shows the gender distribution of patients. Out of 60 patients, 31 (52%) patients were male and 29 (48%) patients were female.

Table 1: Age and gender distribution of the study population (n=60)

Sr. No	Age Group	Males	Females	Total
1	20-35	6(19.4%)	4(13.8%)	10(16.7%)
2	36-50	8(25.8%)	0(0%)	8(13.3%)
3	51-65	4(12.9%)	13(44.8%)	17(28.3%)
4	66-80	13(41.9%)	12(41.4%)	25(41.7%)
5	Total	31	29	60

Table 1 shows distribution of patients according to age.10 patients belong to age group 20-35 and amongst them 6 were males and 4 were females. Age group of 66-80 years had the 25 patients i.e. 41.7% followed by 51-65 years (28.3%) followed by 36-50 years (13.3%) and 20-35 years (16.7%) of age group.

Graph 1: Age and gender distribution of the study population (n=60)

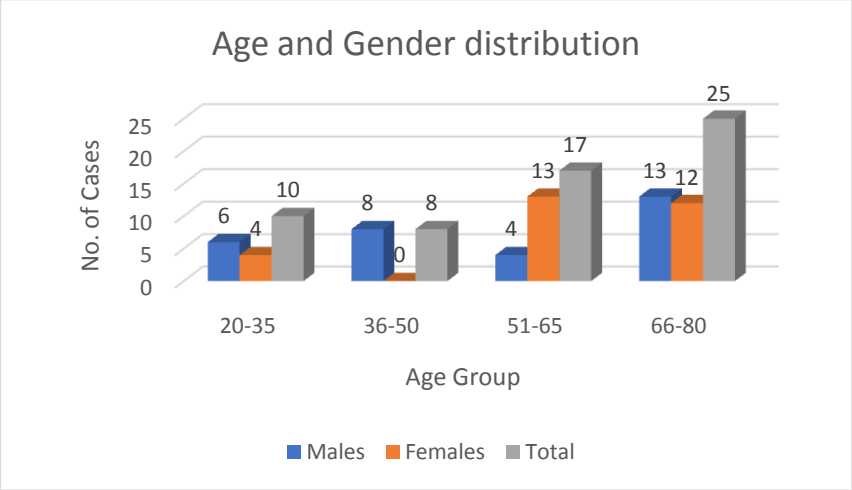


Table 2: Co-morbidity distribution of the study subjects (n=60)

Sr. No	Co-morbidity	No. of cases	Percentage
1	NIL	37	61.7%
2	Diabetes	13	21.7%
3	Hypertension	13	21.7%
4	Hypothyroidism	3	5.0%
5	COPD	1	1.7%

Table 2 shows preoperative comorbidities of the patients. 13 (21.7%) patients had Diabetes, Hypertension was present in 13 (21.7%) patients, Hypothyroidism in 3 (5%) patients, COPD was found in 1 (1.7%) study subject.

Graph 2: Co-morbidity distribution of the study subjects (n=60)

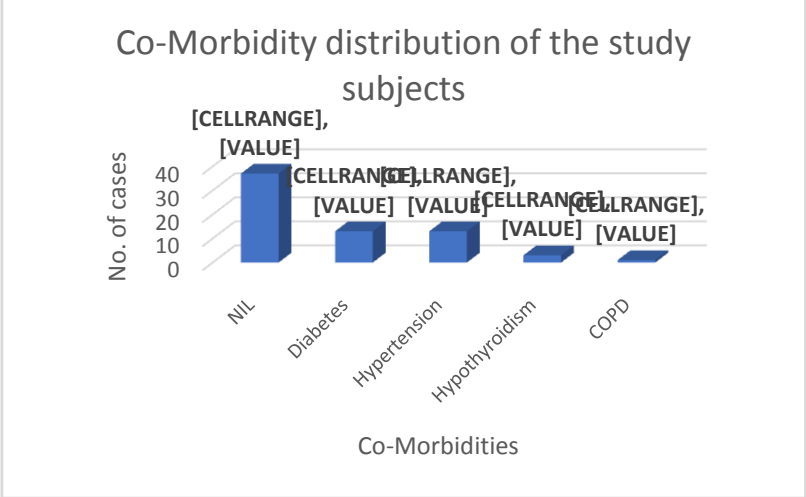


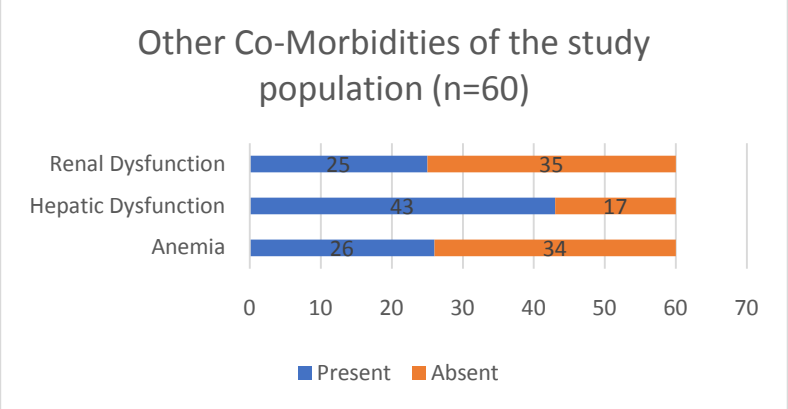
Table 3: Group C predictors of the study population (n=60)

Sr. No	Group C predictors	Present	Absent
1	Anemia	26(43.33%)	34(56.67%)

2	Hepatic dysfunction	43(71.7%)	17(28.3%)
3	Renal dysfunction	25(41.66%)	35(58.33%)

Table 3 shows Group C predictors in study population and it was found that hepatic dysfunction was present in 43 (71.7%) subjects, anaemia was found in 26 (43.33%) patients and renal dysfunction was evident in 25 (41.66%) subjects.

Graph 3: Group C of the study population (n=60)



Echocardiographic findings: Group D predictors

Table 4: MV Stenosis Grade Distribution (n=60)

Sr. No	MVA Grade	No. of cases	Percentage
1	Moderate	29	48.3%
2	Severe	31	51.7%

Mitral valve stenosis was categorized into moderate and severe categories according to mitral valve area. It was seen that 31 (51.7%) patients had severe mitral valve stenosis and 29 (48.3%) patients had moderate mitral valve stenosis.

Graph 4: MV Stenosis Grade Distribution (n=60)

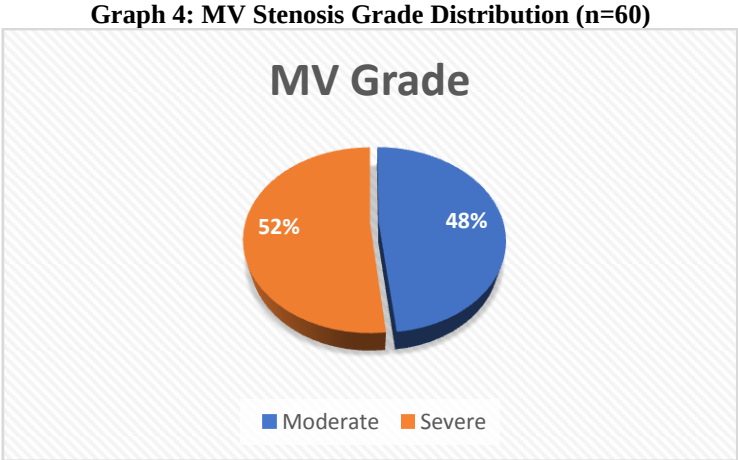


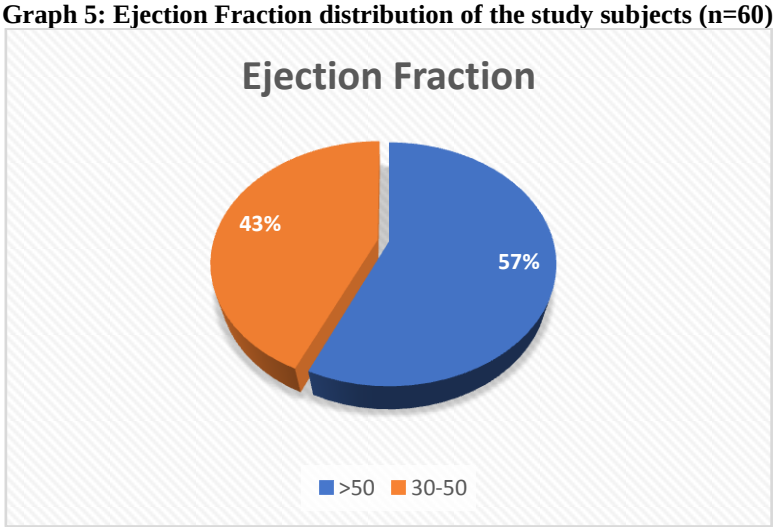
Table 5: Ejection Fraction distribution of the study subjects (n=60)

Sr. No	EF	No. of Cases	Percentage
1	>50	34	56.7%

2	30-50	26	43.3%
3	**Total**	**60**	100.0%

Patients were categorized into EF >50, EF between 30-50 and EF below 30. Total 34 patients i.e. 56.7% had EF >50 and remaining 26 (43.3%) patients had EF between 30-50.

Graph 5: Ejection Fraction distribution of the study subjects (n=60)



Group E predictors:

Table 6: Intra-Operative Blood Transfusion(n=60)

Sr. No	Intra-Op Blood Transfusion	No. of cases	Percentage
1	Transfused	20	33.3%
2	Not- Transfused	40	66.7%
3	**Total**	**60**	100.0%

In our study, 20 (33.3%) patients required intra-operative blood transfusion and 40 (66.7%) patients did not require blood transfusion.

Graph 6: Intra-Op blood transfusion(n=60)

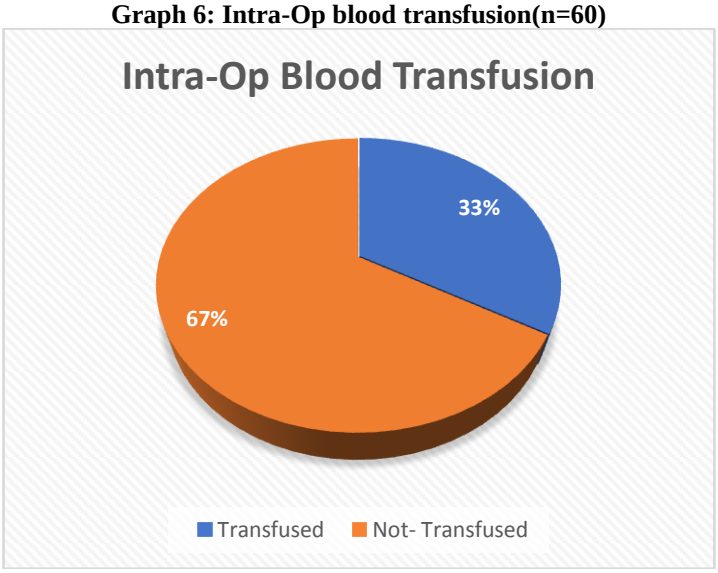
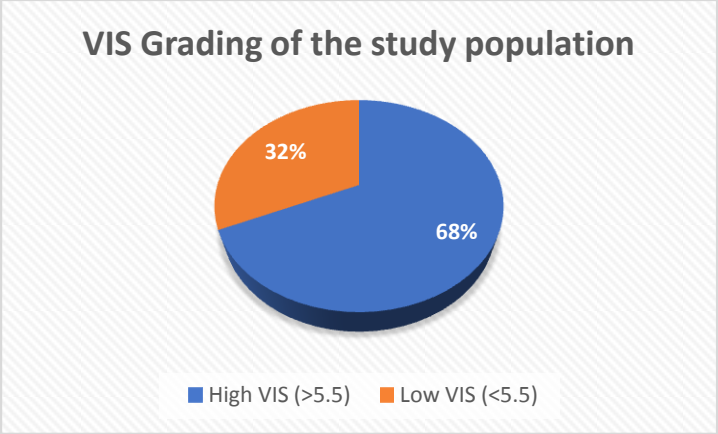


Table No 7: VIS grading of the study population (n=60)

Sr. no	VIS	No. of cases	Percentage
1	High VIS (>5.5)	41	68.3%
2	Low VIS (<5.5)	19	31.7%

Patients were categorized into 2 groups low VIS (< 5.5) and high VIS (> 5.5). In our study, total 41 (68.3%) patients required high VIS in postoperative period and 19 (31.7%) patients required low VIS.

Graph No 7: VIS grading of the study population (n=60)



GROUP A PREDICTORS:

1) Gender vs VIS

Gender vs VIS	High VIS		Total
	NO	YES	
Female	4(13.8%)	25(86.25%)	29
Male	15(48.4%)	16(51.6%)	31
Total	19	41	60

$\chi 2 = 8.287$, df = 1, p = 0.004; odds ratio: 5.89(1.68-17.98)

In this study, 25 out of 29 i.e. 86.25% patients were females and 16 out of 31 i.e. 51.6% were male who required high VIS. Chi-square test was found to be significant (p = 0.004) when gender distribution was compared.

2) Age vs VIS

Age	High VIS		Total
	NO	YES	
Age >60	0(0%)	38(100%)	38
Age <60	19(86.36%)	3(13.63%)	22
Total	19	41	60

$\chi 2 = 48.03$, df = 1, p = <0.0001;

In this study, all 38 (100%) patients above 60 years and 3 out of 22 i.e. 13.63% patients with Age <60 years required high VIS. Age >60 years was found to be a risk factor for high VIS requirement, when Chi-square test was applied (p = <0.0001)

GROUP B PREDICTORS:

Comorbidities vs VIS

Co-morbidities vs VIS	High VIS		Total
	NO	YES	
Absent	18(48.6%)	19(51.4%)	37
Present	1(4.3%)	22(95.75%)	23
Total	19	41	60

$\chi 2 = 12.864$, df = 1, p = <0.0001; odds ratio: 20.8(2.75-170.02)

In this study, 22 out of 23 i.e. 95.75% patients with comorbiditiesand 19 out of 37 i.e. 51.4% patients without comorbidities required high VIS. When chi-square test was applied result was significant. (p = <0.0001)

GROUP C PREDICTORS:

1) Anaemia vs VIS

Anaemia vs VIS	High VIS		Total
	NO	YES	
Absent	14(41.2%)	20(58.8%)	34
Present	5(19.2%)	21(80.8%)	26
Total	19	41	60

$\chi 2 = 3.27$, df = 1, p = 0.07;

Anaemia was present in 21 (80.8%) patients who required high VIS and was absent in 20 (58.8%) patients who required high VIS. When chi-square test was applied, association of anaemia and high VIS was not found significant. (p = 0.07)

2) Hepatic dysfunction vs VIS

Hepatic Dysfunction vs VIS	High VIS		Total
	NO	YES	
Absent	9(52.9%)	8(47.1%)	17
Present	10(23.3%)	33(76.7%)	43
Total	19	41	60

$\chi 2 = 4.962$, df = 1, p = 0.026; odds ratio: 3.7(1.33-12.16)

In our study, 33 (76.7%) out of 43 patients with hepatic dysfunction and 8 (47.1%) out of 17 patients without hepatic dysfunction required high VIS. According to chi-square test, this association was found to be significant with p = 0.026.

3) Renal dysfunction vs VIS

Renal Dysfunction vs VIS	High VIS		Total
	NO	YES	
Absent	16(39.02)	25(60.98)	41

Present	1(5.26)	18(94.74)	19
Total	19	41	60

$\chi 2 = 7.288$, df = 1, p = 0.006; odds ratio: 11.52(1.751-127.2)

In our study, 18 (94.74%) out of 19 patients with renal dysfunction and 25 (60.98%) out of 41 patients without renal dysfunction required high VIS. When Chi-square test was applied, it was found that renal dysfunction was not associated with increased risk of high VIS. (p = 0.006)

GROUP D PREDICTORS:

1) MV stenosis grade vs VIS

MV Grade vs VIS	High VIS		Total
	NO	YES	
Moderate	7(24.1%)	22(75.9%)	29
Severe	12(38.7%)	19(61.3%)	31
Total	19	41	60

$\chi 2 = 1.477$, df = 1, p = 0.225

In our study, 19 (61.3%) out of 31 patients with severe MV stenosis and 22 (75.9%) out of 29 patients with moderate MV stenosis required high VIS. When Chi-square test was applied, Severity of Mitral valve stenosis did not predict need for high VIS. (p = 0.225)

2) Ejection fraction vs VIS

EF vs VIS	High VIS		Total
	NO	YES	
>50	18(52.9%)	16(47.1%)	34
30-50	1(3.8%)	25(96.25)	26
Total	19	41	60

$\chi 2 = 16.41$, df = 1, p = <0.0001; Odds ratio 28.125(3.413-231.79)

25 (96.25%) patients in 30-50 % EF group required high VIS and 16 (47.1%) patients with EF above 50% required high VIS. When Chi-square test was applied, it was seen that reduced ejection fraction i.e. patients in group of EF between 30-50 were associated with increased risk of high VIS. (Chi square test; p = <0.0001)

3) Pulmonary hypertension vs VIS

Pulmonary HTN vs VIS	High VIS		Total
	NO	YES	
Mild	15(75%)	5(25%)	20
Moderate	4(13.8%)	25(86.2%)	29
Severe	0	11(100%)	11
Total	19	41	60

$\chi 2 = 26.735$, df = 2, p = <0.0001

In our study, we found that patients having severe pulmonary hypertension were associated with increased risk of high VIS. (Chi square test; p = <0.0001)

GROUP E PREDICTORS:

1) Blood transfusion vs VIS

Blood Transfusion vs VIS	High VIS		Total
	NO	YES	
Transfused	4(20%)	16(80%)	20
Not- Transfused	15(37.5%)	25(62.5%)	40
Total	19	41	60

$\chi 2 = 1.887$, df = 1, p = 0.170

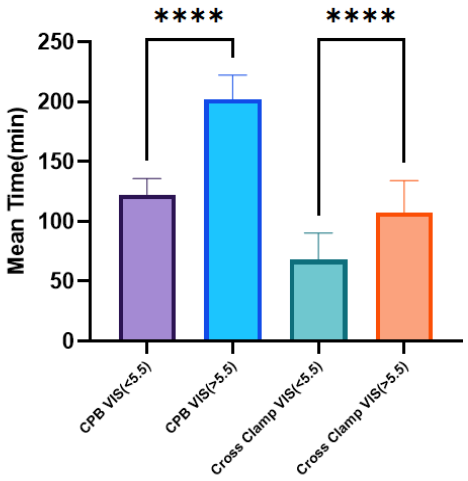
Our study found no association between perioperative blood transfusion and high VIS. (Chi square test; p = 0.170)

2) CPB and Cross clamp time vs VIS

Sr. No	Parameter	VIS (<5.5)	VIS (>5.5)	p Value
1	CPB	122.5(13.21)	201.7(20.48)	<0.0001
2	Cross Clamp	67.84(22.56)	107.1(27.06)	<0.0001

Mean cardio-pulmonary bypass (CPB) time was 201.7 in high VIS group. It was 122.5 minutes in low VIS group. When unpaired t-test was applied, difference was found to be significant.

Similarly, mean aortic cross-clamp time was 107.1 minutes in high VIS group and was 67.84 minutes in low VIS group. Unpaired t-test result for this parameter was found to be significant.



Linear regression of Mean VIS vs Duration of Mechanical Ventilation

A simple linear regression was calculated to see the effect of mean VIS on duration of mechanical ventilation. A significant regression equation was found. [F (1,58) = 15.109, p < 0.000] with r^2 of 0.207. Individual parameter i.e. mean VIS was examined further and t was found that mean VIS (t=3.887, p=0.00) was a significant predictor of duration of mechanical ventilation.

Model Summary

R	R Square	Adjusted R	Std. Error of	Change Statistics

		Square	the Estimate	R Square Change	F Change	df1
0.455	0.207	0.193	4.257	0.207	15.109	1

ANNOVA

	Sum of Squares	Df	Mean Square	F	Sig.
Regression	273.737	1	273.737	15.109	.000[b]
Residual	1050.846	58	18.118		
Total	1324.583	59			

Coefficient Parameters

	Unstandardized Coefficients		Standardized Coefficients	T	Sig.
	B	Std. Error	Beta		
Mean VIS	0.906	0.233	0.455	3.887	0

Linear regression of Mean VIS vs Duration of ICU Stay

A simple linear regression was calculated to see the effect of mean VIS on duration of mechanical ventilation. A significant regression equation was found. [F (1,58) = 34.901, $p < 0.000$] with r^2 of 0.307. Individual parameter i.e. mean VIS was examined further and it was found that mean VIS (t=5.908, p=0.00) was a significant predictor of duration of ICU stay.

Model Summary

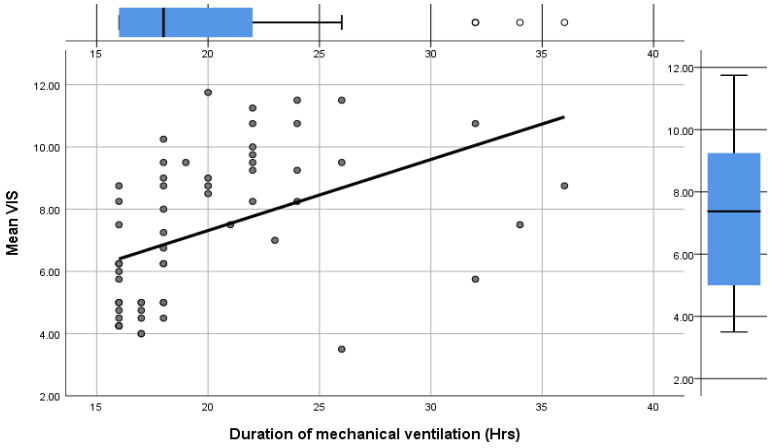
R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics		
				R Square Change	F Change	df1
0.613	0.307	0.365	0.973	0.376	34.901	1

ANNOVA

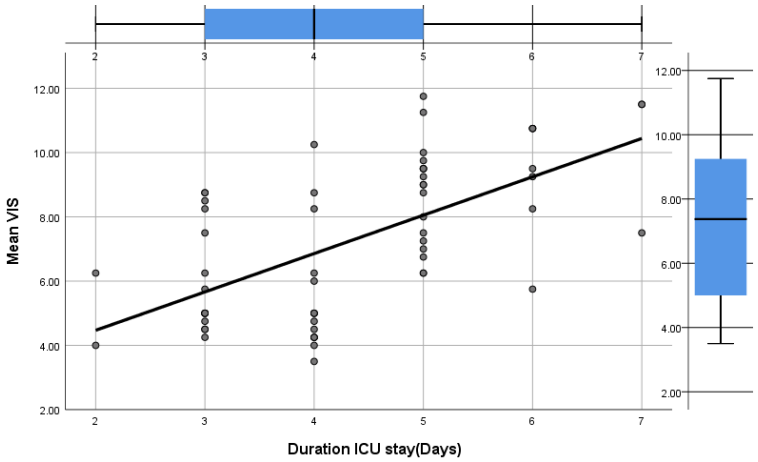
	Sum of Squares	Df	Mean Square	F	Sig.
Regression	33.035	1	33.035	34.901	.000[b]
Residual	54.899	58	.947		
Total	87.933	59			

Coefficient Parameters

	Unstandardized Coefficients		Standardized Coefficients	T	Sig.
	B	Std. Error	Beta		
Mean VIS	0.315	0.053	0.613	5.908	.0000



Graph: Duration of mechanical ventilation vs Mean VIS



Graph: Duration of ICU stay vs Mean VIS

DISCUSSION

Mitral valve replacement surgery is usually performed in patients with moderate or severe mitral stenosis mostly belonging to American society of anaesthesiologist physical status II or III and IV. Many comorbid conditions increase the risk for developing poor myocardial contractility leading to Left ventricular dysfunction, which is common after valve replacement surgeries using cardiopulmonary bypass (CPB). Deterioration of ventricular dysfunction requires ionotropic drugs to maintain adequate hemodynamic status. There is only a small amount of blood that remains in the left atrium. With the contraction of the left atrium (the "atrial kick") during late ventricular diastole, this small amount of blood fills the left ventricle.

Mitral valve areas less than 2 cm^2 causes an impediment to the blood flow from the left atrium into the left ventricle. This creates a pressure gradient across the mitral valve. As the gradient across the mitral valve increases, the left ventricle requires the atrial kick to fill with blood. Mitral valve area less than 1 cm^2 causes an increase in left atrial pressure. The normal left ventricular diastolic pressure is 5 mmHg. A pressure gradient across the mitral valve of 20 mmHg due to severe mitral stenosis will cause a left atrial pressure of about 25 mmHg. This left atrial pressure is transmitted to the pulmonary vasculature resulting in pulmonary hypertension. Due to hypoxemia, there may be pulmonary vasoconstriction as well that further elevates right heart pressures. The elevated pulmonary capillary wedge pressure leads to rise in interstitial edema which also increases the load on right ventricle. Finally, intimal hyperplasia and medial hypertrophy develop in the pulmonary vascular bed. All these changes leads to rise in pulmonary arterial pressure and right ventricle begins to dilate and fail. As a result of the dilation of the right ventricle, tricuspid regurgitation develops. The jugular venous pressure may be elevated. Other signs of right heart failure such as hepatic congestion and pedal edema may also eventually develop.

As left atrial pressure remains elevated, the left atrium will increase in size. As the left atrium increases in size, there is a greater chance of developing atrial fibrillation. If atrial fibrillation develops, the atrial kick is lost.

Thus, in severe mitral stenosis, the left ventricular filling is dependent on the atrial kick. With the loss of the atrial kick, there is a decrease in cardiac output and sudden development of congestive heart failure. Mitral stenosis progresses slowly from initial signs of mitral stenosis to NYHA functional class II symptoms to atrial fibrillation to NYHA functional class III or IV symptoms. The severity of mitral stenosis can be assessed on the basis of several parameters such as mitral valve area, severity of PAH and LA size. The preoperative evaluation is accomplished by echocardiographic examination.

The vasoactive-inotropic score (VIS) objectively quantifies the degree of cardiovascular support using a simple formula that standardizes the dose of different inotropes required to take the patient off pump and in the intensive care unit. Requirement of inotropes and vasopressors correlates not only with disease severity and its consequences, but also with other comorbid conditions. The need for vasoactive drugs is included in mortality prediction scores such as SOFA score, EuroSCORE II or REMEMBER score.

Hence, in this prospective, observational study, we evaluated various predictors which necessitated the requirement of high inotropes in the post bypass period and in the intensive care unit. We also assessed the duration of mechanical ventilation and ICU stay in patients requiring high VIS.

In our study, out of 60 patients, 41 (68.3%) patients needed high VIS and 19(31.7%) needed low VIS.

Predictors associated with requirement of high VIS:

GROUP A PREDICTORS:

1) Gender

Muller et al (2002) conducted a retrospective study to analyse the effects of preoperative and intraoperative factors on the requirement of inotropic support after cardiopulmonary bypass (CPB). They found that females were more prone to require high VIS. **Imdad Ahmed et al (2009)** also found that female gender was one of the risk factors associated with need for inotropic support. In our study, 25 out 29 patients i.e. 86.25% females required high VIS and 16 out of 31 i.e. 51.6% males required high VIS which was found to be statistically significant.

2) Age

Previous studies by **Muller et al (2002)** found that age of >65 year indicates an increased risk for inotropic support. **Imdad Ahmed et al (2009)** found that age ≥ 70 years was significantly associated with inotropic use in patient had undergone concomitant coronary artery bypass graft and aortic valve replacement. Similar to these studies, in our study, all patients (100%) with Age >60 years required high VIS. Statistical analysis showed, Age >60 was found to be a risk factor for high VIS requirement.

Advanced age is always accompanied by a general decline in organ function, especially because of changes in the structure and function of the heart and vasculature that will ultimately affect cardiovascular performance, even in the absence of overt coexisting diseases.

GROUP B PREDICTORS:

Co-morbidities

Muller et al (2002) demonstrated that patients with COPD had an increased risk of use of positive inotropic drugs as patients with COPD commonly had mild-to-moderate increase in pulmonary artery pressure. An increased afterload may influence right ventricular performance after CPB.In our study, 22 out of 23 patients i.e. 95.75% patients with comorbiditiesand 19 out of 37 i.e. 51.4% patients without comorbidities required high VIS. When chi-square test was applied result was significant (p = <0.0001) and patients with comorbidities like Hypertension, COPD, DM, Hypothyroidism were more likely to require high VIS.

GROUP C PREDICTORS:

1) Preoperative Ejection fraction (EF)

Muller et al (2002) concluded that low preoperative ejection fraction as a predictor of low cardiac output after CPB in patients undergoing CABG surgery as well as in those undergoing valve surgery. **Imdad Ahmed et al (2009)**study revealed that patients with left ventricular ejection fraction (LVEF) ≤ 40% were more likely to receive inotropic support (p = 0.001).In our study, patients were categorized according to preoperative Ejection fraction (EF) into EF >50, EF between 30 to 50. 25 patients in 30-50 % EF group required high VIS and only one did not require high VIS. It was found that reduced ejection fraction i.e. patients in group of EF between 30-50 were associated with increased risk of high VIS.

2) Pulmonary hypertension

Imdad Ahmed et al (2009) found that presence of pulmonary hypertension was not associated with increased use of inotropic support. In our study, we classified the patients into mild, moderate and severe pulmonary hypertension categories. 11 out of 11 in severe category, 25 out of 29 in moderate category and 5 out of 20 in mild category required high VIS support. Statistical analysis revealed that patients having severe pulmonary hypertension were associated with increased risk of high VIS.

3) Severity of Mitral valve stenosis

In our study, 19 out of 31 patients with severe MV stenosis and 22 out of 29 patients with moderate MV stenosis required high VIS. We found that, severity of Mitral valve stenosis did not predict need for high VIS.

GROUP D PREDICTORS:

1) Anaemia

In our study, 20 out of 34 non-anaemic patients and 21 out of 26 anaemic patients required high VIS. When statistical analysis was done, we did not find anaemia as a risk factor for high VIS requirement.

2) Hepatic & Renal Dysfunction

Muller et al (2002) Their study included 1471 adult patients undergoing elective cardiac surgery with CPB. Chronic renal failure was analysed for predictive power of the need for positive inotropic drugs. Also, **Imdad Ahmed et al (2009)** identified chronic kidney disease stage 3 to 5 as a independent predictors of inotrope use in their study.

In our study, 18 out of 19 patients with renal dysfunction and 25 out of 41 patients without renal dysfunction required high VIS. Statistical analysis showed that renal dysfunction was significantly associated with requirement of high VIS.

In our study, 33 out of 43 patients with hepatic dysfunction and 8 out of 17 patients without hepatic dysfunction required high VIS. On statistical analysis, it was seen that hepatic dysfunction was significantly associated with requirement of high VIS.

GROUP E PREDICTORS:

1) Mean cardio-pulmonary bypass (CPB) time

Depressed myocardial function is common after cardio-pulmonary bypass (CPB). Inotropes are frequently administered to improve post-bypass ventricular dysfunction.

Muller et al (2002) in their study of the 1471 patients, 1140 underwent CABG surgery, 231 had cardiac valve surgery and 100 underwent cardiac valve surgery and CABG. They concluded that increased CPB time was associated with requirement for high VIS. In our study, mean cardio-pulmonary bypass (CPB) time was 201.7 in high VIS group and 122.5 minutes in low VIS group. After statistical analysis, it was found that mean cardio-pulmonary bypass (CPB) time determines the need for high VIS.

2) Mean aortic cross-clamp time

Muller et al (2002) found that an aortic cross-clamping time of >90 min was an independent predictor of post-CPB need for positive inotropic drugs with regards to intraoperative factors.

Moh'd, A.F. et al. (2021) studied 609 adult patients posted for elective cardiac surgery between December 2019 and December 2020 were enrolled. Most patients (87.2%) underwent coronary artery bypass grafting (CABG) and 78 patients (12.8%) underwent single heart valve procedure. Operative time ranged from 120 to 402 min and averaged 259.4 min (SD ± 45.9 min). ACC time ranged from 15 to 159 min and averaged 50.56 min (SD ± 19.4 min). Factors associated with significantly longer ACC time were smoking (OR = 1.89 (95% CI 1.3–2.74), *p* value = 0.01), respiratory disease (OR = 0.48 (95% CI 0.24–0.96), *p* value = 0.039), obesity (OR = 1.76 (95% CI 1.18–2.63), *p* value = 0.005) and AVR (OR = 2.11 (95% CI 1.17–3.83), *p* value = 0.013). Low cardiac output syndrome (LCOS) was observed in 19.2% of patients. Longer than average ACC time was associated with increased use of inotropes (*p* value < 0.001), intra-aortic balloon pump (*p* value < 0.001) The average intensive care unit length of stay (ICULOS) was 1.64 days (SD ± 1.1 days).

In our study, mean aortic cross-clamp time was 107.1 minutes in high VIS group and it was 67.84 minutes in low VIS group. Statistical analysis found the association of duration of aortic cross-clamping and requirement of high VIS to be significant.

3) Perioperative blood transfusion

In our study, we found that there was no association between perioperative blood transfusion and high VIS requirement.

4) Duration of mechanical ventilation

In a retrospective study by **Gaies et al (2002**) where they studied One hundred seventy-four patients between 0 to 6 months of age admitted to the cardiothoracic intensive care unit after cardiac surgery with cardiopulmonary bypass found that patients in the high VIS category were more likely than those in the low VIS category to have a longer time to initial extubation.

In our study, a simple linear regression was used to calculate the effect of mean VIS on duration of mechanical ventilation. A significant regression equation was found. [F (1,58) = 15.109, $p < 0.000$] with r^2 of 0.207. Individual parameter i.e. mean VIS was examined further and it was found that mean VIS (t=3.887, p=0.00) was a significant predictor of duration of mechanical ventilation.

5) Duration of ICU stay

In the similar study by Gaies et al (2002), amongstone hundred seventy-four patients between 0 to 6 months of age, in the high VIS group longer ICU stay was found as compare to low VIS group.

Yumiko Yamazaki et al. (2018), in their retrospective cohort study of 129 adult cardiac surgery patients, after adjusting for the EuroSCORE, preoperative ejection fraction, and cardiopulmonary bypass time, a high VIS at the end of surgery was associated with a poor outcome with an adjusted odds ratio of 4.87 (95% confidence interval 1.51-18.94; p = 0.007). After controlling for the EuroSCORE and bypass time, patients with a high VIS experienced longer ICU stay (hazard ratio 1.62; 95% confidence interval 1.10-2.39; p = 0.015) and needed longer ventilation (hazard ration 1.87; 95% confidence interval 1.28-2.74, p = 0.001).

Koponen et al. (2019), in their single-centre retrospective cohort study included 3213 cardiac surgery patients and found that VIS predicted the length of ICU stay.

In our study, a simple linear regression was used to calculate the effect of mean VIS on duration of ICU stay. A significant regression equation was found. [F (1,58) = 34.901, $p < 0.000$] with r^2 of 0.307. Individual parameter i.e. mean VIS was examined further and it was found that mean VIS (t=5.908, p=0.00) was a significant predictor of duration of ICU stay.

CONCLUSION

Hence, through our study, we concluded that patients with the abovementioned predictors should be treated with caution because they are more likely to require a high VIS during mitral valve replacement surgery.

Patients who require high VIS during mitral valve replacement surgery were at risk for prolonged mechanical ventilation and an extended ICU stay.

ETHICS APPROVAL: Approved by Institutional Ethics Committee

INFORMED CONSENT FORM

I have been explained about this study in the language which I understand. I have been told that my participation in above study is voluntary and I am aware that I can opt out of the study at any time without giving any reason to do so. I am also hereby informed that my refusal to participate in the above study will not affect my treatment by any means.

I hereby give you the permission for academic presentation or publication of information obtained as a result of my participation in the study. I understand that medical records that reveal my identity will remain confidential unless required by the law or as stated above. I understand that I will not get any financial incentives for participation in this study. I hereby agree to participate in the study and I shall fully cooperate with my doctors throughout the study.

Investigator's sign:	Patient's sign:
Name:	Name:
Date:	Date:

सहमतीपत्र

मुझेइसअध्ययनकेबारेमेंउसभाषामेंसमझायागयाहैजिसेमैंसमझताहूं।मुझेबतायागयाहैकिउपरोक्तअध्ययनमेंमेरीभागीदारीस्वैच्छिक हैऔरमुझेपताहैकिमैंऐसाकरनेकाकोईकारणदिएबिनाकिसीभीसमयअध्ययनसेबाहरनिकलसकताहूं।मुझेयहभीबतायागयाहैकिउपरो क्तअध्ययनमेंभागलेनेसेमेरेइनकारकामेरेउपचारपरकोईप्रभावनहींपड़ेगा।

मैंआपकोअध्ययनमेंमेरीभागीदारीकेपरिणामस्वरूपप्राप्तशैक्षिकप्रस्तुतियासूचनाकेप्रकाशनकीअनुमतिदेताहूं।मैंसमझताहूंकिमेरीपह चानबतानेवालेमेडिकलरिकॉर्डतबतकगोपनीयरहेंगेजबतककिकानूनद्वाराआवश्यकनहोयाजैसाकिऊपरकहागयाहै।मैंसमझताहूंकिमु झेइसअध्ययनमेंभागलेनेकेलिएकोईवित्तीयप्रोत्साहननहींमिलेगा।मैंइसअध्ययनमेंभागलेनेकेलिएसहमतहूंऔरमैंअपनेडॉक्टरोंकेसा थपूरेतन्मयतासेसहयोगकरूंगा।

जांचकर्ताकेहस्ताक्षर - रुग्णकेहस्ताक्षर -

नाम – नाम –

तारीख - तारीख-

माहितीसंमतीपत्र

मलासमजलेल्याभाषेतयाअभ्यासाबद्दलमलास्पष्टकेलेआहे.

मलासांगितलेगेलेआहेकीवरीलअभ्यासामध्येमाझासहभागऐच्छिकआहेआणिमलायाचीजाणीवआहेकीअसेकोणतेहीकारणनदेतामीक धीहीअभ्यासातूनबाहेरपडूशकतो.

वरीलअभ्यासातभागघेण्यासनकारदेण्यानेमाझ्याउपचारांवरकोणत्याहीप्रकारेपरिणामहोणारनाहीहेमलायाद्वारेदेखीलकळविण्यातआ लेआहे.

अभ्यासामध्येमाझ्यासहभागाच्यापरिणामीमीशैक्षणिकसादरीकरणासाठीकिंवामिळविलेल्यामाहितीच्याप्रकाशनासमीयाद्वारेपरवान गीदेतो.

मलासमजलेआहेकीवैद्यकीयनोंदीजीमलाओळखतआहेतकायद्यानुसारआवश्यकअसल्याशिवायकिंवावरसांगितल्याशिवायगोपनीय राहतील. मलासमजलेकीयाअभ्यासामध्येभागघेण्यासाठीमलाकोणतीहीआर्थिकप्रोत्साहनमिळणारनाही.

मीयाद्वारेअभ्यासातभागघेण्याससहमतआहेआणिसंपूर्णडॉक्टरांकडेमीसंपूर्णपणेसहकार्यकरेन.

तपासकर्त्याचीसही - रुग्णाचीसही-

नाव - नाव-

दिनांक - दिनांक-

ABBREVIATIONS

	VIS		Vasoactive Inotropic Score
	CPB		Cardio Pulmonary Bypass
	ASA		American Society of Anaesthesiology
	PMV		Prolonged Mechanical Ventilation
	ICU		Intensive Care Unit
	MV		Mitral Valve
	PMBV		Percutaneous Mitral Balloon Valvuloplasty
	MVR		Mitral Valve Replacement
	MS		Mitral Stenosis
.	CMC		Closed Mitral Commissurotomy
.	MR		Mitral Regurgitation
.	LCOS		Low Cardiac Output Syndrome
.	BMI		Body Mass Index
.	OR		Odds Ratio
.	CABG		Coronary Artery Bypass Grafting
.	NYHA		New York Heart Association
.	COPD		Chronic Obstructive Pulmonary Disease
.	XCL		Cross Clamp
.	PDE		Phosphodiesterase

.	ECMO		Extra Corporeal Membrane Oxygenation
.	MODS		Multiple Organ Dysfunction Syndrome
.	RFT		Renal Function Test
.	LFT		Liver Function Test
.	HTN		Hypertension
.	DM		Diabetes Mellitus
.	SGPT		Serum Glutamic Pyruvic Transaminase
.	SGOT		Serum Glutamic Oxaloacetic Transaminase
.	BUN		Blood Urea Nitrogen
.	EF		Ejection Fraction
30.	Hb		Haemoglobin
31.	TB		Total Bilirubin
32.	ACC		Aortic Cross Clamp
33.	T		Hypothyroidism

Conflict of interest: None

Authors contribution: SG collected all the data and did thorough examination. VA and BB analysed the data and did interpretation of results. SB was a major contributor in writing the manuscript. All the authors read and approved the final manuscript.

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