Elevate Series

ANNALS OF MEDICINE
2024, VOL. 56, NO. 1, 2426752
https://doi.org/10.1080/07853890.2024.2426752

RESEARCH ARTICLE

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Comparing nSOFA, CRIB-II, and SNAPPE-II for predicting mortality and short-term morbidities in preterm infants ≤32 weeks gestation

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ABSTRACT

Background: Neonatal illness severity scores are not extensively studied for their ability to predict mortality or morbidity in preterm infants. The aim of this study was to compare the Neonatal Sequential Organ Failure Assessment (nSOFA), Clinical Risk Index for Babies-II (CRIB-II), and Score for Neonatal Acute Physiology with Perinatal extension-II (SNAPPE-II) for predicting mortality and short-term morbidities in preterm infants ≤32 weeks.

Methods: In this retrospective study, infants born in 2017–2018 with gestational age (GA) ≤32 weeks were evaluated. nSOFA, CRIB-II, and SNAPPE-II scores were calculated for each patient, and the ability of these scores to predict mortality and morbidities was compared. The morbidities were categorized as mod/sev bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC) requiring surgery, early-onset sepsis (EOS), late-onset sepsis (LOS), retinopathy of prematurity (ROP) requiring treatment, and severe intraventricular hemorrhage (IVH). Calculating the area under the curve (AUC) on receiver operating characteristic curves (ROC) analysis to predict and compare scoring systems' accuracy.

Results: A total of 759 preterm infants were enrolled, of whom 88 deceased. The median nSOFA, CRIB-II, and SNAPPE-II scores were 2 (0, 3), 6 (4, 8), and 13 (5, 26), respectively. Compared with infants who survived, these three scores were significantly higher in those who deceased ($p < 0.05$). For predicting mortality, the AUC of the nSOFA, SNAPPE-II, and CRIB-II were 0.90, 0.82, and 0.79, respectively. The nSOFA scoring system had significantly higher AUC than CRIB-II and SNAPPE-II ($p < 0.05$). However, short-term morbidities were not strongly correlated with these three scoring systems.

Conclusion: In infants ≤32 weeks gestation, nSOFA scoring system is more valuable in predicting mortality than SNAPPE-II and CRIB-II. However, further studies are required to assess the predictive power of neonatal illness severity scores for morbidity.

KEY MESSAGES

- This is the first study comparing nSOFA, SNAPPE-II, and CRIB-II for their ability to predict mortality and short-term morbidities in preterm infants ≤32 weeks.
- The nSOFA scoring system is more valuable in predicting mortality than SNAPPE-II and CRIB-II.
- Preterm infant mortality can be effectively predicted using the nSOFA scoring system.

ARTICLE HISTORY
Received 14 July 2023
Revised 21 September 2024
Accepted 9 October 2024

KEYWORDS
Morbidity; mortality; newborn; neonatal illness severity score; organ dysfunction score

Introduction

Globally, the number of preterm infants born each year is ~15 million, according to the World Health Organization [1]. Premature infants have immature organ systems and poor compensatory abilities, resulting in a series of complications and high mortality rates. The evaluation of a newborn's illness severity upon admission and prompt identification of neonates at higher risk of death in neonatal intensive care units (NICUs) have the potential to enhance patient care and disease prognosis. Various scoring systems have been designed to predict mortality and severe morbidity in neonates, such as Score for Neonatal Acute Physiology (SNAP) [2], Clinical Risk Index for Babies (CRIB) [3], Score for Neonatal Acute Physiology with Perinatal extension (SNAPPE) [4], Clinical Risk Index for Babies-II (CRIB-II) [5], and Score for Neonatal Acute Physiology with Perinatal extension-II (SNAPPE-II) [6]. Among them, the most widely used are SNAPPE-II and CRIB-II, which are simpler and more accurate [7]. In 2020, the Neonatal Sequential Organ Failure Assessment (nSOFA) score was originally introduced as a tool for

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predicting mortality in very low birth weight infants who developed late-onset sepsis [8]. Subsequently, a growing number of studies have demonstrated the value of nSOFA in predicting neonatal mortality [9–11]. Lavilla et al. [10] demonstrated a direct correlation between nSOFA and death, by quantifying organ dysfunction from birth to death or discharge at hourly intervals among preterm infants. Similarly, the validity of nSOFA in predicting neonatal mortality was also confirmed in a multicenter study [11].

Recently, neonatal care aims to reduce mortality as well as increase survival without morbidity. Previous studies have validated CRIB-II, SNAPPE-II, and nSOFA for predicting mortality, and compared CRIB-II with SNAPPE-II. However, very few studies evaluated these scoring systems for predicting neonatal morbidity, and studies comparing these three scoring systems are lacking. The aim of this study was to systematically assess and compare the effectiveness of the nSOFA, SNAPPE-II, and CRIB-II scoring systems in predicting mortality and short-term morbidities in preterm infants ≤32 weeks.

Materials and methods

Study subjects

This retrospective, observational study was conducted in the First Affiliated Hospital of Zhengzhou University from January 2017 to December 2018. This study adheres to the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University (No. 2021-KY-1003). Written informed consent to participate in this study was obtained from the participants' guardians. Inclusion criteria were: preterm newborns ≤32 weeks of gestation and admitted to NICUs within 24 h after birth. Newborns with congenital malformations or congenital metabolic disorders, those who were automatically discharged for any other reasons with unknown prognosis, and those with incomplete data were excluded.

Definitions

Mortality was defined as any death occurring before hospital discharge. Morbidities were defined as follows: moderate or severe bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC) requiring surgery [12], early-onset sepsis (EOS) (sepsis that appears within 72 h of life) [13], late-onset sepsis (LOS) (sepsis that appears after 72 h of life), retinopathy of prematurity (ROP) requiring treatment (which follows the ETROP study recommendations) [14], and severe intraventricular hemorrhage (IVH) (more than grade II) [15].

BPD was defined with supplemental oxygen therapy or oxygen combined respiratory support at 36 weeks of postmenstrual age. It was categorized based on the pattern of respiratory support and oxygen concentration at this time [16].

Sepsis was defined by the positive blood culture and clinical signs of infection.

Calculation of scores

The nSOFA score (ranging from 0 to 15) is determined by assessing respiratory dysfunction through the need for mechanical ventilation and oxygen supplementation, cardiovascular dysfunction based on the use of vasoactive medications and/or corticosteroids, and hematologic dysfunction by evaluating platelet count (Table 1) [17]. The nSOFA score was calculated using an online tool available at https://peds.ufl.edu/apps/nsofa/default.aspx. The assessment was based on the worst nSOFA score recorded within the first 12 h of admission.

The SNAPPE-II score (ranging from 0 to 162) is calculated using nine variables measured during a 12-h

Table 1. Neonatal Sequential Organ Failure Assessment (nSOFA) components and scoring.

Component	Scores				
Respiratory score	0	2	4	6	8
Criteria	Not intubated or intubated, $SpO_2/FiO_2 \geq 300$	Intubated, $SpO_2/FiO_2 < 300$	Intubated, $SpO_2/FiO_2 < 200$	Intubated, $SpO_2/FiO_2 < 150$	Intubated, $SpO_2/FiO_2 < 100$
Cardiovascular score	0	1	2	3	4
Criteria[a]	No inotropes and no systemic corticosteroid treatment	No inotropes and systemic corticosteroid treatment	1 inotrope and no systemic corticosteroid treatment	≥ 2 inotropes or 1 inotrope and systemic corticosteroid treatment	≥2 inotropes and systemic corticosteroid treatment
Hematologic score	0	1	2	3	NA
Criteria[b]	Platelet count $\geq 150\times10^3$	Platelet count $100–149\times10^3$	Platelet count $<100\times10^3$	Platelet count $<50\times10^3$	

[a]Medications considered as inotropic or vasoactive: dopamine, dobutamine, epinephrine, norepinephrine, vasopressin, milrinone, and phenylephrine.
[b]Most recent platelet count is available.

period: birth weight (BW), small-for-gestational-age (SGA) status, lowest mean blood pressure, Apgar score at 5 min, lowest serum PH, lowest body temperature, occurrence of multiple seizures, partial pressure of oxygen in arterial blood (PaO_2)/fraction of inspired oxygen (FiO_2) ratio, and urine output [6].

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 [3].

Statistical analysis

Statistical analyses were performed using GraphPad Prism 8.0 software. Quantitative variables are presented as mean and standard deviation and categorical variables are expressed as percentages. The univariate analysis was conducted by Student *t*, Mann–Whitney *U*, chi-square, and Fisher exact tests, according to data type. The predictive accuracy of the scoring systems for neonatal mortality was evaluated through receiver operating characteristic (ROC) curves and the corresponding area under the curves (AUC). Furthermore, for each scoring system, the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated at different cut-off points to evaluate their effectiveness in predicting mortality.

Results

A total of 759 infants with gestational age ≤32 weeks were finally included in the study and 88 babies died (11.59%). The median postnatal age at the time of death was 5 days (IQR, 2–12). Of the preterm infants who died, 58 (65.9%) passed away within the first week following birth. The flow diagram outlining the study participants is presented in Figure 1. The baseline characteristics of the study population are detailed in Table 2. The mean gestational age was (30.01 ± 1.52) weeks, and the mean birth weight was (1266.98 ± 270.62) g. The gestational age, birth weight, and Apgar score were significantly lower in non-survivors compared to the survivors ($p < 0.001$). The incidence of major morbidities was 1.8% (14 patients) for mod/sev BPD, 13.2% (100 patients) were diagnosed with EOS, 9.6% (73 patients) were occurred LOS, 8.6% (65 patients) had severe IVH, 4.3% (33 patients) with ROP requiring treatment, and 1.2% (9 patients) with NEC requiring surgery.

The median scores for nSOFA, CRIB-II, and SNAPPE-II were 2 (0, 3), 6 (4, 8), and 13 (5, 26), respectively. Non-survivors had significantly higher nSOFA, SNAPPE-II, and CRIB-II scores compared to survivors (Figure 2a). Table 3 and Figure 2b present the ROC curve and corresponding AUC values comparing the predictive accuracy of nSOFA, SNAPPE-II, and CRIB-II for mortality. The AUC of the nSOFA, SNAPPE-II, and CRIB-II were 0.90 (95%CI: 0.87–0.93), 0.82 (95% CI:

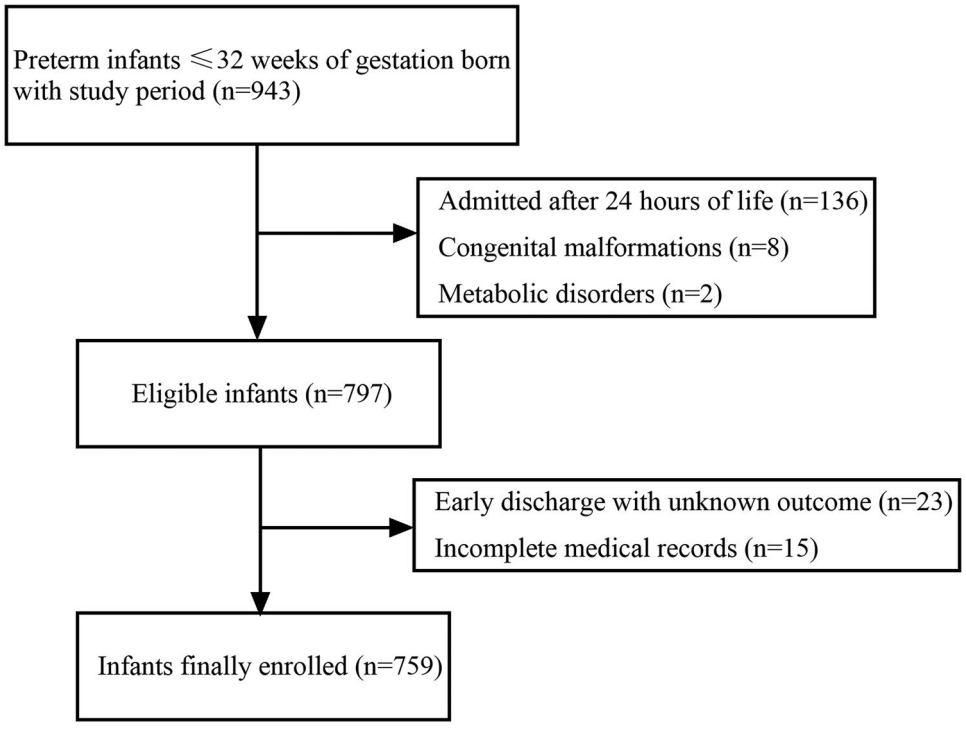

Figure 1. The flow diagram of the study participants.

0.76–0.87), and 0.79 (95% CI: 0.74–0.84), respectively. For predicting mortality, nSOFA had significantly higher AUC than CRIB-II and SNAPPE-II ($p < 0.05$); however, no significant difference was observed between the CRIB-II and SNAPPE-II.

Table 2. The baseline characteristics of the study population.

Parameter	Survivors ($n = 671$)	Non-survivors ($n = 88$)	p-Value
Gestational age, week, mean (*SD*)	30.17 ± 1.39	28.81 ± 1.90	<0.001
Birth weight, g, mean (*SD*)	1293.50 ± 261.55	1064.77 ± 253.93	<0.001
Male, *n* (%)	372 (55.44)	51 (57.95)	0.655
Multiple birth, *n* (%)	126 (18.78)	17 (19.32)	0.903
Caesarean section, *n* (%)	525 (78.24)	61 (69.32)	0.061
Maternal age, median (IQR)	30 (27, 35)	30 (27, 33)	0.101
Spontaneous pregnancy, *n* (%)	591 (88.08)	75 (85.23)	0.443
Gestational hypertension, *n* (%)	298 (44.41)	39 (44.32)	0.987
Gestational diabetes, *n* (%)	58 (8.64)	6 (6.82)	0.562
Premature rupture of membranes, *n* (%)	167 (24.89)	21 (23.86)	0.834
Apgar score at 1 min, median (IQR)	8 (7, 9)	6 (3, 8)	<0.001
Apgar score at 5 min, median (IQR)	9 (8, 10)	8 (5, 9)	<0.001
SNAPPE-II, median (IQR)	12 (5, 22)	36.5 (20.25, 54)	<0.001
CRIB-II, median (IQR)	6 (4, 8)	9 (7, 11)	<0.001
nSOFA, median (IQR)	1 (0, 2)	5 (4, 8)	<0.001

SNAPPE-II: Score for Neonatal Acute Physiology with Perinatal Extension-II; CRIB-II: Clinical Risk Index for Babies-II; nSOFA: Neonatal Sequential Organ Failure Assessment.

Table 4 shows the AUC values for the predictive ability of different illness severity scores in relation to short-term morbidities. For predicting mod/sev BPD, CRIB-II had good predictive ability (AUC 0.81), whereas nSOFA and SNAPPE-II showed fair predictive performance. Overall, these three scoring systems had fair to poor predictive power when it came to predicting ROP requiring treatment. For predicting other morbidities like NEC requiring surgery, EOS, LOS, and severe IVH, the three scoring systems all showed poor predictive abilities. As shown in Figure 3, the mortality increased with the elevation in nSOFA, SNAPPE-II, and CRIB-II scores, while a similar trend was not observed for morbidities.

Discussion

To the best of our knowledge, this is the first study to compare the predictive abilities of nSOFA, SNAPPE-II, and CRIB-II in forecasting mortality and short-time morbidities among preterm infants ≤32 weeks. In the present study, our results suggested that these three scoring systems

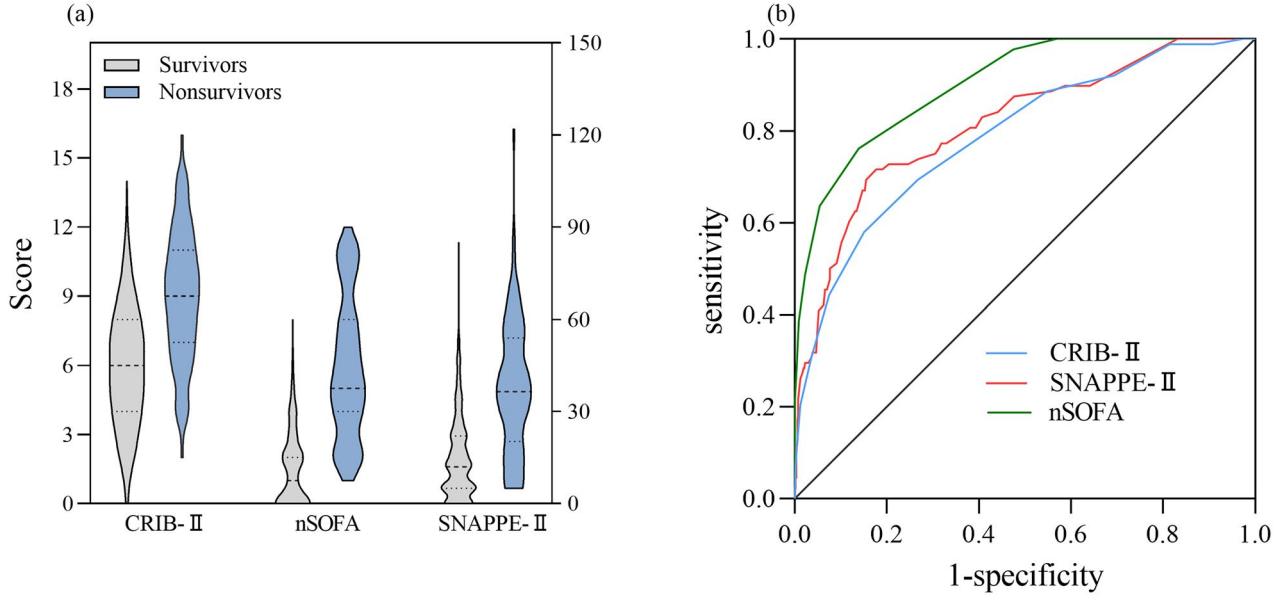

Figure 2. nSOFA, SNAPPE-II, and CRIB-II scores among survivors and non-survivors. (a) Median, quartiles, and probability density of these three scores for survivors and non-survivors. (SNAPPE-II scores are based on the right Y-axis as a reference standard, and CRIB-II and nSOFA scores are based on the left Y-axis.) (b) ROC curve analysis of nSOFA, SNAPPE-II, and CRIB-II for predicting mortality.

Table 3. Cutoff points, AUC, sensibility, specificity, predictive values, and accuracy for the three scores as a mortality predictor.

	Cutoff point	AUC (95% CI)	Sensitivity	Specificity	PPV	NPV	Accuracy	p-Value
SNAPPE-II	26.5	0.82 (0.76–0.87)	0.72	0.82	0.80	0.75	0.77	<0.001
CRIB-II	8.5	0.79 (0.74–0.84)	0.58	0.85	0.79	0.67	0.72	<0.001
nSOFA	3.5	0.90 (0.87–0.93)	0.76	0.86	0.84	0.78	0.81	<0.001

SNAPPE-II: Score for Neonatal Acute Physiology with Perinatal Extension-II; CRIB-II: Clinical Risk Index for Babies-II; nSOFA: Neonatal Sequential Organ Failure Assessment; AUC: area under the curve; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value.

Table 4. Analysis of ROC curves for adverse outcomes.

	SNAPPE-II		CRIB-II		nSOFA	
Variable	AUC (95% *CI*)	*p*-Value	AUC (95% *CI*)	*p*-Value	AUC (95% *CI*)	*p*-Value
BPD (mod/sev)	0.71 (0.60–0.82)	0.007	0.81 (0.72–0.89)	<0.001	0.77 (0.66–0.88)	0.001
ROP requiring treatment	0.72 (0.64–0.80)	<0.001	0.78 (0.70–0.86)	<0.001	0.66 (0.58–0.75)	0.002
NEC requiring surgery	0.56 (0.38–0.73)	0.571	0.56 (0.40–0.72)	0.526	0.71 (0.55–0.86)	0.035
EOS	0.56 (0.50–0.62)	0.073	0.47 (0.41–0.53)	0.309	0.59 (0.53–0.65)	0.003
LOS	0.56 (0.49–0.63)	0.096	0.61 (0.55–0.68)	0.001	0.57 (0.50–0.64)	0.066
Severe IVH	0.59 (0.52–0.66)	0.014	0.56 (0.49–0.63)	0.126	0.62 (0.55–0.70)	0.001

SNAPPE-II: Score for Neonatal Acute Physiology with Perinatal Extension-II; CRIB-II: Clinical Risk Index for Babies-II; nSOFA: Neonatal Sequential Organ Failure Assessment; ROC: curve receiver operating characteristics curve; AUC: area under the curve; CI: confidence interval; BPD: bronchopulmonary dysplasia; ROP: retinopathy of prematurity; NEC: necrotizing enterocolitis; EOS: early-onset sepsis; LOS: late-onset sepsis; IVH: intraventricular hemorrhage.

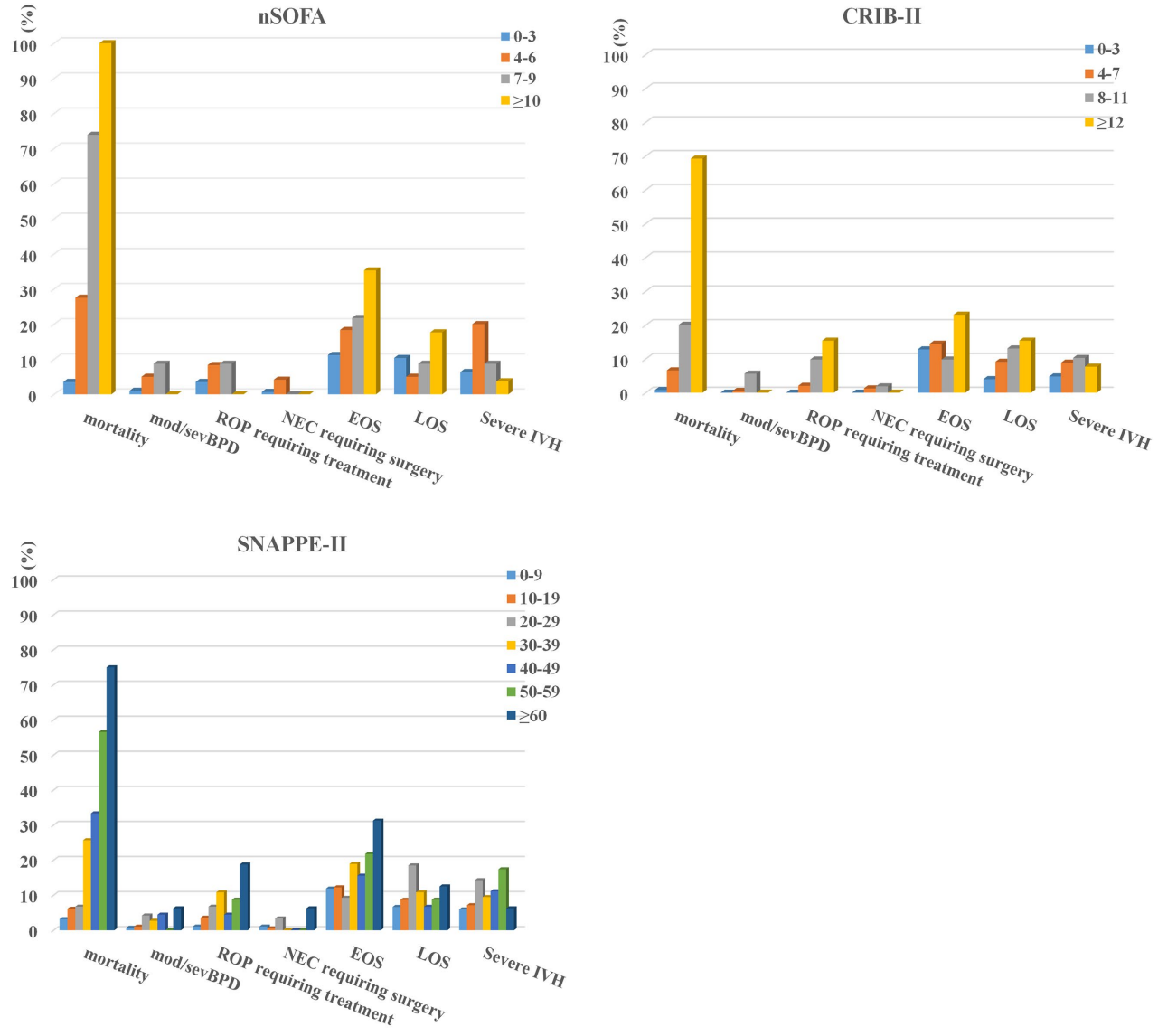

Figure 3. Bar charts of nSOFA, CRIB-II, and SNAPPE-II scores trend in predicting mortality and morbidities. SNAPPE-II: Score for Neonatal Acute Physiology with Perinatal Extension-II; CRIB-II: Clinical Risk Index for Babies-II; nSOFA: Neonatal Sequential Organ Failure Assessment; BPD: bronchopulmonary dysplasia; ROP: retinopathy of prematurity; NEC: necrotizing enterocolitis; EOS: early-onset sepsis; LOS: late-onset sepsis; IVH: intraventricular hemorrhage.

were reliable predictors of mortality in preterm infants, with the nSOFA showing the strongest predictive power. However, in predicting short-term morbidities, they showed poor predictive performance in general.

Early identification of increased risk of death facilitates clinical decision-making. In the past, gestational age and birth weight were considered important determinants of newborn death [18], whereas neonatal

mortality is also influenced by a range of perinatal factors and the infant's physiological condition, particularly the severity of illness during the first hours of life [19]. Thus, neonatal illness severity scoring systems are generated to evaluate the risk of mortality. Based on previous research [7,20], there are two widely used scoring systems. One routinely applied score is the CRIB-II, an adjusted and streamlined version of the CRIB. SNAPPE-II, a simplified iteration of SNAPPE, is the other commonly used score.

Previously, many studies have compared the predictive accuracy of SNAPPE-II and CRIB-II in assessing neonatal mortality, but their results were inconsistent. A meta-analysis comparing six mortality scoring systems found that CRIB-II and SNAPPE-II exhibited similar predictive performance, with CRIB-II showing an AUC of 0.85 and SNAPPE-II an AUC of 0.87, respectively [21]. Vardhelli et al.'s study showed that the AUC for CRIB-II was 0.79 and for SNAPPE-II was 0.78 [22]. A recent study by Sotodate et al. indicated that SNAPPE-II and CRIB-II were strong mortality predictors, with AUCs of 0.85 and 0.81, respectively [23]. In the present study, we found that AUCs of 0.82 (95% CI: 0.76–0.87) for SNAPPE-II and 0.79 (95% CI: 0.74–0.84) for CRIB-II, showing a good predictive ability for mortality, which is generally consistent with previous studies [24–26].

However, these traditional scoring systems were developed considerably earlier, and neonatal intervention has since undergone significant advancements. According to recent studies [22,27], their mortality prediction accuracy may now be suboptimal. In addition, these parameters are based on static variables. Thus, it is reasonable to question the application of old scoring systems in the modern world.

The SOFA scoring system, an operational description of malfunctioning organs, has been universally acknowledged as a reliable indicator of in-hospital mortality in adult and pediatric patients [28,29]. The nSOFA is an attempt to provide an assessment of organ dysfunction appropriate for premature newborns, which is getting increasing attention in recent years. A reputable study by Fleiss N et al. demonstrated that there was an association between the nSOFA score and late-onset infection mortality in preterm infants [17]. Subsequently, a Brazilian study found that the nSOFA score within the first 24 h had an AUC of 0.92 for predicting late-onset sepsis mortality among neonates with very low birth weight [30]. Based on a study examining the predictive value of nSOFA for mortality in preterm infants with necrotizing enterocolitis, its AUC was 0.87 [31]. However, there were no studies comparing the predictive ability of nSOFA, SNAPPE-II, and CRIB-II. Our study revealed that nSOFA had strong predictive ability for mortality, with an AUC of 0.90, significantly higher than SNAPPE-II and CRIB-II. This may be because nSOFA includes more parameters concerning the infant's emergency condition.

Very limited research has evaluated the predictive performance of nSOFA, SNAPPE-II, and CRIB-II for neonatal morbidity. Ozcan et al. [32] demonstrated that higher SNAPPE-II is associated with BPD and ROP. In Carvalho et al.'s study [33], SNAPPE-II was shown to be able to predict morbidities, such as NEC, ROP, and IVH, but the AUC showed only fair-to-poor accuracy. Lee et al. [34] reported that the CRIB-II was significantly predictive of moderate-to-severe BPD and severe IVH; however, it was not associated with NEC, sepsis, or ROP. In the present study, we found that CRIB-II had better prediction power for moderate-to-severe BPD and ROP requiring treatment compared to SNAPPE-II and nSOFA, with moderate to good predictive accuracy. This finding aligns with the study conducted by Vardhelli et al. [22]. However, in predicting other morbidities, such as EOS, LOS, NEC requiring surgery, and severe IVH, these three scoring systems all showed poor predictive ability. Overall, we found that short-term morbidities are not strongly correlated with neonatal critical illness scoring systems, which is in accordance with the Sotodate et al.'s study [23]. We considered that the predictability of the short-term morbidities risk is determined not only by the neonatal disease severity score but also by the interaction of multiple postnatal medical factors, such as breastfeeding, which can reduce the risk of NEC.

This study had several limitations. These three scores might have been subject to the effects of differences particular to each institution, encompassing their respective care protocols and laboratory surveillance methods. One advantage of nSOFA scoring system is that it's based on dynamic variables, thus it may be more meaningful to continuously assess the nSOFA scores at different time points. Another limitation is its retrospective, single-center design. The study was conducted in only one institution, so it might not be representative of the characteristics of infants elsewhere. There is a need for further confirmation of these results to determine whether these scoring models are independent of the institution. Further studies are required to assess the prediction ability of neonatal illness severity scores for morbidity.

Conclusion

In infants ≤32 weeks gestation, nSOFA scoring systems are more valuable in predicting mortality than SNAPPE-II and CRIB-II and it may be helpful in

identifying preterm infants requiring intervention. However, further studies are required to assess the predictive power of neonatal illness severity scores for morbidity.

Ethical approval

This study adheres to the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University (No. 2021-KY-1003). Written informed consent to participate in this study was obtained from the participants' guardians.

Authors contributions

Qingfei Hao and Jing Chen are co-first authors and contributed equally to this work. They contributed to the conceptualization, data curation, and writing of the original draft. Haoming Chen contributed to methodology, data curation, and formal analysis. Jing Zhang and Yanna Du contributed to the methodology and resources. Xiuyong Cheng contributed to conceptualization, supervision, reviewing, and editing. All the authors approved the final version of the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was supported by the Natural Science Foundation of Henan Province (232300420226).

Data availability statement

The data underlying this article are available from the corresponding author on reasonable request.

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