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A New Mortality Score in Preterm Infants: The Vasoactive Inotropic Score

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Abstract: Background: Can vasoactive inotropic score (VIS) be a new mortality score in preterm infants weighing less than 1000 grams? Method:This study was designed as a retrospective study. A total of 280 preterm infants under 1000 grams admitted to the neonatal intensive care unit over a five-year period were included in the study. For each patient, CRIB-II score and VIS were calculated, and their ability to predict mortality was compared. To predict and compare the accuracy of the scoring systems, Receiver Operating Characteristic (ROC) analysis was used, and the area under the curve (AUC) was calculated. Results:In infants who died within the first 28 days postnatally, CRIB-II Score (p=0.0001) and VISmax (p=0.0001) were higher compared to those who survived. The AUC for CRIB-II and VIS in predicting mortality were 0.86/0.81, with cutoffs of >12/>5, sensitivity 79/70, specificity 82/87, positive predictive value (PPV) 81/85, and negative predictive value 80/75, respectively. There was no statistically significant difference between the AUC values of the CRIB-II Score and VIS variables (p=0.160). Conclusion: VIS can predict mortality in very low birth weight preterm infants as accurately as the CRIB-II score.

Keywords: vasoactive inotrope score

Introduction

The rapid identification of high-risk infants in neonatal intensive care units (NICUs) has the potential to improve patient care and disease prognosis. Various scoring systems have been developed to predict mortality and severe morbidity in neonates. Among the scores used to predict preterm mortality, the Clinical Risk Index for Babies-II (CRIB-II) score is both accurate and simple, making it a commonly used tool in routine practice (1). The CRIB-II score was developed by Parry et al. in 2003. This score (ranging from 0 to 27) is calculated based on five parameters: birth weight, gender, admission temperature, gestational age, and the worst base deficit during the first hour of life (2). While many studies have shown that the CRIB-II score predicts neonatal mortality, differences exist in terms of the area under the ROC curve, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and cutoff values (3-13).The vasoactive-inotrope score (VIS) is not yet routinely used to predict mortality in preterm infants. Davidson et al. (14) developed VIS, calculated as follows: 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 their study, VIS was calculated at 24, 48, and

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72 hours, and a strong correlation was found between high VIS values and longer hospital stays, duration of mechanical ventilation, and mortality. Several studies have shown that VIS predicts mortality in neonates and infants following cardiac/diaphragm surgery and in sepsis (15,16,17). However, there are few studies demonstrating that VIS predicts preterm morbidity and mortality (18,19).The primary aim of our study is to determine whether VIS predicts mortality in preterm infants weighing less than 1000 grams. The secondary aim is to compare the predictive abilities of VIS and the widely used CRIB-II score in preterm mortality.

Materyal - Method

Settings and Study Population

This was a retrospective study conducted at Zeynep Kamil Women and Children's Health Training and Research Hospital. A total of 280 preterm infants born with a birth weight below 1000 grams between 2019 and 2024 were included in the study. The study was conducted in compliance with the Declaration of Helsinki and was approved by the Ethics Committee of Zeynep Kamil Women and Children's Health Training and Research Hospital (Approval No. 2021-32).Inclusion criteria included: preterm infants with a birth weight <1000 grams admitted to the NICU within 24 hours of birth. Exclusion criteria were: infants with congenital malformations or congenital metabolic disorders, those discharged automatically for unknown prognostic reasons, and those with incomplete data.The following data were collected retrospectively: Demographic findings: birth weight, gestational age, gender, and mode of delivery;Antenatal findings: antenatal steroid use, presence of preeclampsia, and chorioamnionitis; Postnatal findings: admission temperature, maximum base deficit during the first postnatal hour, 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) administered within the first 24 hours, resuscitation frequency, and mortality rates.

Definitions

Antenatal corticosteroid use: Administering 2 doses of corticosteroids within 1 week for all women at risk of preterm labor between 24 and 34 weeks of gestation is recommended. Betamethasone and dexamethasone are used antenatally (20).Chorioamnionitis: Defined as fever (>38°C) without a clear focus of infection, accompanied by at least two additional criteria such as uterine tenderness, foul-smelling vaginal discharge, maternal leukocytosis (white blood cells >15,000/mm^3), elevated C-reactive protein, maternal tachycardia (>100 beats/min), and fetal tachycardia (>160 beats/min) (21).Preeclampsia: Defined as new-onset proteinuria and/or edema with hypertension (blood pressure >140/90 mmHg and mean arterial pressure >105 mmHg) (22).Mortality: Defined as any death occurring before hospital discharge.

Score Calculation

The CRIB-II score (ranging from 0 to 27) is calculated based on five parameters: birth weight, gender, body temperature at the time of admission, gestational age, and the worst base deficit within the first hour of life (2).

VISwas calculated using the maximum inotrope doses administered within the first 24 postnatal hours.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)(14).

Statistical analysis

Statistical analyses in this study were performed using the NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA). In the evaluation of the data, descriptive statistical methods (mean, standard deviation, median, and interquartile range) were used. The distribution of

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variables was assessed with the Shapiro–Wilk normality test. For comparisons between two groups with normally distributed variables, an **independent t-test** was used.For non-normally distributed variables, time-based comparisons were analyzed with the **Friedman test**, subgroup comparisons with **Dunn's multiple comparison test**, and two-group comparisons with the **Mann–Whitney U test**. The **chi-square test** was used for categorical data comparisons.The area under the ROC curve (AUC) was calculated to determine the diagnostic accuracy of mortality predictors. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and LR(+) values were calculated, and cutoff points for variables were determined.Results were evaluated at a significance level of $p<0.05$.

Results

The mean birth weight of the 280 infants was 684.49±193.2 grams, and the mean gestational age was 26.4±2.2 weeks. Of the infants, 56.79% were male, and 66% were delivered via cesarean section. Resuscitation was performed on 87% of the infants at least once. Antenatal steroid therapy was administered to 53% of the infants. The incidence of preeclampsia was 18%, and chorioamnionitis was 13%. The mean maximum base deficit during the first postnatal hour was -6.5±-5.7. Dopamine was administered to 28% of the infants, dobutamine to 46%, adrenaline to 20%, norepinephrine to 20%, and milrinone to 1%. The mean CRIB II score was 12.32±4.08, and the mean VIS was 53.75±89.57. The overall mortality rate was 49% (Table 1). Infants who died within the first 28 postnatal days had significantly lower birth weights, gestational ages, and antenatal steroid use rates compared to survivors (p=0.0001 for all). In contrast, infants who died had significantly higher rates of resuscitation, male gender, preeclampsia, chorioamnionitis, spontaneous vaginal delivery, and administration of dopamine, dobutamine, adrenaline, and norepinephrine (p-values: 0.0001; 0.001; 0.0001; 0.008; 0.0001; 0.0001; 0.0001; 0.0001, respectively). Dopamine and dobutamine doses, as well as the mean base deficit, were significantly higher in infants who died compared to survivors (p=0.004, p=0.0001, p=0.0001, respectively). The mean CRIB-II score and VIS were significantly higher in infants who died compared to those who survived (p=0.0001 for both, Table 2). Logistic regression analysis identified high CRIB-II scores (p=0.0001) and high VIS (p=0.0001) as independent factors affecting mortality (Table 3). To evaluate the importance of CRIB-II and VIS in predicting mortality, the area under the ROC curve (AUC) was calculated. The AUC for CRIB II in predicting mortality was 0.860 (0.814-0.898), while the AUC for VIS was 0.816 (0.765-0.859) (Table-4). Both variables had an AUC above the desired threshold of 0.700. No statistically significant difference was observed between the AUC values of CRIB II and VIS (p=0.160).

The cutoff values for predicting mortality were calculated for CRIB-II and VIS. For CRIB II with a cutoff >12, sensitivity was 79.86%, specificity 82.27%, positive predictive value (PPV) 81.60%, negative predictive value (NPV) 80.60%, and LR (+) was 4.50. Patients with a CRIB-II score >12 were found to have a 4.5 times higher risk of mortality compared to those with a CRIB-II score <12. For VIS with a cutoff >5, sensitivity was 70.50%, specificity 87.94%, PPV 85.20%, NPV 75.20%, and LR (+) was 4.50 (Table 5, Figure 1).A premature infant with a VIS of >5 was found to have a 5.85 times higher risk of mortality compared to an infant with a VIS of <5.

Discussion

This study demonstrated that the Vasoactive Inotropic Score (VIS) predicts mortality in preterm infants. It is the first study to show that VIS, similar to CRIB-II, predicts mortality in preterm infants. The quantitative value of VIS in preterm mortality increases its significance.Numerous studies have shown that CRIB-II predicts preterm mortality. These studies reported cut-off values of 4, 11, 4, and 5; AUC values of 0.84, 0.96, 0.69, and 0.69; sensitivity rates of 85, 95, 81, and 69; specificity rates of 83, 82, 75, and 63; positive predictive values (PPV) of 75, 74, 83, and 76; and negative predictive values (NPV) of 90, 96, 82, and 54 (3, 4, 5, 6). In the study conducted by researchers from the Korean Neonatal Network (KNN), the CRIB-II score performed strongly in predicting mortality within the first 30 days (AUC: 0.8435). However, its effectiveness diminished beyond the 90-day threshold (AUC: 0.6576) (7). Other studies demonstrating the predictive ability of CRIB-II for mortality reported AUC values of

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0.84 (8), 0.85 (9), 0.91, 0.92, 0.96, and 0.92 (2, 10, 11, 12). In the study with an AUC of 0.84, sensitivity was 75%, specificity was 78%, and the cut-off value was determined to be 8.5 (8). Some studies have also reported cut-off values of 6.5 and 7 (9, 13). In our study, the CRIB-II score for predicting preterm mortality had an AUC of 0.860 (0.814–0.898). For a cut-off value of >12, sensitivity was 79.86%, specificity was 82.27%, positive predictive value (PPV) was 81.60%, negative predictive value (NPV) was 80.60%, and LR(+) was 4.50. These findings are consistent with those reported in other studies. The variation in CRIB-II cut-off values among studies may stem from differences in study settings, populations from diverse centers, and variations in birth weights and gestational ages.

VIS, originally used as a hemodynamic support score in postoperative pediatric cardiac patients in intensive care, has been shown in studies to predict mortality following cardiac surgery in infants, neonates, and preterm infants. Gaies et al. (15) showed that the frequency of death, cardiac arrest, mechanical circulatory support, and need for renal replacement therapy increased significantly in patients who reached VIS within 48hours among postoperative cardiac patients, 43% of whom were neonates. Butts et al. identified a correlation between the 36-hour VIS and the duration of mechanical ventilation, length of ICU stay, and total hospital costs in a study of 76 pediatric patients following cardiac surgery (23). Sanil et al. found that the 48-hour VIS was associated with adverse outcomes in infants undergoing heart transplantation (24). In the study by Friesland-Little et al., a 48-hour VIS >27 was shown to predict the need for ECMO after cardiac surgery (25). Gaies et al.demonstrated in their 2014 study that a 24-hour VIS >20 after cardiac surgery was associated with neonatal mortality and morbidity (26). Grow et al., in a study of 244 infants under 1 year of age, showed that VISmax after cardiac surgery predicted poor prognosis (27). In the study by Dilli et al. involving 119 neonates, a 72-hour VIS after cardiac surgery was found to be associated with mortality and the duration of ventilation (28). In the study conducted by Koponen et al., 117 patients who underwent cardiovascular surgery, were markedly hypotensive, and were born before 33 weeks of gestation were examined. It was emphasized that a VIS value >25 showed 66% sensitivity and 92% specificity for mortality, with 32.5% of the patients dying (29).

There are also studies linking VIS with poor prognosis in congenital diaphragmatic hernia (CDH). Gospel et al. demonstrated that VIS was associated with poor clinical and echocardiographic findings in neonates with CDH (16). Similarly, Lig et al. showed that a 24-hour VIS in neonates with CDH was associated with worsening cardiac function and a higher risk of mortality (30).

Studies have also associated VIS with poor prognosis in pediatric and neonatal sepsis. In the study by Demirhan et al., VIS was found to be a poor prognostic factor in neonatal sepsis (17).In another study conducted by Haque et al. (31) 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. (32) 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.

The number of studies linking VIS with preterm morbidity and mortality is limited. The study conducted by Aziz et al.,(19) 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 between 0–5, by 5.1 times in patients with a VIS be- tween 5–10, by 13.3 times in patients with a VIS between 10–15, by 23.8 times in patients with a VIS between 20–25, by 37.7 times in patients with a VIS between 25–30, and by 46.1 times in patients with a VIS >30 compared to infants with a normal VIS. In the study by Kharrat et al., it was shown that a 48-hour VIS greater than 20 was associated with poor prognosis in 192 neonates born at less than 35 weeks of gestation (33). In our study, we found that preterm infants with a VIS >5 at 24 hours had a mortality rate 5.85 times higher. Despite differences in cut-off values, the common finding across these studies is that VIS predicts mortality in preterm infants.

Conclusion: In our study, VIS predicted preterm mortality with low sensitivity and NPV, but high specificity and PPV compared to the CRIB-II score. With its equivalent quantitative predictive ability, VIS can be used as a preterm mortality score.

Table 1. Demographic, Antenatal, Postnatal Findings, VIS, and CRIB II Score.

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Bİrth weight	mean±SD	684,49±193,21	
Bİrth weeks	mean±SD	25,39±2,93	
Resuscitation	none	33	%11,79
	1	241	%86,07
	>2	6	%2,14
Gender	female	159	%56,79
	male	121	%43,21
Preeclampsia		51	%18,21
Chorioamnionitis		39	%13,93
Antenatal steroid dose	none	85	%30,36
	1	46	%16,43
	>2	149	%53,21
Mode of delivery	vaginal delivery	95	%33,93
	C/S	185	%66,07
CRİB II Score	mean±SD	12,32±4,08	
	median (IQR	12 (9-16)	
VIS	mean±SD	53,75±89,57	
	median (IQR	5 (0-110)	
BE	mean±SD	-6,5±5,7	
	Median (IQR	-6 (-9,75--2)	
Dopamin in first hour 24		79	%28,21
Dobutamin in first hour 24		130	%46,43
Adrenalin in first hour 24		58	%20,71
Noradrenalin in first hour 24		57	%20,36
Milrinon in first hour 24		3	%1,07

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Mortality in postnatal 28 days	139	%49,64

Table 2. Comparison of Demographic, Antenatal, and Postnatal Findings, VIS and CRIB II ScoreAverages in Infants Who Died and Survived Within the first 28 days postnatally .

		Mortalite (-) n:141		Mortalite (+) n:139		p
Bİrth week	mean±SD	26,99±2,36		23,77±2,55		0,0001
Bİrth weight	mean±SD	797,25±160,27		570,11±152,47		0,0001
Resuscitation	none	26	%18,44	7	%5,04	0,0001
	1	115	%81,56	126	%90,65	
	>2	0	%0,00	6	%4,32	
Gender	Male	66	%46,81	93	%66,91	0,001
	Female	75	%53,19	46	%33,09	
Preeclampsia		37	%26,24	14	%10,07	0,0001
Chorioamnionitis		12	%8,51	27	%19,42	0,008
Antenatal steroid dose	none	24	%17,02	61	%43,88	0,0001
	1	19	%13,48	27	%19,42	
	>2	98	%69,50	51	%36,69	
Mode of delivery	vaginal delivery	24	%17,02	71	%51,08	0,0001
	C/S	117	%82,98	68	%48,92	
CRİB II Score	mean±SD	9,85±3,01		14,82±3,46		0,0001
	Median (IQR)	10 (8-11,5)		15 (13-17)		
VIS	mean±SD	10,07±33,04		98,05±105,76		0,0001
	Median (IQR)	0 (0-5)		100 (5-140)		
BE	mean±SD	-5±5,12		-8,01±5,87		0,0001

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	Median (IQR)	-4 (-7--1,5)		-6,5 (-11,5--4)		
Dopamin		17	%12,06	62	%44,60	0,0001
Dopamin dose in postnatal 24h	Ort±SS	10,59±5,83		15,24±5,78		0,004
	Median (IQR)	10 (5-15)		20 (10-20)		
Dobutamin		31	%21,99	99	%71,22	0,0001
Dobutamin dose in postnatal 24h	Ort±SS	8,71±4,83		13,81±5,47		0,0001
	Median (IQR)	5 (5-10)		10 (10-20)		
Adrenalin		5	%3,55	53	%38,13	0,0001
Adrenalin dose in postnatal 24h	Ort±SS	0,64±0,49		1,07±0,47		0,061
	Median (IQR)	1 (0,1-1)		1 (1-1)		
Noradrenalin		6	%4,26	51	%36,69	0,0001
Noradrenalin dose in postnatal 24h	Ort±SS	0,93±0,19		1,06±0,27		0,156
	Median (IQR)	1 (1-1)		1 (1-1)		
Milrinon		0	%0,00	3	%2,16	0,079

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Table 3. Logistic Regression Analysis for Predictors of Mortality Within 28 Days Postnatally.

	OR (%95 G.A)	p
Bİrth week	1,05 (0,75-1,48)	0,786
Birth weight	1 (0,99-1,01)	0,155
Resuscitation	1,42 (0,39-5,11)	0,594
Gender	0,48 (0,21-1,07)	0,074
Preeclempsia	0,42 (0,15-1,20)	0,104
Chorioamnionitis	0,81 (0,27-2,38)	0,699
Antenatal steroid		0,853
1	0,83 (0,25-2,74)	0,758
>2	0,77 (0,31-1,9)	0,573
Mode of delivery	0,87 (0,35-2,12)	0,753
Dopamin	0,44 (0,14-1,36)	0,154
Dobutamin	1,89 (0,76-4,71)	0,173
Adrenalin	0,37 (0,03-5,07)	0,456
Noradrenalin	0,17 (0,01-3,84)	0,267
CRİB II Score	1,55 (1,38-1,73)	0,0001
VIS	1,02 (1,01-1,02)	0,0001
BE	1,04 (0,94-1,15)	0,416

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Table 4. AUC, Cut-off, Sensitivity, Specificity, PPV, and NPV values of the CRIBII score and VIS.

	AUC	SE	95% CI
CRİB II Skoru	0,860	0,023	0,814 - 0,898
VIS	0,816	0,026	0,765 - 0,859

	Cut-off	Sensitivity	Specificity	PPV	NPV	LR (+)
CRIB II Skoru	>12	79,86	82,27	81,60	80,60	4,50
VIS	>5	70,50	87,94	85,20	75,20	5,85

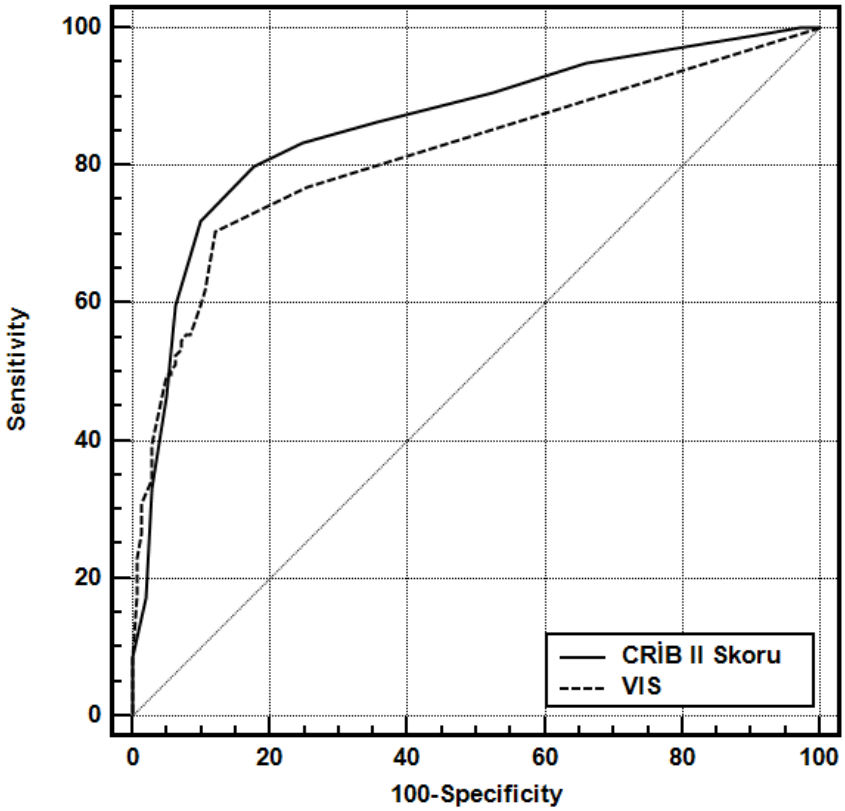

Figure 1. ROC analysis of the CRIBII score and VIS for predicting mortality.

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References

1. Baker, S.; Xiang, W.; Atkinson, I. Hybridized neural networks for non-invasive and continuous mortality risk assessment in neonates. *Comput. Biol. Med.* **2021**, *134*, 104521. https://doi.org/10.1016/j.compbiomed.2021.104521.
2. The CRIB (clinical risk index for babies) score: a tool for assessing initial neonatal risk and comparing performance of neonatal intensive care units. The International Neonatal Network. *Lancet.* 1993, 342, 193–8. Erratum in: Lancet **1993**, *342*, 626. PMID: 8100927.
3. Rahman, A.; Hamid, M.H. Accuracy of CRIB II Score in Predicting the Neonatal Mortality in very Preterm Babies. *PJMHS* 2022, 16;564-566.
4. Ezz-Eldin, Z.; Hamid, T.; Youssef, M.; Nabil, H. Clinical Risk Index for Babies (CRIB II) Scoring System in Prediction of Mortality in Premature Babies. *JCDR* **2015**, *9*.
5. Marete, I.K.; O Wasunna, A.; A Otieno, P. Clinical risk index for babies (CRIB) II score as a predictor of neonatal mortality among low birth weight babies at Kenyatta National Hospital. *East Afr Med J.* **2011**, *88*, 18–23.
6. Mohkam, M.; Afjeii, A.; Payandeh, P.; Zadkarami, M.; Kazemian, M.; Fakhraii, H. A comparison of CRIB, CRIB II, SNAP, SNAPII and SNAP-PE scores for prediction of mortality in critically ill neonates. *Med J Islamic Republ Iran.* **2011**, *24*, 193–199.
7. Lee, S.M.; Lee, M.H.; Chang, Y.S. The Clinical Risk Index for Babies II for prediction of time-dependent mortality and short-term morbidities in very low birth weight infants. *Neonatology.* **2019**, *116*, 244–51.
8. Faridpour, F.; Farahani, A.S.; Rassouli, M.; Shariat, M.; Nasiri, M.; Ashrafzadeh, M. Clinical risk index for babies (CRIB-II) scoring system in prediction of mortality risk in preterm neonates in the first 24 hour.. Evidence Based Care **2020**, *10*, 58–63, 2020
9. Babaei, H.; Jafrasteh, A. The evaluation of CRIB II scoring system in predicting mortality in preterm newborns. *Yafteh.* **2015**, *16*, 27–35
10. Gagliardi, L.; Cavazza, A.; Brunelli, A.; Battaglioli, M.; Merazzi, D.; Tandoi, F.; Cella, D.; Perotti, G.F.; Pelti, M.; Stucchi, I.; et al Assessing mortality risk in very low birthweight infants: a comparison of, C.R.I.B.; CRIB-II; SNAPPE-II Arch Dis Child Fetal Neonatal Ed. **2004**, *89*, F419–F422. https://doi.org/10.1136/adc.2003.031286.
11. EzzEldin, Z.M.; Hamid, T.A.; Youssef, M.R.; Nabil, H.E. Clinical risk index for babies (CRIB II) scoring system in prediction of mortality in premature babies. *J Clin Diagn Res.* 2015, 9, SC08–SC11.
12. Felice C, Del Vecchio A, Latini G. Evaluating illness severity for very low birth weight infants: CRIB or CRIB-II? *J Maternal Fetal Neonatal Med.* **2005**, *7*, 257–60.
13. Fouladinejad, M.; Behnampour, N.; Zanjani, A.P.; Gharib, M.H.; Kamrani, M.A. The evaluation of predicting mortality risk of premature infants with very low birthweight by CRIB score. *J Gorgan Univ Med Sci.* **2009**, *10*, 40–89.
14. Davidson, J.; Tong, S.; Hancock, H.; Hauck, A.; da Cruz, E.; Kaufman, J. Pro- spective validation of the vasoactive-inotropic score and correlation to short-term outcomes in neonates and infants after cardiothoracic sur gery. *Intensive Care Med* **2012**, *38*, 1184–1190.
15. Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, et al. Vasoactive-inotropic score as a predictor of morbidity and mor- tality in infants after cardiopulmonary bypass. *Pediatr Crit Care Med* **2010**, *11*, 234–238.
16. Hari Gopal S, Toy CL, Hanna M, Furtun BY, Hagan JL, Nassr AA, Fernandes CJ, Keswani S and Gowda SH Inotropic score and vasoactive inotropic score as predictors of outcomes in congenital diaphragmatic hernia: A single center retrospective study. *Front. Pediatr.* **2023**, *11*, 1101546.
17. Demirhan, S.; Topçuoğlu, S.; Karadağ, N.; Özalkaya, E.; Karatekin, G. Vasoactive inotropic score as a predictor of mortality in neonatal septic shock. *J Trop Pediatr.* 2022, 68. https://doi.org/10.1093/tropej/fmac100.
18. Amer, R.; Seshia, M.M.; Elsayed, Y.N. A vasoactive inotropic score predicts the severity of compromised systemic circulation and mortality in preterm infants. *J. Neonatal Perinat. Med.* **2022**, *15*, 529–535. https://doi.org/10.3233/npm-210932.

19. Aziz, K.B.; Lavilla, O.C.; Wynn, J.L.; Lure, A.C.; Gipson, D.; de la Cruz, D. Maximum vasoactive-inotropic score and mortality in extremely premature, extremely low birth weight infants. *J Perinatol* **2021**, *41*, 2337–2344. https://doi.org/10.1038/s41372-021-01030-9.
20. Kliegman, R.M.; Stanton, B.F.; St Gene, J.W.; Schor, N.F.; Behrman, R.E. Nelson textbook of pediatrics. Philadelphia: Saunders Elsevier; 2011.
21. Been JV, Rours IG, Kornelisse RF, Lima Passos V, Kramer BW, Schnei- der TA, et al. Histologic chorioamnionitis, fetal involvement, and antena- tal steroids: Effects on neonatal outcome in preterm infants. *Am J Obstet Gynecol* **2009**, *201*, 587.e1–8.
22. Romero R, Gomez R, Galasso M, Munoz H, Acosta L, Yoon BH, et al. Macrophage inflammatory protein-1 alpha in term and preterm partu- rition: Effect of microbial invasion of the amniotic cavity. *Am J Reprod Immunol* **1994**, *32*, 108–113.
23. Butts, R.J.; Scheurer, M.A.; Atz, A.M.; Zyblewski, S.C.; Hulsey, T.C.; Bradley, S.M.; Graham, E.M. Comparison of maximum vasoactive inotropic score and low cardiac output syndrome as markers of early postoperative outcomes after neonatal cardiac surgery. *Pediatr Cardiol.* **2012**, *33*, 6. https://doi.org/10.1007/s00246-012-0193-z.
24. Y Sanil et al Vasoactive-inotropic score after pediatric heart transplant: a marker of adverse outcome. *Pediatr Transplant.* **2013**, *17*, 567–72.
25. Friesland-Little, J.M. et *al.* Risk factors for requiring extracorporeal membrane oxygenation support after a Norwood operation. *J Thorac Cardiovasc Surg.* **2019**, *122*, 428–436.
26. Gaies MG et al. Vasoactive-inotropic score is associated with outcome after infant cardiac surgery: an analysis from the Pediatric Cardiac Critical Care Consortium and Virtual PICU System Registries. *Pediatr Crit Care Med.* **2014**, *15*, 52
27. Crow SS et al. Duration and magnitude of vasopressor support predicts poor outcome after infant cardiac operations. *Ann Thorac Surg.* **2014**, *98*, 655–61.
28. Dilli D et.al. Predictive Value of Vasoactive-inotropic Score for Mortality in Newborns Undergoing Cardiac Surgery. *Indian Pediatr.* **2019**, *56*, 735–740.
29. Koponen, T.; Karttunen, J.; Musialowicz, T.; Pietiläinen, L.; Uusaro, A.; Laht- inen, P. Vasoactive-inotropic score and the prediction of morbidity and mortality after cardiac surgery. *Br J Anaesth* **2019**, *122*, 428–436.
30. Liu, C.; Li, J.; Wei, Y.; Wang, Y.; Zhang, H.; Ma, L. Preliminary study on the predictive value of the vasoactive-inotropic score for the prognosis of neonatal congenital diaphragmatic hernia. *BMC Surg.* **2023**, *23*, 69. doi: 10.1186/s12893-023-01970-3.
31. Haque, A.; Siddiqui, N.R.; Munir, O.; Saleem, S.; Mian, A. Association between vasoactive-inotropic score and mortality in pediatric septic shock. *Indian Pediatr* **2015**, *52*, 311–313. https://doi.org/10.1007/s13312-015-0630-1.
32. Kallekkattu, D.; Rameshkumar, R.; Chidambaram, M.; Krishnamurthy, K.; Selvan, T.; Mahadevan, S. Threshold of inotropic score and vasoac- tive-inotropic score for predicting mortality in pediatric septic shock. *Indian J Pediatr* **2022**, *89*, 432–437.
33. Kharrat, A.; Ripstein, G.; Baczynski, M.; Zhu, F.; Ye, X.Y.; Joye, S.; Jain, A. VAlidity of the vasoactive-inotropic score in preterm neonates receiving cardioactive therapies. *Early Hum Dev.* **2022**, *173*, 105657. https://doi.org/10.1016/j.earlhumdev.2022.105657.