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ORIGINAL ARTICLE

Does Vasoactive Inotrope score predict morbidity and mortality in premature babies weighing less than 1000 grams?

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ABSTRACT

Objective: The vasoactive inotropic score (VIS) was first used to assess inotropic exposure in neonates with congenital heart disease and was subsequently shown to predict postoperative mortality. The aim of this study is to evaluate the relationship between VIS and morbidity and mortality in preterm infants.

Material and Methods: This is a retrospective and cross-sectional study. The files of 77 premature babies weighing less than 1000 grams, who were hospitalized in the Neonatal Intensive Care Unit at the University of Health Sciences Zeynep Kamil Maternity and Children's Training and Research Hospital between January 2019 and January 2020, were evaluated retrospectively. Demographic data, antenatal and perinatal findings, postnatal clinical findings, postnatal 1st and 48th hour systolic, diastolic, and mean blood pressures, pH, base deficit, and lactate values were recorded. The maximum VIS (VIS_{max}) at the postnatal 48th hour was calculated.

Results: In the preterm infants, a VIS_{max} value of 80 (85% sensitivity, 47% specificity) and a VIS_{max} value of 7.5 (97% sensitivity, 57% specificity) were found to be predictive for pulmonary hypertension and mortality, respectively.

Conclusion: A VIS_{max} value of 7.5 and a VIS_{max} value of 80 predict mortality and pulmonary hypertension in preterm infants with extremely low birth weight. Further studies are needed.

Keywords: Inotropic score, mortality, premature.

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INTRODUCTION

The inotrope score (IS=dopamine dose (mcg/kg/min) + dobutamine dose (mcg/kg/min) + 100×epinephrine dose (mcg/kg/min)) was defined to calculate the total inotrope exposure of newborns in post-cardiac surgery. It was found that IS helped to predict death, cardiac arrest, prolonged mechanical ventilation, renal replacement therapy, and neurological damage. It was also observed that it provided accurate information about prolonged hospital stay and negative fluid balance.[1] By modifying the inotrope score, Davidson et al.[2] created the vasoactive inotrope score (VIS=dopamine dose (mcg/kg/min) + dobutamine dose (mcg/kg/min) + 100×epinephrine dose (mcg/kg/min) + 10×milrinone dose (mcg/kg/min) + 10,000×vasopressin dose (u/kg/min) + 100×norepinephrine dose (mcg/kg/min)). In this study, IC and VIS calculations were made at 24, 48, and 72 hours, and as a result, a strong correlation was found between high VIS values and length of hospital stay, mechanical ventilation time, and mortality. Some authors observed that VIS was superior to IC in predicting short-term prognosis.

Hemodynamic failure is involved in the etiology of respiratory distress syndrome (RDS), need for mechanical ventilation, intraventricular hemorrhage (IVH), patent ductus arteriosus (PDA), pulmonary hypertension, necrotizing enterocolitis (NEC), hypotension, and sepsis, which are among the morbidities of extremely low birth weight (ELBW) premature infants. The most commonly used vasoactive inotropes in ELBW preterm infants with hemodynamic insufficiency include dopamine, dobutamine, norepinephrine, epinephrine, milrinone, and vasopressin.

Do vasoactive inotropes used in the treatment of hemodynamic insufficiency predict morbidity and mortality in preterm infants? Can VIS, which is the sum of vasoactive inotropes and is used as a prognostic factor for post-cardiac hospital stay and mortality in newborns, predict mortality and morbidity in preterm infants? In this study, we aimed to reveal the relationship between VIS and premature morbidity and mortality.

MATERIAL AND METHODS

This study is a retrospective and cross-sectional study. Premature babies who were born with a birth weight of less than 1000 grams between 01/01/2019 and 01/01/2020 and hospitalized in the Neonatal Intensive Care Unit at the Health Sciences University Zeynep Kamil Gynecology and Pediatrics Training and Research Hospital were included in the study. This study was approved by the Zeynep Kamil Maternity and Children's Disease Health Training and Research Center, Clinical Research Ethics Committee (2021/32). Infants with congenital anomalies, those referred to another center, and those whose families refused to participate in the study were not included. A total of 77 ELBW premature babies were included in the study.

Demographic findings of the patients (birth weight, gestational week, gender, mode of delivery), antenatal findings (antenatal steroid use, preeclampsia, chorioamnionitis, presence of diet- and insulin-regulated diabetes, umbilical artery/vein flow disorder on Doppler USG), perinatal findings (1st and 5th minute APGAR scores, positive pressure ventilation (PPV) in the delivery room, cardiac massage, and adrenaline use), and postnatal findings (RDS, type and duration of invasive ventilation (Synchronous Intermittent Mandatory Ventilation (SIMV), High Frequency Oscillatory Ventilation (HFO)), type and duration of noninvasive ventilation (nasal Continuous Positive Airway Pressure (nCPAP), nasal Synchronous Intermittent Mandatory Ventilation (nSIMV)), PDA and its treatment, pulmonary hypertension, frequency of prostaglandin use, frequency of INO (inhaled nitric oxide), frequency of hypotension and hypotension with shock, bronchopulmonary dysplasia (BPD), frequency of postnatal steroid use, IVH, frequency and treatment of retinopathy of prematurity (ROP), clinical and culture-positive sepsis, NEC and its treatment, duration of total parenteral nutrition (days), length of hospital stay, presence of mortality, and day of death) were recorded.

The frequency and maximum doses of dopamine (mcg/kg/min), dobutamine (mcg/kg/min), adrenaline (mcg/kg/min), noradrenaline (mcg/kg/min), milrinone (mcg/kg/min), and vasopressin (u/kg/min) treatment initiated within the postnatal 48 hours and VIS_{max} values were calculated in 61 patients. The postnatal 1st and 48th hour blood pH, BE, and lactate values, as well as postnatal 1st and 48th hour systolic, diastolic, and mean arterial pressures, were recorded retrospectively. Demographic data (gender, mode of birth), antenatal (antenatal steroid administration, presence of preeclampsia, presence of chorioamnionitis, presence of diet-regulated DM, presence of findings on Doppler USG), perinatal (delivery room PPV, cardiac massage, presence of adrenaline), and postnatal findings (RDS, SIMV, HFO, nCPAP, nSIMV, hypotension and hypotension with shock, PDA and its treatment, presence of pulmonary hypertension, presence of prostaglandin, presence of INO, presence of BPD, presence of IVH, ROP and its treatment, presence of clinical and culture-positive sepsis, presence of NEC, and mortality) were compared for VIS maximum. For cases with VIS_{max}, the predictive value of VIS was analyzed.

It is recommended to administer 2 doses of corticosteroids to all women at risk of preterm labor within 1 week between 24 and 34 weeks of gestation. Betamethasone and dexamethasone are used antenatally.[3] The Apgar score is a scoring system consisting of 5 parameters assessed at the 1st and 5th minutes after birth. Sixty seconds after the birth of the infant (ignoring the cord and placenta), these 5 parameters (heart rate, respiration, muscle tone, response to the nasogastric catheter, and color) are evaluated, with each receiving 0, 1, or 2 points. A total of 10 points indicates that a newborn is in the best possible condition. An infant with a score of 0–3 requires immediate intervention.[4]

Chorioamnionitis was defined as the presence of fever (>38 °C) without a clear focus, along with two or more criteria for infection and uterine tenderness, foul-smelling vaginal discharge, maternal leukocytosis (white blood cells >15,000/mm³), elevated C-reactive protein, maternal tachycardia (>100 beats/min), and fetal tachycardia (>160 beats/min).[5] Preeclampsia was defined as the presence of new-onset proteinuria and/or edema with hypertension (blood pressure >140/90 mmHg and a mean arterial pressure of >105 mmHg).[6] Clinical course, chest X-ray findings, and blood gas values were used to diagnose RDS.[7] BPD was defined as continuing oxygen demand at postconceptional 36 weeks.[8] IVH was diagnosed in line with the criteria described by Volpe.[9] ROP was defined according to the International Classification of Retinopathy of Prematurity.[10]

Table 1: Demographic, antenatal and perinatal findings (n=77)

Patient number, n(%)	77 (100)
Birth weight (Mean±SD)	642.3±200.5
Gestational week (Mean±SD)	24.6±2.8
Gender, n (%)	
Boy	44 (57.1)
Girl	33 (42.9)
Mode of delivery, n (%)	
C/S	41 (53.2)
NSVB	36 (46.8)
Antenatal steroid, n (%)	
No	42 (54.5)
1 dose	12 (15.6)
2 doses	22 (28.6)
Preeclampsia, n (%)	13 (16.9)
Chorioamnionitis, n (%)	13 (16.9)
Diet-regulated diabetes mellitus, n (%)	4 (5.2)
Insulin-regulated diabetes mellitus, n (%)	0 (0.0)
Umbilical artery/vein flow disorder in Doppler USG, n (%)	13 (16.9)
Apgar 1st, Min (mean±SD)	3.57±1.30
Apgar 5th, Min (mean±SD)	5.79±1.57
Delivery room PPV, n (%)	71 (92.2)
Delivery room cardiac masage, n (%)	12 (15.6)
Delivery room adrenalin, n (%)	8 (10.4)

SD: Standard deviation; PPV: Positive pressure ventilation; C/S: Cesarean section; NSVB: Normal spontaneous vaginal birth; USG: Ultrasonography.

The clinical diagnosis of NEC was based on the presence of the most characteristic clinical features (abdominal bloating, biliary vomiting or gastric aspiration, and rectal bleeding [bloody stools in the absence of heme or anal fissures]) and radiological findings such as intramural gas (pneumatosis intestinalis), pneumoperitoneum, or abdominal imaging of sentinel intestinal loops.[11] Pulmonary hypertension was diagnosed by the pediatric cardiology clinic within the framework of echocardiographic findings or by the presence of acute and end-stage clinical findings when the pediatric cardiology clinic could not be reached.

Hemodynamically significant PDA, based on echocardiographic findings, was defined as an internal ductal diameter of ≥1.5 mm and/or a left atrium (LA)/aortic root (AO) ratio of ≥1.5. An amniotic fluid index of <5 cm was considered oligohydramnios. Culture-positive sepsis was defined as the presence of clinical and laboratory findings consistent with sepsis within the first week with a causative agent grown in culture, while clinical sepsis was defined as the presence of clinical and laboratory findings compatible with sepsis within the first week without a causative agent grown in culture. Hypotension was defined as a mean blood pressure of <30 mmHg in the first 72 hours in preterm infants with a gestational age of <32 weeks. A lactate value over 2.5 mmol/L in patients with hypotension was defined as shock. This study was conducted in accordance with the Declaration of Helsinki.

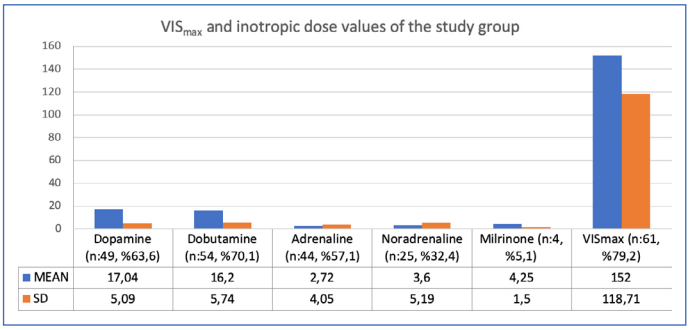

Figure 1: VIS_{max} and vasoactive inotropic dose and frequency (n=61).

Statistical Analysis

The data obtained in this study were analyzed using SPSS version 22.0 (SPSS, Statistical Package for Social Sciences, IBM Inc., Armonk, NY, USA) statistical software. The descriptive data were expressed as frequency (n,%) and numerical data were expressed as mean±SD or median (min–max). Normality of the data was evaluated with the Kolmogorov-Smirnov test. Differences between the mean values of the study group were evaluated using the t-test. ROC analysis was used to determine the significance of parameters in terms of predicting VIS scores. The Pearson test was used for correlations between the baseline and 48th-hour blood pressure, lactate, pH, and BE values in the study group. The data were presented in the 95% confidence interval, and a p value of <0.05 was considered statistically significant. p=0.000 values were presented as p<0.001.

RESULTS

The demographic, antenatal, perinatal, and postnatal findings in the study group (n=77) are shown in Table 1 and Table 2.

The VIS_{max} score was calculated in 61 (79.2%) patients in the study group, and the mean VIS_{max} was found to be 152.71±118.71. The mean dose was found to be 17.04±5.09 for dopamine (n=49, 63.6%), 16.2±5.74 for dobutamine (n=54, 70.1%), 1.19±0.43 for adrenaline (n=44, 57.1%), 1.44±1.1 for noradrenaline (n=25, 32.4%), and 0.42±0.15 for milrinone (n=4, 5.1%) (Fig. 1).

There is an inverse, weak, but statistically insignificant correlation between VIS_{max} and birth weight (p=0.08, r=0.22). There is an inverse, weak, but statistically insignificant correlation between VIS_{max} and gestational week (p=0.86, r=0.02) (Table 3).

When the baseline and 48th-hour blood pressure mean values were compared, both systolic and diastolic blood pressure mean values measured at the 48th hour (systolic: 48.96±9.75 mmHg; diastolic: 28.52±6.99 mmHg) were found to be statistically significantly higher compared to the mean systolic and diastolic blood pressures measured at baseline (systolic: 38.4±11.47; diastolic: 19.48±6.56) (p<0.001 and p<0.001, respectively) (Fig. 2). There is a statistically significant correlation between both systolic and diastolic blood pressure values measured at baseline and at 48 hours (correlation coefficients: 0.78 and 0.80; p values: <0.001 and <0.001, respectively).

Table 2: Postnatal clinical findings (n=77)

Patient number, n (%)	77 (100)
RDS, n (%)	68 (88.3)
Invasive ventilation type, n (%)	
SIMV	65 (83.3)
HFO	10 (13.0)
Days of invasive ventilation, (Mean±SD)	22.17±39.11
Noninvasive ventilation type, n (%)	
CPAP	11 (14.3)
SIMV	18 (23.3)
Days of noninvasive ventilation, (Mean±SD)	7.10±11.74
PDA, yes, n (%)	19 (37.3)
PDA treatment, n (%)	
Medical	21 (91.3)
Surgical	2 (8.7)
PH, n (%)	21 (27.3)
Frequency of ilomedine, n (%)	22 (28.6)
Frequency of INO, n (%)	9 (11.7)
Hypotension, n (%)	30 (69.7)
Hypotension with shock, n (%)	7 (23.3)
BPD, n (%)	26 (33.8)
Frequency of postnatal steroids, n (%)	24 (31.2)
IVH, n (%)	30 (39.0)
ROP, n (%)	12 (15.6)
ROP treatment, n (%)	2 (2.6)
Clinical sepsis, n (%)	45 (58.4)
Culture positive sepsis, n (%)	37 (48.0)
Feeding intolerance, n (%)	36 (46.8)
NEC, n (%)	26 (27.3)
Treatment of NEC, n (%)	
Surgical	6 (22.3)
Medical	21 (77.7)
Mortality	48 (62.3)

SD: Standard deviation; RDS: Respiratory distress syndrome; HFO: High frequency oscillatory; CPAP: Continuous positive airway pressure; SIMV: Synchronous intermittent mandatory ventilation; PDA: Patent ductus arterius; PH: Pulmonary hypertension; INO: Inhale nitrik oksit; BPD: Broncopulmonary dysplasia; IVH: Intraventricular hemorrhage; ROP: Premature of retinopathy; NEC: Necrotizing enterocolitis.

When the baseline and 48th-hour blood gas values were compared, it was found that the mean baseline lactate concentration was 6.12±4.07, while the mean 48th-hour lactate concentration was 3.34±2.81. There was a statistically significant correlation between the mean lactate values measured at baseline and at the 48th hour (p<0.001) (Fig. 3). There was also a statistically significant correlation between pH values measured at baseline and at the 48th hour (r=0.39, p=0.02).

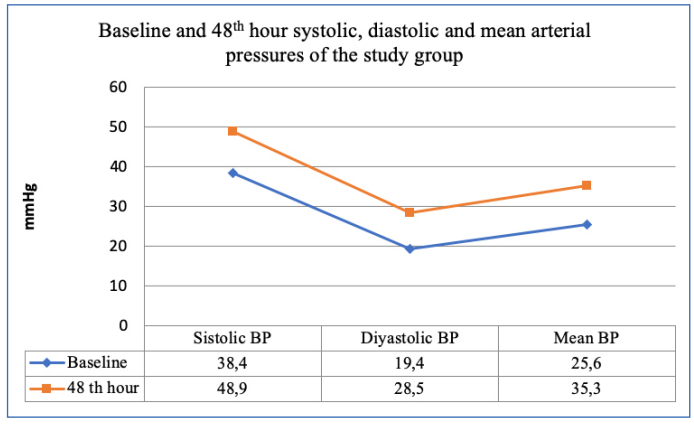

Figure 2: Systolic, diastolic and mean blood pressure values measured at baseline and 48th hour (n=61)

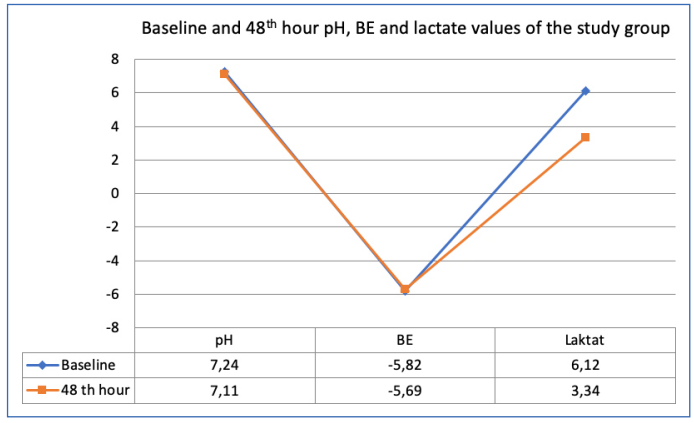

Figure 3: Blood gas values measured at baseline and 48th hour (n=61).

Table 3: The relationship between VIS score and birth weight and week of birth

	Correlation coefficient	p*
Gestational week	0.22	0.08
Birth weigh	0.02	0.86

*: Pearson Correlation Test was applied; VIS: Vasoactive inotropic score.

When VIS_{max} was evaluated in terms of demographic, antenatal, perinatal, and postnatal clinical findings, it was found that the mean VIS_{max} value was statistically significantly higher in the patients in whom PPV was applied in the delivery room compared to the patients who did not undergo PPV (mean VIS values: 156.72±117.83 and 12.50±10.60, respectively; p<0.001). The mean VIS_{max} values were statistically significantly lower in the patients in whom NCPAP was applied compared to the patients who did not undergo NCPAP (mean VIS_{max} values: 5.00±0.00 and 147.44±123.04, respectively; p=0.003). The mean VIS_{max} values were statistically significantly lower in the patients in whom NSMIV was applied compared to the patients who did not undergo NSMIV (mean VIS_{max} values: 40.00±67.85 and 179.42±112.50, respectively; p<0.001). The mean

Table 4: The correlations between demographic, antenatal and perinatal findings of the study group and VIS_{max} means (n=61)

Parameter	n	%	VIS, Mean±SD	p
Gender				0.98
Boy	36	59.01	152.22±110.95	
Girl	25	40.98	151.68±131.44	
Mode of delivery				0.82
C/S	28	45.90	148.28±130.92	
NSVB	33	54.09	155.15±109.26	
Administration of antenatal steroids				0.25
Yes	27	44.26	130.20±115.30	
No	34	55.73	83.5±95.65	
Preeclampsia				0.07
Yes	10	16.39	89.11±104.07	
No	51	83.60	163.33±119.72	
Chorioamnionitis				0.64
Yes	12	19.67	166.25±106.43	
No	49	80.32	148.51±122.30	
Diet regulated DM				0.97
Yes	4	6.55	150.00±132.41	
No	57	93.44	152.14±118.99	
Findings in Doppler USG				0.50
Yes	11	18.03	175.00±122.78	
No	50	81.96	146.94±118.47	
PPV in delivery room				**<0.001**
Yes	59	96.72	156.72±117.83	
No	2	3.27	12.50±10.60	
Cardiac masage in delivery room				0.79
Yes	10	16.39	159.70±94.77	
No	51	83.60	150.49±123.61	
Adrenalin in delivery room				0.92
Yes	6	9.83	147.83±105.50	
No	55	90.16	152.45±120.94	

SD: Standard deviation; VIS: Vasoactive inotropic score; D: Diabetes mellitus; C/S: Cesarean section; NSVB: Normal spontaneous vaginal birth; USG: Ultrasonography; PPV: Positive pressure ventilation.

VIS_{max} value was statistically significantly higher in the patients who had pulmonary hypertension compared to the patients who did not have pulmonary hypertension (mean VIS values: 212.14±115.41 and 120.42±108.99, respectively; p=0.005). The mean VIS_{max} value was statistically significantly higher in the patients who had hypotension compared to the patients who did not have hypotension (mean VIS_{max} values: 166.56±110.03 and 57.69±89.08, respectively; p=0.003). The mean VIS_{max} value was statistically significantly higher in the infants who died compared to the infants who survived (mean VIS_{max} values: 191.85±105.57 and 18.21±24.30, respectively; p<0.001) (Table 4, Table 5).

The VIS score prediction values determined for the variables with significant differences in mean VIS scores, along with sensitivity and specificity values, 95% confidence intervals (CI), area under the curve (AUC), positive predictive values (PPV), and negative predictive values (NPV) are shown in Table 6. The VIS ROC analysis related to pulmonary hypertension and mortality is shown in Figure 4 and Figure 5, respectively.

DISCUSSION

The vasoactive inotrope score (VIS), used to calculate inotrope exposure and determine prognosis in newborns with post-cardiac surgery

Table 5: The relationship between postnatal findings of the study group and VIS_{max} score mean values (n=61)

Parameter	n	%	VIS, Mean±SD	p
RDS				0.38
Yes	57	93.44	155.82±119.04	
No	4	6.55	97.50±114.34	
SIMV				0.39
Yes	52	85.24	147.44±123.04	
No	9	14.75	178.33±90.96	
HFO				0.39
Yes	9	14.75	178.33±90.96	
No	52	85.24	147.44±123.04	
NCPAP				**0.003**
Yes	3	4.91	5.00±0.00	
No	58	95.08	159.60±116.78	
NSMIV				**<0.001**
Yes	12	19.67	40.00±67.85	
No	49	80.32	179.42±112.50	
PDA				0.75
Yes	24	39.34	158.00±124.51	
No	37	60.65	148.19±116.38	
PDA medical treatment				0.51
Yes	15	24.59	135.46±109.11	
No	46	74.40	157.39±122.33	
PDA surgical treatment				0.27
Yes	2	3.27	243.50±2.12	
No	59	96.72	148.89±119.50	
PH				**0.005**
Yes	21	35.00	212.14±115.41	
No	40	65.00	120.42±108.99	
Prostacyclin				**0.005**
Yes	21	35.00	212.14±115.41	
No	40	65.00	120.42±108.99	
Hypotension				**0.003**
Yes	30	69.7	166.56±110.03	
No	13	31.3	57.69±89.08	
Hypotension with shock				0.92
Yes	7	23.3	170.00±158.11	
No	23	76.6	165.52±110.03	
INO				0.89
Yes	9	14.75	147.77±99.47	
No	52	85.24	152.73±122.57	
BPD				0.06
Yes	12	85.8	20.41±25.71	
No	2	14.2	5.00±0.00	

Table 5 (cont): The relationship between postnatal findings of the study group and VIS_{max} score mean values (n=61)

Parameter	n	%	VIS, Mean±SD	p*
IVH				0.14
Yes	26	42.62	178.34±124.03	
No	35	57.37	132.42±112.40	
ROP				0.87
Yes	7	50.00	19.28±31.67	
No	7	50.00	17.14±16.54	
ROP Treatment				0.78
Yes	2	14.2	15.00±14.14	
No	12	85.8	18.75±26.03	
Clinical sepsis				0.50
Yes	32	52.45	161.62±128.85	
No	29	47.54	141.37±107.67	
Culture positive sepsis				0.44
Yes	27	44.26	139.14±110.75	
No	34	55.73	162.20±125.36	
Presence of NEC				0.30
Yes	18	29.50	127.61±118.87	
No	43	70.49	162.20±118.54	
Mortality				**<0.001**
Yes	47	77.04	191.85±105.57	
No	14	22.95	18.21±24.30	

SD: Standard deviation; RDS: Respiratory distress syndrome; SIMV: Synchronous intermittent mandatory ventilation; HFO: High frequency oscillatory ventilation; nCPAP: Nasal continuous positive airway pressure; NSIMV: Nazal Synchronous intermittent mandatory ventilation; PDA: Patent ductus arterius; PH: Pulmonary hypertension; INO: Inhale nitrik oksit; BPD: Broncopulmonary displasia; IVH: Intraventricular hemorrhage; ROP: Premature of retinopathy; NEC: Necrotizing enterocolitis.

or infants in septic shock, was evaluated in this study to assess morbidity in preterm infants below 1000 g (RDS, invasive/noninvasive ventilation, pulmonary hypertension, prostaglandin frequency, BPD, IVH, PDA, ROP, NEC, sepsis) and to determine mortality. As a result, we found that systolic and diastolic arterial pressures increased and lactate levels decreased at 48 hours with inotropic exposure. VIS_{max} was higher in preterm infants below 1000 g who received positive pressure ventilation in the delivery room and who had a high incidence of hypotension, pulmonary hypertension, and mortality. A VIS_{max} value of >80 predicted pulmonary hypertension with 85% sensitivity and 47% specificity, and a VIS_{max} value of >7 predicted mortality with 97% sensitivity and 57% specificity. The contribution of this study to the literature is that it is the second study to evaluate whether VIS predicts morbidity and mortality in preterm infants. The limitation of the study was the high mortality rate and its small sample size of premature babies under 1000 grams.

In our study, the mean gestational age was 24.6±2.8 weeks, and the mean VIS_{max} was 152±118.71. In the study conducted by Aziz et al.,[12] a relationship was found between a decrease in gestational age and birth weight and an increase in VIS_{max}. In our study, there was a statistically insignificant relationship between VIS_{max}, gestational age, and birth weight, and the increase in VIS_{max}.

In our study, systolic and diastolic arterial pressures increased, and lactate levels decreased at the 48th hour with hemodynamic support. VIS_{max} was high in hypotensive preterms; however, VIS_{max} was not higher in hypotensive preterms with a high lactate level. This finding is attributed to the decrease in lactate at the 48th hour with hemodynamic support, which was initiated in preterm infants, most of whom were only hypotensive. Although it is recommended that hemodynamic support should be monitored rather than initiated, especially in the first 72 hours due to hypotension, we believe that early hemodynamic support should be started only in hypotensive preterm infants in light of studies showing that lactate level is an independent risk factor for mortality in preterms.[13]

There are many studies evaluating the relationship between VIS and mortality. Gaies et al.[14] showed that the frequency of death, cardiac arrest, mechanical circulatory support, and need for renal replacement therapy increased significantly in patients who reached VIS_{max} within 48

Table 6: VIS_{max} score estimation, sensitivity and specificity values, 95% confidence intervals, area under the curve, positive and negative predictive values of variables with statistically significant differences (n=61)

Parameter	VIS_{max}	Sensitivity	Specificity	%95 CI	AUC	Pozitive predictive value	Negative predictive value
PPV	7.50	86%	50%	0.74–0.99	0.86	98.1%	11.1%
PH	80.00	85%	47%	0.58–0.84	0.71	46.2%	86.4%
Hypotension	15.00	46%	6%	0.03–0.34	0.19	82.4%	77.8%
Prostacyclin	80.00	85%	47%	0.58–0.84	0.71	46.2%	86.4%
Mortality	7.50	97%	57%	0.90–1.00	0.95	88.5%	88.9%

PPV: Positive pressure ventilation; PH: Pulmonary hypertension; CI: Confidence interval; VIS: Vasoactive inotropic score; AUC: Area under curve.

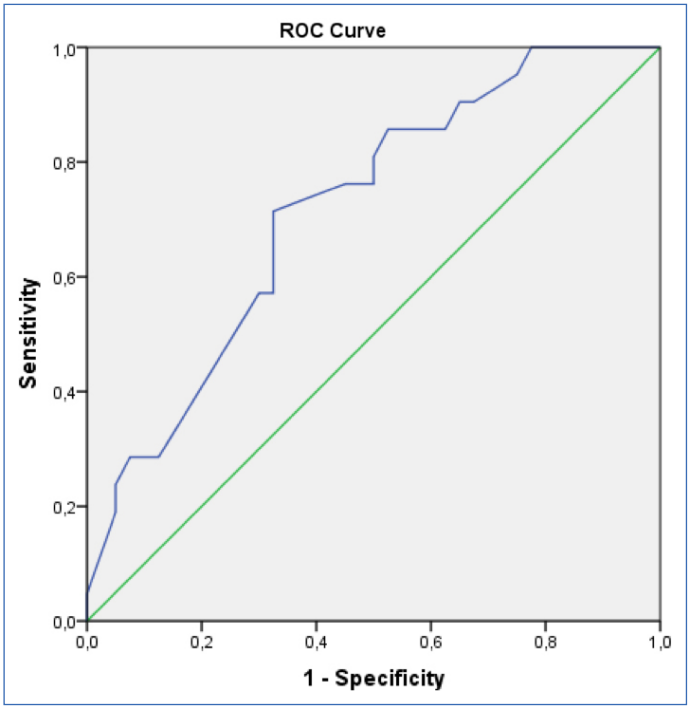

Figure 4: ROC analysis associated with pulmonary hypertension.

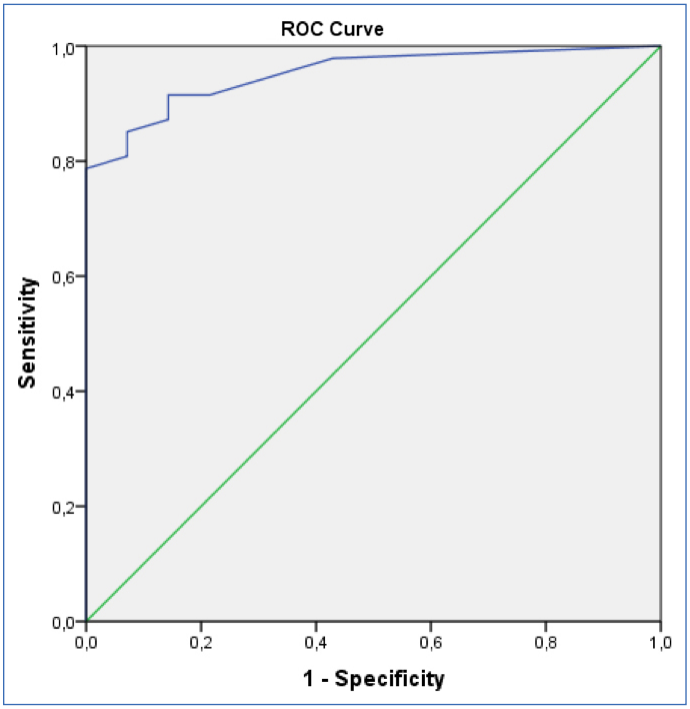

Figure 5: ROC analysis related to mortality.

hours among postoperative cardiac patients, 43% of whom were neonates. In the study conducted by Koponen et al.,[15] 117 subjects who underwent cardiovascular surgery, were markedly hypotensive, and were born before 33 weeks of pregnancy were examined. It was emphasized that a VIS value of >25 showed 66% sensitivity and 92% specificity in terms of mortality, with 32.5% of the patients dying. In another study conducted by Haque et al.,[16] a VIS value of >20 was found to be associated with 100% mortality in sepsis patients admitted to the pediatric intensive care unit. In their study, Kallekkattu et al.[17] showed that a VIS value of >42.5 determined an area under the curve of 88% in terms of mortality in sepsis patients admitted to the pediatric intensive care unit.

Although the mean VIS score was found to be 15 in the study conducted by Öztürk et al.,[18] one of the studies evaluating the VIS score in the pediatric cardiac intensive care unit in our country, there is no data related to mortality. In the study conducted by Öncü et al.,[19] which retrospectively evaluated risk factors and short-term outcomes in very low birth weight premature babies with early postnatal hypotension, it was found that 41% of the patients had a VIS value of >15, and the presence of metabolic acidosis accompanying hypotension and a VIS value of >15 were independent risk factors for the development of secondary acute renal failure.

The study conducted by Aziz et al.,[12] published in 2021, provides the most up-to-date data on this subject. In this study, 436 VLBW infants were examined, and mortality increased by 3.3 times in patients with a VIS_{max} between 0–5, by 5.1 times in patients with a VIS_{max} between 5–10, by 13.3 times in patients with a VIS_{max} between 10–15, by 23.8 times in patients with a VIS_{max} between 20–25, by 37.7 times in patients with a VIS_{max} between 25–30, and by 46.1 times in patients with a VIS_{max} >30 compared to infants with a normal VIS_{max}. Although there are differing opinions about the VIS score cut-off value that determines mortality in the literature, a VIS value of >15 or >20 is generally considered as the cut-off.

In our study, it was found that a VIS_{max} value of 7.50 predicted mortality with 97% sensitivity and 57% specificity, with the area under the curve at 95%.

Aziz et al.[12] conducted the first study to evaluate VIS in premature infants in terms of VIS and morbidities, prior to our study. Unlike our study, VIS scores were divided into three groups as 0, <10, and ≥10 in this study, and the relationship between demographic, antenatal, perinatal, postnatal clinical findings, and mortality was investigated. In the study conducted by Aziz et al.,[12] the 5-minute Apgar score among perinatal findings was 7 in those with VIS=0, while it was lower in those with VIS<10 and ≥10. In our study, VIS_{max} was found to be higher in infants who underwent PPV in the delivery room, although the study design was different.

In our study, statistically significant values were found in preterm infants who were not administered NCPAP and NSMIV, and high VIS_{max} values were found in preterm infants with RDS and BPD, though the differences were not statistically significant. The reason for this may be respiratory distress (RDS) in premature infants, requiring invasive ventilation support, hemodynamic support, and high inotrope dosages.

In the study conducted by Aziz et al.,[12] an increased incidence of intestinal perforation and NEC was found with high VIS, reflecting the expected relationship between hemodynamic dysfunction and VIS. It is known that parameters such as IVH and NEC are associated with hemodynamic dysfunction. Interestingly, in our study, VIS_{max} was found to be significantly lower in infants who had NEC compared to those who did not have NEC. Infants with IVH had a high VIS_{max} in our study, although this difference was not statistically significant.

In our study, there was a significant difference between the frequency of pulmonary hypertension and prostaglandin use and VIS_{max}. Detection sensitivity for pulmonary hypertension was found to be 85% and specificity 47% in cases with VIS_{max} ≥80. Although an increase in VIS is common in a pathology affecting the vascular system, such as pulmonary hypertension, it is crucial to detect the presence of pulmonary hypertension before such a high VIS is reached. The incidence of pulmonary hypertension in our study was found to be 27%. Further studies evaluating the VIS score in a pulmonary hypertension-based cohort may shed light on this issue. The main purpose of our study was to determine the relationship between VIS and mortality in cases with ELBW. According to our results, the VIS score has an important role in determining the risk of mortality. It is challenging to evaluate ELBW patients admitted to the NICU using objective, quantitative, and reproducible scoring tools. In this context, the VIS score may emerge as a valuable parameter.

CONCLUSION

In conclusion, VIS is a quantitative parameter that has been shown to be directly related to mortality in premature ELBW patients and serves as an objective indicator of hemodynamic/cardiovascular support. The combination of VIS scores with other disease scores may contribute to risk stratification for ELBW patients hospitalized in the NICU.

Statement

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Ethics Committee Approval: The Istanbul Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center Clinical Research Ethics Committee granted approval for this study (date: 17.02.2021, number: 2021/32).

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