Original Article

Inotropes Score (IS) And Vasoactive Inotropes Score (VIS) After Congenital Heart Disease Surgery: Association and Outcome at PCICU of A Tertiary Cardiac Hospital

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ABSTRACT

Background and objectives

Children with congenital heart diseases (CHD) undergoing surgical correction are at high risk for serious post-operative morbidity and mortality. This study was conducted to figure out the association of inotropes score (IS) and vasoactive inotropes score (VIS) with clinical outcomes after congenital heart surgery.

Materials and methods

This is a retrospective observational study (total study population 477, April-December 2017) were done in a pediatric cardiac ICU (PCICU) of a tertiary cardiac hospital. Along with several demographic, operative and post-operative variables, doses of inotropic and vasoactive medications were documented for the first 48hrs after PCICU admission. Maximum IS and VIS level in the first 48hrs was also recorded. Linear and multivariant regression analyses were done to find the association of IS / VIS with pre-operative, intra-operative and post-operative variables in order to determine the association between IS / VIS and clinical outcome after pediatric cardiac surgery.

Results

A total 477 patients underwent cardiac surgery for CHD during the study period and among them 5.4% (3) neonate, 14.67% (70) infant and 80.08% (382) were children. Optimum cut-off value of high IS and VIS was detected by ROC curve, 7.2 (sensitivity 58%, specificity 94%) and 17.5 (sensitivity 86%, specificity 92%) respectively. Study population with early age, high level of cardiac complexity, high CPB time, high cross clamp time, kept open sternum in post-operative period were strongly associated with high VIS (≥17.5) level and statistically significant (p value <0.001). On linear regression analysis patient with high VIS level had more incidence of re-intubation, prolong period ventilation, prolong ICU stay, higher incidence AKI and high mortality and all were found statistically significant (p-value <0.05).Low body weight at the time of surgery, higher cardiac complexity, high CPB and cross clamp time, open sternum in post-operative period were strongly associated high IS (p value <0.05). Similarly, needed re-open after surgery, higher re-intubation, prolong ventilation, prolong ICU stay and high mortality were statistically significant with high IS level (p-<0.05). On multiple regression analysis revealed longer CPB time, needed kept open sternum after surgery, longer cross clamp time was a self-dependent risk factor for high level of IS and VIS respectively. Both high level of IS and VIS is an important predictor for re-intubation after extubation whether VIS was an independent predictor of prolong duration of mechanical ventilation and mortality, was found to be statistical significant (p-value <0.05).

Conclusions: Patients with high IS and VIS was strongly associated with early age of surgery, high cardiac complexity, increasing CPB and cross clamp time; and required prolong mechanical ventilator support, prolong ICU stay, suffered from increased morbidity and mortality.

Keywords

PCICU; inotropic score; vasoactive inotropic score; mortality.

INTRODUCTION

Among all of the congenital problem in children, congenital heart disease (CHD) is one of the top most congenital problem and worldwide incidence was 0.8% to 1.2% of live births[1]. In developing countries incidence was relatively high and one study showed the prevalence was 7.8/1000 live births in Bangladesh[2]. Due to recent advancement of medical sciences, a large number of child get relief from this miser with dramatic reduction in morbidity and mortality[3]. Despite tremendous technologic advancement in medicine and surgical management, infant and children undergoing cardiac surgery with or without bypass are still at high risk for notable disability as well as lethality immediate period of surgery[4,5]. During early post-operative period

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inotropes and vasopressors are routinely used to improve the severity of illness[6]. Children after cardiac surgery treated with inotropes that are scored and proposed firstly by Wernovsky[7]. The score was modified by Davidson et al. including the vasoactive medications and inodilator, popularly known as vasoactive inotropes score[8]. Several studies were done in developed country and found high level of inotropic score, vasoactive inotropic score in first 48hr was associated with prolong ICU stay, longer period of mechanical ventilation and is good predictor of poor clinical outcome[9].

There has been very few validated research work done for postoperative markers of short and long-term outcomes. In post-operative care, it is important to point out and quantify the factors which can predict the short-term as well as long-term outcomes and study showed that the VIS level is more forecast of awful short-term outcome than IS level [8,10]. There are several studies done in the developed country for evaluating that the to evaluate the IS and VIS as a strong indicator of early postsurgical outcome after CHDs surgery[11]. But in developing country, there was scarcity of such type of study. In Bangladesh, there was too limited study regarding IS and VIS to predict the morbidity and mortality of children under going CHDs surgery. The objective of the study was to determine the association of inotropes score or vasoactive-inotropes score with clinical outcomes after congenital heart surgery.

METHODOLOGY

This is a retrospective analysis of the 477 patients who underwent cardiac surgery for CHD and admitted in PCICU (April - December 2017) of a tertiary cardiac hospital. The patient not underwent surgical correction during the study period were excluded. The diagnosis was established by echocardiography, and if needed cardiac catheterization done by pediatric cardiologist. Preoperative clinical findings, age and sex of patient, weight and nutritional status at surgery and cardiac diagnosis were recorded in medical record sheet during the period of hospital admission. Severity and complexity of the diseases were assessed by Aristotle Basic Score (ABS) and RACHES-1 score. Intraoperative characteristics included the detail document of the note of operation, CPB time, aortic cross clamp (ACC) time, redo surgery, kept open sternum were documented.

Following inotropic and vasopressors were used: dopamine, dobutamine, epinephrine, norepinephrine, milrinone and vasopressin. The initiation of inotropes and vasoactive medication was done by pediatric cardiac surgeon and anesthesiologist in the operation room (OR) and patient shifted to PCICU. The infusion of the medication was titrated and discontinue based on clinical condition, hemodynamics, ABG status and echocardiographic findings by the attending pediatric intensivist. The doses of inotropic and vasoactive medications were recorded hourly in the ICU flow chart along with other parameters. Post-operative variables included needed reoperation, mechanical ventilation duration, time and type of extubation, reintubation, septicemia, length of ICU stay, renal replacement therapy and ultimate discharge status were recorded.

Calculation of IS and VIS were documented hourly and maximum IS and VIS level over the first 48hr were recorded after admission to PCICU. To specify the hemodynamic status after surgery, Wernovsky developed inotropes score (IS) which is calculated by the following formula; IS = dopamine (µg/kg/min dose) + dobutamine (µg/kg/min dose) +100 × epinephrine (µg/kg/min dose)[7]. Vasoactive inotrope score is reform with adding more vasopressors by Gaies et al. and calculated as VIS = IS + 10 X milrinone (µg/kg/min dose) +10,000 x vasopressin (U/kg/min dose) + 100 × norepinephrine (µg/kg/min dose) [8].

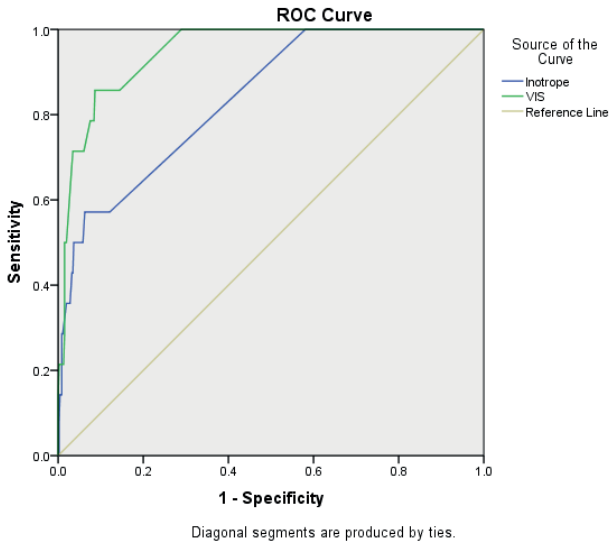

Fig-1: ROC curve for IS and VIS within 48hr

Fig-2: Calculated Vasoactive Inotropic Score (VIS) and Inotropic Score (IS) at ROC values

Area Under the Curve					
Test Result Variable(s)	Area	Std. Error	P value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
IS	0.838	0.051	<0.001	0.739	0.937
VIS	0.948	0.020	<0.001	0.908	0.988

The diagnostic accuracy of IS and VIS values were further analyzed by calculating the area under the receiver operating characteristics (ROC) curve in the first 48hr period and the best cut-off value were determined by utilizing sensitivity and specificity. The high level of IS was ≥7.2 (sensitivity 0.571 and specificity 0.937) and VIS was ≥17.5 (sensitivity 0.857 and specificity 0.914).

Fig-3: Determination of cut off value with youden index.

Cutoff value	Sensitivity	Specificity	youden index (j=sen+spe-1)
17.5	0.857	0.914	0.771
7.2	0.571	0.937	0.508

All recorded data in the flow sheet were collected and stored in the departmental computer in Excel sheet, after that data transformed in SPSS data sheet. All study variable including demographic characteristics, perioperative data were expressed as mean ± SD. Data analysis was done by Statistical Program for Social Science Software (SPSS, version 23.0); Linear and multiple logistic regression analyses used to predict the relation of IS and VIS with pre-operative, intra-operative and immediate post-operative variables to determine the association between inotropic/vasoactive inotropic support and clinical outcome in children after cardiac surgery. Result consider statistically significant, when p-value was <0.05.

Ethical clearance

Consent obtained for publication of this research.

RESULTS

A- 477 patients underwent cardiac surgery for CHD during the study period and among them 5.4% (3) neonate, 14.67% (70) infant and 80.08% (382) were children. Male and female were 54% (259) and 46% (218) respectively. Optimum cut-off value of high IS and VIS was detected by ROC curve 7.2 (sensitivity 58%, specificity 94%) and 17.5 (sensitivity 86%, specificity 92%) respectively. Table-1 showed the list of CHDs surgery done during the study period in our center and most common diagnoses are VSD were 31.03% (n=148), ASD were 15.51% (n= 74) and TOF were 15.51% (n= 74).

In this study, the study population mean ages were 66 months and mean weight were 15.19 kg. CPB not needed fifty-nine patients and mean CPB time, aortic cross clamp time and hospital stay was 97.29 min, 67.62 min and 4.62 days respectively. During surgery, pump failure developed to eight patients and 2.30% (n=7) patients died following cardiac surgery.

Table-1: Type of congenital heart diseases (CHD) enrolled in the study (n=477)

Type of congenital heart diseases (CHD)	Number (%)
Atrial Septal Defect	74 (15.51)
Ventricular Septal Defect	148 (31.03)
Patent Ductus Arteriosus	58 (12.16)
Tetralogy of Fallot's	74 (15.51)
Transposition of Great Arteries	25 (5.24)
Double Outlet Right Ventricle (TOF, TGA, VSD type)	35 (10.06)
Total Anomalous Pulmonary Venous Return	14 (2.94)
TOF with Absent Pulmonary Valve Syndrome	05 (1.05)
Atrioventricular Septal Defect	05 (1.05)
Others (Pulmonary Stenosis, Truncus Atresia, Pulmonary Atresia, DCRV, Truncous Arteriosus, COA, Aortopulmonary Window, Single Ventricle, Ebstein, Heterotaxy, Taussig Bing Anomalies, Hypoplastic Branch Pulmonary Artery)	25 (5.24)

A-425 and 52 patients had a low (VIS < 17.5) and high VIS score (VIS ≥ 17.5) respectively. All neonate and

significant number of infants underwent cardiac surgery had high level of VIS score. On linear regression analysis, CHDs surgery at younger ages were associated with maximum VIS (69.06 ± 69.44 Vs 44.33 ± 65.62; p value <0.004), LBW significantly associated with maximum VIS (15.72 ± 10.60 Vs 11.63 ± 11.80; p value <0.001) but gender has no association [Table-2]. The high level of RACHS score and ABS (2.53 ± 0.83 Vs 1.84 ± 0.70; 5.87 ± 2.16 Vs 8.26 ± 1.62; p value <0.001) both score is associated with high VIS score.

Among the intra-operative variables, high CPB (88.47 ± 59.43 Vs 169.5±65.56 min; p value <0.001) and cross clamp time (60.80 ± 45.19 Vs 123.46±49.54 min; p value <0.001), open sternum in post-operative period were strongly associated (1 (0.2) Vs 8 (15.4); p value <0.001) with high VIS (≥17.5).

Regarding postoperative outcome, high VIS level had more incidence of re-open after surgery (3.1% Vs 7.7%), re-intubation (3.1% Vs 34.6%), prolong ventilator support (6.28 ± 5.38 Vs 33.88 ± 15.85hrs), prolong ICU stay (4.14 ± 4.32 Vs 11.96 ± 8.90 days), AKI (4.7% Vs 50%) and high mortality (0.5% Vs 23.2%) and all were found statistically significant; p value <0.001.

Table-2: Association of different parameters with VIS (linear regression analysis).

	<17.5 (n=425) (%)	>17.5 (n=52) (%)	P value
Pre-operative parameters			
Age	69.06 ± 69.44	44.33 ± 65.62	0.004
Neonate (0-1 month)	0 (0)	3 (5.8)	
Infant (1-12 month)	51 (12)	19 (36.5)	
Child (13-216 month)	363 (5.4)	29 (55.8)	
Adult (>216 month)	11 (2.6)	1 (1.9)	
Gender (Male)	233 (54.8)	26 (50.0)	0.573
Weight	15.72 ± 10.60	11.63 ± 11.80	<0.001
RACHS score	2.53 ± 0.83	1.84 ± 0.70	<0.001
Aristotle score (Basic)	5.87 ± 2.16	8.26 ± 1.62	<0.001
Intra-operative parameters			
Type of operation (CPB)	363 (85.4)	51 (98.1)	<0.001
CPB time (min)	88.47 ± 59.43	169.42 ± 65.56	<0.001
X cIamp time (min)	60.80 ± 45.19	123.46 ± 49.54	<0.001
Redo surgery	7 (1.6)	0 (0)	0.644
Open sternum	1 (0.2)	8 (15.4)	<0.001
Post-operative parameters Reopen	13 (3.1)	4 (7.7)	<0.001
Re-intubation	13 (3.1)	18 (34.6)	<0.001
MV Duration (hrs)	6.28 ± 5.38	33.88 ± 15.85	<0.001
ICU stay (days)	4.14 ± 4.32	11.96 ± 8.90	<0.001
AKI	20 (4.7)	26 (50)	<0.001
Death	2 (0.5)	12 (23.1)	<0.001

MV= Mechanical ventilation, RACHS=Risk Adjustment for Congenital Heart Surgery

On linear regression, no association was found among high IS, gender and early age of surgery of the patients [Table-3] but a remarkable association was found between LBW at the time of surgery and higher cardiac complexity with maximum IS level ($p < 0.02$) [Table-3]. Children with high CPB and cross clam time, open sternum in post-operative period were strongly associated high IS ($p < 0.001$). In postoperative outcome needed re-open after surgery, higher re-intubation rate, prolong ventilator support, prolong ICU stay, AKI and high mortality, all were found statistically significant; ($p < 0.001$).

Table-3: Association of different parameters with Inotrope (linear regression analysis).

Inotrope Scores (IS)	<7.2 (n=440)(%)	>7.2 (n=37) (%)	P value
Pre-operative parameters			
Age	67.91 ± 66.51	47.91 ± 96.76	0.186
Neonate (0-1month)	1 (0.2)	2 (5.4)	
Infant (1-12month)	56 (12.7)	14 (37.8)	
Child (13-216month)	373 (84.8)	19 (51.4)	
Adult (>216month)	10 (2.3)	2 (5.4)	
Gender (Male)	240 (54.5)	19 (51.4)	0.944
Weight	15.65 ± 10.67	10.84 ± 11.47	0.027
RACHS score	1.87 ± 0.72	2.48 ± 0.83	<0.001

Inotrope Scores (IS)	<7.2 (n=440)(%)	>7.2 (n=37) (%)	P value
Aristotle Basic score	5.98 ± 2.19	7.92 ± 1.87	<0.001
Intra-operative parameters			
Type of operation (CPB)	379 (86.1)	35 (94.6)	<0.001
CPB time (min)	91.47 ± 59.98	166.51 ± 83.15	<0.001
X cIamp time (min)	63.57 ± 46.32	115.92 ± 61.86	<0.001
Redo surgery	7 (1.6)	0 (0)	0.595
Open sternum	2 (0.5)	7 (18.9)	<0.001
Post-operative parameters			
Re-open Re-intubation	13 (3) 23 (5.2)	4 (10.8) 8 (21.6)	<0.001 <0.001
MV Duration (hrs)	3.09 ± 0.89	2.45 ± 9.05	<0.001
ICU stay (days)	4.52 ± 4.82	10.62 ± 9.61	<0.001
AKI	30 (6.8)	16 (43.2)	<0.001
Death	6 (1.4)	8 (21.6)	<0.001

MV= Mechanical ventilation

On multiple regression analysis [table-4] revealed, longer CPB time and cross cIamp time during surgery, kept open sternum in post-surgical period was an independent risk factor for high level of IS and VIS. Both high level of IS and VIS significantly associated with reintubation whether VIS was an independent predictor of prolong duration of MV and mortality (p <0.001).

DISCUSSION

In the early postoperative period after CHDs surgery, children often suffered in low cardiac output and the condition having highest mortality[10]. In operation room and PCICU, multiple measures are employed for the proper management of these patients, vasopressors and inotropes are regularly started to reduce the possibility of the postoperative hazards and to promote favorable outcome[12].

The comparism between maximum level of IS and VIS in the first 24hr and 48hr done by Gaies et al. and found that highest level of VIS in the first 48hr was the best indicator of poor clinical outcome[9]. Davidson et al. study showed, maximum level of VIS at 48hr after congenital heart disease surgery had significant correlation with unsatisfactory outcome compared with VIS and IS level at 24hr and 72hr after surgery[8]. In our study, we found highest level VIS during 48hr is significantly associated poor outcome as well as a predominant predictor of mortality.

In our study, re-intubation has a strong correlation with both high IS and VIS level, though several study supported that failure of extubation is significantly associated with longer period of mechanical ventilation[13]. In our study many child need prolong period of mechanical ventilation and the re-intubated patients belongs this group. Article from Harris et al, and Preisman et al, found that early extubation associated with good outcome and limited number of children needed re-intubation[14,15].

Kumer M et al, found a strong association between requirement of prolong period of respiratory support and high VIS level, Gaies et al. study also showed high VIS associated with delayed period of first-time extubation and several studies also revealed that requirement of higher inotropic support is to be significantly associated with delayed extubation[16-18]. We also found that the children had high VIS score in first 48hr required prolonged duration of respiratory support but our study cannot rule out other causes which also influences the longer duration of mechanical ventilator support like bronchomalacia, upper air way diseases, diaphragmatic palsy.

In linear regression analysis, we found that higher IS and VIS level associated with prolong post-operative ICU stay but another study in simple shunt lesion showed type of incision also affect length of ICU stay[19]. The mean duration of ICU stay has been found to be significantly prolong in the group with high VIS level in earlier studies[9]. On multivariate regression analysis, our study did not found that high IS and VIS level is an independent risk factor for prolong ICU stay, though several study result identify as a strong identifiable risk factors[16-18]. This is supported by Davidson et al. study and they identified other factors like poor feeding, vocal cord paralysis, diaphragm palsy, septicemia might be the responsible for longer days ICU stay after cardiac surgery [8]. One study by Butts et al. also did not found any association between length of hospital stay and highest level of VIS in neonate and explained that feeding difficulties, malnutrition affecting longer hospital stay in the neonatal population[20].

Table-4: Multivariate regression analysis for inotrope score and vasoactive inotrope score.

	IS				VIS			
Variables	**Standardized Coefficients**	**t**	**P value**	**VIF**	**Standardized Coefficients**	**t**	**P value**	**VIF**
Age (month)	0.081	0.915	0.361	5.027	-0.008	-0.123	0.902	5.027
Weight	-0.112	-1.248	0.213	5.133	-0.095	-1.460	0.145	5.133
Redo surgery	-0.034	-0.771	0.441	1.235	-0.006	-0.189	0.850	1.235
Operation Type (CPB)	-0.079	-1.503	0.134	1.732	-0.056	-1.483	0.139	1.732
CPB time (min)	0.349	2.404	0.017	13.383	0.084	0.806	0.421	13.383
X clamp time (min)	-0.092	-0.660	0.510	12.328	0.230	2.285	0.023	12.328
RACHS score	-0.100	-1.253	0.211	4.038	-0.085	-1.470	0.142	4.038
Aristotle score	0.216	2.336	0.020	5.416	0.230	3.444	0.001	5.416
Open sternum	0.144	3.014	0.003	1.447	0.012	0.352	0.725	1.447
Re open	0.084	1.871	0.062	1.278	0.016	0.480	0.631	1.278
Re intubation	0.125	2.572	0.010	1.504	0.154	4.382	<0.001	1.504
MV Duration(hrs)	0.073	1.081	0.280	2.931	0.325	6.636	<0.001	2.931
AKI	0.055	1.144	0.253	1.451	0.032	0.936	0.350	1.451
PCICU stay (days)	0.038	0.622	0.534	2.317	-0.009	-0.198	0.843	2.317
Death	-0.035	-.723	0.470	1.443	-0.176	-5.124	<0.001	1.443

MV= Mechanical ventilation

There are several scoring systems to evaluate the severity and complexity of congenital heart diseases. Aristotle Basic Scoring system allows a precise scoring system to evaluate and classify according to the complexity of congenital heart surgery procedures and also give detailed analysis to evaluate the surgical outcome like morbidity, mortality[21]. We observe in our study that high Aristotle Basic Score is strong predictor for high IS and VIS level. We also found that the RACHEs score also significantly associated with maximum level of both score.

Children with congenital heart surgery are needed CPB and is a well-established cause of systemic inflammatory response syndrome (SIRS), LCOS and longer pump time (CPB) contributes to an increased inotropic support[22-24]. In our study, although surgery needed CPB and longer CPB time was significantly associated with high IS and VIS level but these were not used to be an independent predictor of high VIS level but longer CPB time used for high IS level.

In our study, low body weight is associated with both high IS and VIS score and early age at surgery needed maximum level of vasopressor, although the number of participant infant and children are more in low VIS group but statistically the association of early age and high VIS level is significant. Although, multiple linear regression analysis failed to establish that the age was an independent determinant for high VIS level.

Study limitations: It is a retrospective, single-center study; multiple surgeons and pediatric cardiologist contributing related variations cannot be ruled out.

CONCLUSIONS

Patients with high IS and VIS was strongly associated with early age of surgery, severe cardiac complexity, longer CPB time, cross clamp time and kept open sternum after surgery; higher IS and VIS required prolong mechanical ventilator support, prolong ICU stay, morbidity and mortality. High level of IS and VIS, are excellent tool to measure illness severity of cardiac surgery patients. Maximum level IS and VIS in early post-operative period, have an increased chance of significant morbidity and mortality. During the parent counselling, it may also guide the physician regarding prognosis and outcome of PCICU stay.

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Data analysis: NAH, AT, NT

Manuscript preparation: AT

Manuscript review: AT, NAH, SK, TA

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