Research Article

Türk Fen ve Sağlık Dergisi
Turkish Journal of Science and Health

Volume 5
Number 2
Year 2024
Pages 95-103

e-ISSN: 2717-7173 https://dergipark.org.tr/tr/pub/tfsd

Received: 20.02.2024 *Accepted:* 19.04.2024 https://doi.org/10.51972/tfsd.1438904

Predictive Value of Different Risk Scores for Mortality and Morbidity in Extremely Preterm Infants

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ABSTRACT:
Purpose: To determine the role of different scoring systems in predicting mortality and morbidity risk of preterms who are younger than 32 weeks and/or have a birth weight of less than 1500 g.
Material and Methods: Preterm infants with a gestational age (GA) of less than 32 weeks and/or a birth weight (BW) of less than 1500 grams, who were admitted to the neonatal intensive care unit (NICU) between June 2014 and June 2016, were included in this study. The SNAP-PE-II and CRIB scores in the first 12 hours of life and the NTISS scores at 24, 48, and 72 hours of life were calculated for all newborns. Mortality rate, length of hospital stay, and morbidities were prospectively recorded. The patients were divided into two groups as survivors (Group 1) and non-survivors (Group 2). The data obtained were then statistically compared between the two groups.
Results: A total of 120 preterm infants constituted the study group. There were significant differences between the groups with respect to all studied risk scores (p<0.001). All scores showed satisfactory discrimination and calibration abilities for mortality. As for the morbidities, all of the scores were found to be higher in patients with morbidities than those without, but the situation changed when the ROC analyses were performed and sensitivity and specificity values were calculated.
Conclusion: This is one of the few studies that evaluated the relationship between the scoring systems used to predict mortality risk and common morbidities in extremely preterm patients.
Keywords: *Scoring systems; CRIB; SNAP-II; SNAP-PE-II; NTISS*

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INTRODUCTION

Improvements in perinatal and neonatal care have increased the survival rate of preterm infants that also have higher rates of mortality and morbidity. Common morbidities due to preterm birth are respiratory distress syndrome (RDS), patent ductus arteriosus (PDA), necrotising enterocolitis (NEC), bronchopulmonary dysplasia (BPD), intraventricular hemorrhage (IVH), and retinopathy of prematurity (ROP) (Chawanpaiboon et al., 2019; Acunaş, Uslu and Baş, 2018). In neonatal intensive care units, predetermination of the mortality risk and the severity of diseases that may lead to mortality is extremely important both for being prepared for severe conditions that may be encountered such as early mortality during follow-up and answering the parents' questions. Various scoring systems have been developed to predict the mortality risk. Scoring systems are used to predict patient prognosis, to compare different groups in clinical trials, to evaluate the performance of different units, to predict early and late complications as well as mortality, and to perform relevant interventions in advance (McLeod et al., 2020; Zeng, Shi and Li, 2023) The desired features of a neonatal scoring system are ease of use, early applicability after birth, and an ability to the calculate the risks of mortality and morbidity and treatment cost. More comprehensive scoring systems have been developed over the years, which are based on physiologic parameters reflecting the initial clinical status of the patient and the treatments applied to the patient (Erdem, 2003). Score for Neonatal Acute Physiology - Perinatal Extension (SNAP-PE-II), which can be administered in the first 12 hours postnatally, consists of nine different parameters including mean blood pressure, lowest body temperature, PO2/FiO2 ratio, serum pH value, presence of convulsions, urine volume, birth weight, fifth-minute Apgar score, and the presence of a small for gestational age (SGA) (Richardson et al., 2001). Clinical Risk Index for Babies (CRIB), uses information about base deficit and oxygen demand in the first 12 hours of life, along with birth weight, gestational age in weeks, and congenital malformation(s) (Brito et al., 2003). Neonatal Therapeuetic Intervention Scoring System (NTISS), a modification of the Adult Therapeuetic Intervention Scoring System (TISS) used in adults, was created to provide a treatment-based disease severity assessment tool for use in neonatal intensive care (Gray et al., 1992).

Our aim is to determine the role of different scoring systems in predicting mortality and morbidity risk of preterms who are younger than 32 weeks and/or have a birth weight of less than 1500 g.

MATERIAL and METHODS

Purpose and Type of the Study

Our purpose is to determine the role of different scoring systems in predicting mortality and morbidity risk of preterms who are younger than 32 weeks and/or have a birth weight of less than 1500 g.

Sampling and participant

Preterm infants with a gestational age (GA) of less than 32 weeks and/or a birth weight (BW) of less than 1500 grams , who were admitted to the neonatal intensive care unit (NICU) between June 2014 and June 2016, were included in this study. The SNAP-PE-II and CRIB scores in the first 12 hours of life and the NTISS scores at 24, 48, and 72 hours of life were calculated for all newborns.

Data Collection Tools

Mortality rate, length of hospital stay, and morbidities including RDS, IVH, NEC, BPD, ROP, and PDA were prospectively recorded. Mode of delivery, 1st and 5th minute Apgar score, gender, gestational age in weeks, and birth weight were obtained from the patients' neonatal epicrises or medical records. Prospectively recorded data were evaluated retrospectively. The patients were divided into two groups as survivors (Group 1) and non-survivors (Group 2). The data obtained were then statistically compared between the two groups.

Statistical Analysis

For descriptive statistical evaluation, percentage (%) and frequency values were used for categorical variables while median, minimum, maximum, mean and standard deviation values were used for numerical variables. Chi-square test was performed for categorical variables and Mann-Whitney U (MWU) test for numerical variables for comparing the groups. A p value of less than 0.05 was considered statistically significant for all statistical tests. Spearman correlation coefficient (r) was used to evaluate the relationship between numerical variables. The area under the ROC curve was calculated to evaluate the discrimination and calibration of mortality scores. The score was considered to be discriminative if the area under the ROC curve was above 0.80. The point on the ROC curve with the highest specificity and sensitivity was determined as the cut-off point. Specificity and sensitivity were calculated for that cut-off point. With this calculation, patients with a mortality risk above the cut-off point constituted the group with expected mortality. Thus, the relationship between scores and the expected and observed mortality rates was evaluated. The same calculations were performed separately for the morbidity rates. All statistical tests were performed using the Statistical Package for Social Science (SPSS) 11.0 software package.

Ethical Approval

Ethics approval for the study was obtained from the Local Ethics Committee on 15.06.2016, with a protocol number of 12/16 and a protocol code of

TUTF-BAEK 2016/160.

RESULTS

A total of 128 preterm infants followed up in the NICU between June 1, 2014 and June 30, 2016 were included in the study. Six patients were excluded from the study because they died before the 72nd hour of life; two patients were also excluded because they were referred from an external center. A total of 120 preterm newborns constituted the study group. Ninety-six surviving infants were considered as Group 1 and 24 non-surviving infants were considered as Group 2.

Mean gestational age in weeks was 29 ± 1.8 weeks in Group 1 and 26 ± 2.3 weeks in Group 2; mean birth weight was 1260 ± 386 g in Group 1 and 833 ± 300 g in Group 2. When the two groups were compared, the difference between BW, GA, presence of SGA, and the 1st and 5th minute Apgar scores were statistically significant (p<0.001). There was no statistically significant difference between the groups in terms of gender and mode of delivery (Table 1).

The mortality rate of the whole study group was 20%. When individual morbidities were analyzed, the most common morbidity was NEC of any stage (60%), which was followed by RDS (58%), IVH of any stage (32%), BPD of any stage (21%), ROP of any stage (12%), and hemodynamically significant PDA (hsPDA) (3%). Stage 1 NEC, RDS, and IVH of any stage were significantly more common in Group 2 compared with Group 1 (p<0.001) (Table 2).

There were significant differences between the groups with respect to all studied risk scores (p<0.001).The areas under the ROC curve of the scores in the Group 2 were calculated as 0.86 for CRIB, 0.85 for NTISS-24, 0.81 for NTISS-48, 0.81 for NTISS-72, 0.84 for SNAP-II, and 0.90 for SNAP-PE-II (p<0.001). All scores showed satisfactory discrimination and calibration abilities for mortality (Table 3).

Table 1. Comparison of Demographic Data

	All patients (n=120)	Group 1 (n=96)	Group 2 (n=24)	p
Caesarean section, n (%)	103 (86)	12 (87)	5 (79)	0,329
Gender (male), n (%)	50 (42)	42 (44)	8 (33)	0,488
Gestational age (week)†	28,8 ± 2,3	29 ± 1,8	26 ± 2,3	<0,001*
Birth weight (gram) †	1175 ± 407	1260 ± 386	833 ± 300	<0,001*
SGA, n (%) †	38 (31,7)	23 (24)	15(62,5)	<0,001**
Apgar 1' †	9 (2-10)	9 (2-10)	3 (2-9)	<0,001*
Apgar 5' †	10 (4-10)	10 (5-10)	7 (4-10)	<0,001*

* Independent Samples T-test ** Chi-square test † (mean±SD)

Tablo 2. Comparison of preterm morbidities

	All patients (n=120)	Group 1 (n=96)	Group 2 (n=24)	p*
NEC, n (%)	72 (60)	61 (63,5)	11 (46)	0,161
Stage 1	36 (30)	36 (37,5)	-	<0,001
Stage 2	34 (28)	24 (25)	10(42)	0,130
Stage 3	2 (2)	1(1)	1(4)	0,361
RDS, n (%)	69 (58)	47 (49)	22 (92)	<0,001
IVH, n (%)	39 (32)	19 (20)	20 (83)	<0,001
Stage 1-2	25 (20)	17 (18)	8 (33)	<0,001
Stage 3	14 (12)	2 (2)	12 (50)	<0,001
hsPDA, n (%)	4 (3)	2 (2)	2 (8)	0,178
BPD, n (%)	25 (21)	22 (23)	4 (16)	0,591
Mild	13 (11)	12 (12)	1 (4)	0,461
Moderate	9 (7,5)	7 (8)	2 (8)	0,572
Severe	3 (2,5)	2 (3)	1 (4)	0,491
ROP, n (%)	15 (12)	12 (12,5)	3 (12,5)	0,652

* Chi-square test **NEC:** Necrotising Enterocolitis, **IVH:** Intraventricular Hemorrhage, hsPDA**:** Hemodynamically Significant Patent Ductus Arteriosus, **BPD:** Bronchopulmonary Displasia, **ROP:** Retinopathy of Preterm

Table 3. Comparison of risk scores

Risk Scores	Group 1 (n=96)	Group 2 (n=24)	p*
CRIB	1,5±2,2	7±4,3	<0,001
NTISS-24	12,3±3,2	16,5±2,5	<0,001
NTISS-48	11,9±2,5	14,5±1,9	<0,001
NTISS-72	12,1±2,5	14,5±1,7	<0,001
SNAP-II	7,2±9,5	27,2±16,5	<0,001
SNAP-PE-II	17,9±19,2	58±23,8	<0,001

* Independent Samples T-test (mean±SD)

Table 4. Distribution of sensitivity and specificity of risk scores for all morbidities

	CRIB	NTISS-24	NTISS-48	NTISS-72	SNAP-II	SNAP-PE-II
RDS						
Sensitivity (%)	87	88	88	73	78	78
Specifity (%)	51	85	79	85	83	73
Cut-off	0,5	11,5	11,5	12,5	6,5	13,5
ROP						
Sensitivity (%)	64	73	80	86	71	86
Specifity (%)	67	72	57	57	70	69
Cut-off	1,5	15,5	12,5	12,5	14	30,5
BPD						
Sensitivity (%)	65	73	68	80	73	72
Specifity (%)	71	62	47	62	65	64
Cut-off	1,5	13,5	12,5	12,5	10	24,5
Moderate-Severe BPD						
Sensitivity (%)	91	75	66	91	67	75
Specifity (%)	69	54	54	56	60	60
Cut-off	1,5	12,5	12,5	12,5	10	24,5
IVH						
Sensitivity (%)	92	92	85	-	92	100
Specifity (%)	80	74	73		69	89
Cut-off	3	15,5	13,5		12,5	47,5

NEC: Necrotising Enterocolitis, **IVH:** Intraventricular Hemorrhage, **hsPDA:** Hemodynamically Significant Patent Ductus Arteriosus, **BPD:** Broncopulmonary Displasia, **ROP:** Retinopathy of Preterm

When the risk scores were evaluated in terms of morbidities, all risk scores were significantly higher in patients with RDS, ROP, and BPD. The discrimination and calibration abilities of all scores were satisfactory only for patients diagnosed with RDS. NTISS-24 was the best scoring system for RDS, having a sensitivity of 88% and a specificity of 85%. The discrimination and calibration abilities of the scores for ROP, BPD, and anaemia were not satisfactory. CRIB, SNAP-II, SNAP-PE-II, SNAP-PE-II, and NTISS scores calculated at 48 hours were significantly different between patients with and without PDA. The discrimination and calibration abilities of these scores were found to be satisfactory. At the cut-off point for the diagnosis of PDA, SNAP-PE-II score was the best scoring system, having a sensitivity of 100% and a specificity of 69%.

The distribution of risk scores was evaluated separately in patients diagnosed with BPD, with and without moderate or severe BPD. Moderate or severe BPD was detected in 12 of 120 patients. When the scores of patients with and without moderate or severe BPD were compared, a significant difference was found between all of the scores. Only the CRIB score had satisfactory discrimination and calibration abilities in this sense. The sensitivity and specificity of the CRIB score at its best cut-off point for the diagnosis were 91% and 69%, respectively. In severe IVH, the prognosis is poor and the likelihood of sequelae is high. Therefore, only patients with severe IVH were selected. When the risk scores were compared in patients with and without IVH, a significant difference was found between all of the scores, except for NTISS, calculated at 72 hours. The discrimination and calibration abilities of all scores were found to be satisfactory. The sensitivity and specificity of the SNAP-PE-II score for the diagnosis of IVH at its best cut-off point were calculated as 100% and 89%, respectively. For all morbidities, the sensitivity and specificity values of the risk scores for those with and without a significant difference between the diagnosed and undiagnosed groups were calculated by a ROC analysis. The distribution of sensitivity and specificity values of the risk scores for all morbidities studied are given on Table 4.

DISCUSSION

Various scoring systems have been developed to predict the mortality risk in various conditions. Scoring systems are used to predict the prognosis of a patient, to compare different groups in clinical studies, to evaluate the performance of different units, to predict early and late complications and mortality, and to perform relevant interventions in advance. The desired features of a neonatal scoring system are ease of use, early applicability after birth, and an ability to calculate the risks of mortality and morbidity and treatment cost. More comprehensive scoring systems have been developed over the years, which are based on physiologic parameters reflecting the initial clinical status of the patient and the treatments applied to the patient (Pollack et al., 2000; Dorling, Field and Manktelow, 2005; Garg, Sharma and Farahbakhsh, 2018).

In our study, we aimed to evaluate the relationship between the scoring systems CRIB, SNAP II, SNAP-PE-II II, SNAP-PE-II II, and NTISS and the mortality and morbidity rates in extremely preterm infants hospitalized in the NICU. The mortality rate of the extremely preterm group in our NICU was found to be 20%. In a multicenter study involving 1668 newborns conducted in Turkey, newborns younger than 32 weeks or weighing less than 1500 grams had a mortality rate of11.3%, while the corresponding mortality rate was 16.8% in a single-center study (Asker et al.,2016; Atasay et al. 2003). In a study published from Portugal, including 100 newborns with a birth weight of less than1500 grams and an age of less than 31 weeks, the mortality rate was 21% (Sarquis, Miyaki and Cat, 2002). In a study of 494 neonates published from Brazil, overall NICU mortality was 8.9%, while infants weighing less than 1500g had a mortality rate of 31.3%. (Zardo and Procianoy, 2003). Our study found a mortality rate that is similar to mortality data on preterm reported both from our country and other countries. The fact that our study group consisted of extremely preterm infants and that more treatments and interventions were performed are probably the main reasons for the high mortality rate found in our study.

In our study, when the scores of the surviving infants were compared with those of the non-surviving infants, a statistically significant difference was found between the two groups for all of the scores studied. When the score distribution of the groups was compared, it was observed that all risk scores were significantly higher in the group of non-surviving infants. All risk scores had satisfactory discrimination and calibration abilities for mortality, with SNAP-PE-II being the best score. These findings were consistent with the literature data. A similar study, which used the NTISS score at 24, 48, and 72 hours and included 172 preterm newborns weighing less than1500 grams, found lower scores in survivors (Wu et al., 2015). In a study using the CRIB, SNAP, SNAP-PE, SNAP-PE-II, and SNAP-PE-II scores, the scores were higher in the non-surviving group compared to the surviving group both in the whole study group and patients having a birth weight of less than 1500 grams (Zardo and Procianoy, 2003). Similar results were reported by a study using the CRIB, CRIB-II and SNAP-PE-II scores in infants weighing less than 1500 grams and (Gagliardi et al., 2004). Karaarslan et al. (Karaarslan et al., 2017) used the CRIB-II and SNAP-PE-II scores in 189 newborns younger than 32 weeks of age and weighing less than 1500 g. A comparison of the surviving and non-surviving groups revealed higher scores in the non-surviving group.

Although many studies have evaluated the relationship between the available scores and mortality, the number of studies evaluating the relationship with the scores and various morbidities is rather limited. In our study, all scores that were studied were found to be higher in patients with morbidities compared to those without, although the situation changed when the ROC analyses were performed and the sensitivity and specificity values were calculated. For the morbidities, all scores had a satisfactory discriminatory power in predicting the risk of IVH and RDS, whereas the CRIB, SNAP-II and SNAP-PE-II scores had a satisfactory discriminatory power for PDA. In terms of sensitivity and specificity, SNAP-PE-II was superior to other scores for IVH and PDA while NTISS-24 was the best one for RDS. The CRIB score was better than the other scores in predicting moderate and severe BPD.

In a recent study with a large sample size, both the CRIB-II and SNAPPE-II scores were found to have good predictive ability while CRIB-II was better than SNAPPE-II for all the morbidities (Vardhelli et al., 2022). The studies evaluating CRIB-II alone showed that the predictive ability of CRIB-II performed well for the important morbidities like ROP, BPD, and IVH (Lee et al., 2019; Phillips, Dewhurst and Yoxall, 2011; Sullivan et al., 2016).

In our study, no significant difference was found between the scores of patients with and without surgical NEC. This may be explained by the low number of patients diagnosed with surgical NEC. When the patient groups with and without NEC of any stage were compared, the CRIB and NTISS-72 scores were significantly higher in the NEC-positive group. In a study including 62 patients diagnosed with NEC, the SNAP-II and SNAP-PE-II scores were found to be higher in the group requiring surgical intervention and lower in the group that survived. It was concluded that the scores could be used to predict the prognosis of NEC and the risk of surgery (Lin et al., 2013)

According to our results, the CRIB, NTISS-48, SNAP-II and SNAP-PE-II scores were significantly higher in the group with PDA. The ROC analysis showed that the CRIB, SNAP-II, and SNAP-PE-II scores had satisfactory discrimination and calibration abilities. In a large study, the treatment approach in patients diagnosed with PDA was evaluated in 1097 preterm infants weighing less than1000 grams and younger than 33 weeks. The SNAP-PE-II score was found to be significantly higher in the conservative approach group compared with the other groups (Sadeck et al., 2014). In a study including 91 patients with a gestational age of less than 28 weeks diagnosed with PDA, the CRIB-II score was found to be significantly higher in the group with clinical findings compared with the group without clinical findings (Yoo et al., 2017).

All the scores studied in our study significantly predicted the diagnosis of ROP. However, when a ROC analysis was performed, and sensitivity and specificity values were calculated according to the cut-off point, it was seen that the scores did not perform well in risk prediction. In our study, patients with and without ROP requiring treatment were evaluated separately in terms of the scores. The difference between all scores except NTISS-48 and NTISS-72 was significant. The ROC analysis showed that discrimination and calibration abilities of the scores fort his diagnosis remained unsatisfactory. In a study that compared the SNAP-PE-II score in very low birth weight infants with and without ROP, it was observed that the score was higher in patients with ROP compared with those without. However, after logistic regression analysis and ROC curve results, it was thought that the score was not capable enough for risk assessment (Fortes Filho et al., 2009). In the study involving 503 preterm infants, 299 patients with ROP were divided into two groups consisting of 35 patients requiring surgical treatment and 264 patients not requiring it. The CRIB score was found to be higher in patients requiring surgical treatment; it was concluded that the score could be used to predict prognosis (Yang, Donovan and Wagge et al., 2006).

In our study, when patients with and without moderate and severe BPD were compared, a significant difference was observed between all of the scores. When a ROC analysis was performed, only the CRIB score was found to have a satisfactory discriminatory power. We found that there was a significant difference between all of the scores when patients with and without moderate and severe BPD were compared. When a ROC analysis was performed, only the CRIB score was found to have a satisfactory discriminatory power. In a study involving 303 preterm newborns younger than 28 weeks of gestational age, the patients were divided into four groups: BPD-free, mild BPD, moderate BPD, and severe BPD. The CRIB score was found to be higher in patients with severe BPD (Bruno et al., 2015). A study from Turkey including 246 preterm infants found that high SNAPPE-II values showed a satisfactory discriminatory power for predicting neonatal morbidities, and as a common and independent risk factor for ROP and BPD (Özcan et al., 2017).

In our study, the CRIB, NTISS-24, NTISS-48, SNAP-II, and SNAP-PE-II scores were higher in the group with severe IVH compared to the IVH-free group. A ROC analysis showed that the discrimination and calibration abilities of these scores were satisfactory. A prospective, multicentre study collected mortality, morbidity and CRIB score data of 10680 preterm newborns weighing less than 1500 grams from 68 units. The predictive ability of the CRIB score for mortality and risk of severe IVH was evaluated in newborns divided into five different groups according to birth weight. They compared the CRIB score, gestational week, and birth weight (Guzmán Cabañas et al., 2009).

CONCLUSION

In conclusion, our study is one of the few studies that evaluated the relationship between the scoring systems used to predict mortality risk and common and important morbidities in severely preterm patients. It was concluded that all of the scores performed well in predicting mortality risk. As for the morbidities, all of the scores were found to be higher in patients with morbidities than those without, but the situation changed when the ROC analyses were performed and sensitivity and specificity values were calculated. Among the morbidities, all of the scores had a satisfactory discriminatory power in predicting the risk of IVH and RDS, whereas the CRIB, SNAP-II, and SNAP-PE-II scores had a satisfactory discriminatory power for PDA. In terms of sensitivity and specificity, SNAP-PE-II was superior to the other scores for predicting IVH and PDA while NTISS-24 performed the best for RDS. The CRIB score was better than the other scores in predicting moderate and severe BPD. This study is a single-center clinical study, and its most important limitation is the small number of patients. A particular limitation is that the NTISS score is based on the assumption that all physicians have similar approaches to neonatal care; furthermore, differences in treatment approaches, training and clinical experience of physicians affect the NTISS score. Further studies are needed to clarify whether these differences affect the predictive power of the scores in predicting mortality and morbidity.

Acknowledgment

We would like to thank Prof. Dr. Burcu TOKUÇ for her support in statistical analysis.

Conflict of Interest

No conflict of interest has been declared by the authors.

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