Assessing mortality risk in very low birthweight infants: a comparison of CRIB, CRIB-II, and SNAPPE-II

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Background: Illness severity scores are increasingly used for risk adjustment in clinical research and quality assessment. Recently, a simplified version of the score for neonatal acute physiology (SNAPPE-II) and a revised clinical risk index for babies (CRIB-II) score have been published.

Aim: To compare the discriminatory ability and goodness of fit of CRIB, CRIB-II, and SNAPPE-II in a cohort of neonates < 1500 g birth weight (VLBWI).

Methods: Data from 720 VLBWI, admitted to 12 neonatal units in Lombardy (Northern Italy) participating in a regional network, were analysed. The discriminatory ability of the scores was assessed measuring the area under the receiver operating characteristic curve (AUC). Outcome measure was in-hospital death.

Results: CRIB and CRIB-II showed greater discrimination than SNAPPE-II (AUC 0.90 and 0.91 vs 0.84, p < 0.0004), partly because of the poor quality of some of the data required for the SNAPPE-II calculation—for example, urine output—but also because of the relative weight given to some items. In addition to each score, several variables significantly influenced survival in logistic regression models. Antenatal steroid prophylaxis, singleton birth, absence of congenital anomalies, and gestational age were independent predictors of survival for all scores, in addition to caesarean section and not being small for gestation (for SNAPPE-II) and a five minute Apgar score of ≥ 7 (for SNAPPE-II and CRIB).

Conclusions: CRIB and CRIB-II had greater discriminatory ability than SNAPPE-II. Risk adjustment using all scores is imperfect, and other perinatal factors significantly influence VLBWI survival. CRIB-II seems to be less confounded by these factors.
were moribund on admission to the NICU (arbitrarily defined as dying within 10 hours of life and receiving only comfort care), and late admissions (> 12 hours from birth) were excluded.

The outcome measure was in-hospital death. Neonates transferred from participating NICUs were tracked to ascertain their outcome; those transferred after 20 days of life or transported back to level I or level II units were considered to be alive. The outcome of two transferred infants remained unknown, and they were excluded from the analysis. The final sample was 720 VLBWI.

**Calculation of scores**

Data used to calculate the scores were prospectively collected, abstracted from charts by one or two trained observers at each centre, and recorded on a customised web database (www.neonatalnet.org) as part of a regional neonatal network. CRIB was calculated from six items: BW; GA; highest temperature at admission; worst base excess; congenital anomalies. The data collection window was the first 12 hours of life. SNAPPE-II was calculated from nine items: BW; being SGA; Apgar score at five minutes; urine output; lowest mean blood pressure; worst PaO2/FIO2 ratio; lowest pH; occurrence of seizures; lowest temperature. The data collection window was the first 12 hours after admission to the NICU. SNAPPE-II data were abstracted following the original description of SNAPPE (data collection was started in 1999, when only abstracts on SNAPPE-II had been published); weights were given to the values after SNAPPE-II publication. To minimise errors in data collection, original values were recorded, and coding and scores were calculated by computer.17

Following the original SNAPPE recommendations,5 items not recorded in charts were treated in the score calculation as a normal value. For CRIB, the only item that could be missing was worst base excess; in this case, following the same line of reasoning and CRIB description,5 a normal value was assumed.

CRIB-II is calculated from five items: sex; BW; GA; worst base excess; temperature at admission. Given that CRIB-II was published after collection of the data, missing data were not assumed to be normal and the case was deleted. Thus 720 neonates were available for the three way comparison.

**Statistical methods**

Discrimination—that is, the ability of the scores to correctly predict life or death—was assessed by calculating receiver operating characteristic curves and their associated area under the curve (AUC).16 An AUC value of 0.5 indicates no ability to discriminate, and larger values indicate increasing ability. A value of 0.8 is considered good.

As a model could have a high AUC, yet systematically overestimate or underestimate risk for some groups of infants, the Hosmer-Lemeshow (HL) test19 was used to measure the goodness of fit of the models. This test compares observed and expected mortality across several strata (usually 10) of the score. A non-significant p value of the HL statistic indicates a model with a constant discriminatory ability across strata. The effect of adding other variables to the scores was assessed with multiple logistic regression models, using in-hospital death as the dependent variable, and calculating as above the AUC and the HL test. Because of the sampling method used (cluster sampling), methods that allow robust estimation of variance were used.

All calculations were carried out with the statistical package Stata 7 (College Station, Texas, USA).

**RESULTS**

Table 1 gives the basic characteristics of the neonates.

The median CRIB value was 1 (interquartile range (IQR) 1–4) for infants who survived and 10 (7–14) for those who died. The corresponding values were 7 (5–9) and 14 (11–16) for CRIB-II and 20 (9–33) and 56.5 (39–71) for SNAPPE-II.

Figure 1 shows the receiver operating characteristic curves comparing the discriminating ability of CRIB, CRIB-II, and SNAPPE-II. CRIB and CRIB-II showed significantly greater discrimination than SNAPPE-II (AUC 0.90 (0.015) for CRIB, 0.91 (0.016) for CRIB-II, and 0.84 (0.020) for SNAPPE-II; p < 0.0004), but had a worse goodness of fit (HL p value = 0.045 for CRIB, 0.04 for CRIB-II, and 0.52 for SNAPPE-II).

Exclusion of babies weighing 400–499 g (n = 15) yielded an AUC of 0.898 for CRIB, 0.905 for CRIB-II, and 0.835 for SNAPPE-II (p = 0.0015).

All the scores did not fully estimate the risk of death, because in addition to the scores, several other variables were significantly associated with survival in multiple logistic regression models. Antenatal steroid prophylaxis, caesarean section, singleton birth, an Apgar score > 7 at five minutes, not being SGA, and not having any congenital anomaly, were significantly associated (or tended to significance) with a better survival in VLBWI (tables 2–4). The influence of these factors was greatest with SNAPPE-II, and least with CRIB-II.

A higher GA was associated with a better survival in CRIB and SNAPPE-II models, and with a worse survival in the CRIB-II model. For the other factors, the direction and magnitude of the odds ratios were similar. Only congenital anomalies, which are included in CRIB but not in SNAPPE-II and CRIB-II, had a clearly smaller odds ratio in CRIB. For CRIB and SNAPPE-II, it must be noted that some factors are highly significant even though they are already included in the score (GA and congenital anomalies for CRIB, SGA, and Apgar score at five minutes for SNAPPE-II), probably indicating poor weighting for these items. For both scores, the addition of these simple factors substantially increased both discrimination (CRIB-based model: AUC = 0.931; SNAPPE-II-based model: AUC = 0.913) and goodness of fit (CRIB: HL p value = 0.26; SNAPPE-II: p = 0.53). For comparison, a logistic model including only these variables and BW, but without CRIB, CRIB-II, or SNAPPE-II, had an AUC of 0.907 with a good fit (HL test p value = 0.49).

**DISCUSSION**

This study addressed two important questions: what are the results of one widely used (CRIB) and two new (CRIB-II and SNAPPE-II) scores in an unselected sample of VLBWI ≤ 32 weeks in terms of discrimination, goodness of fit, and comparative performance; is risk adjustment using these...
scores complete, so that their use effectively removes the confounding due to severity of illness and allows unbiased comparisons between different groups of neonates.

This is the first study to compare CRIB, CRIB-II, and SNAPPE-II for their ability to correctly predict in-hospital death in VLBWI. We show that CRIB and CRIB-II performed better than SNAPPE-II; however, the addition of other perinatal factors considerably improved discrimination of all scores.

The worse SNAPPE-II performance in VLBWI cannot be ascribed to its unexpectedly poor performance, because the discriminatory ability obtained in this study for all scores was in line with published data. The cohort in which our study was carried out (infants of BW 400–1499 g and GA ≤ 32 weeks) was slightly different from the original CRIB cohort (infants of GA ≤ 31 weeks or BW < 1500 g) and CRIB-II cohort (infants of GA ≤ 32 weeks). On the other hand, SNAPPE and SNAPPE-II were developed and validated on all acute neonatal admissions, irrespective of GA or BW. Although these differences should not influence the risk adjusted mortality prediction (our inclusion criteria defined a subset of those with the three scores), some SNAPPE-II items may have a lower sensitivity in VLBWI. Richardson et al have acknowledged that urine output is less useful in VLBWI than in bigger neonates, probably because of difficulties in obtaining complete and precise spontaneous urine collection in a relatively short timespan (12 hours from admission) in tiny babies. A recent report confirms that urine output is an unreliable item. A similar problem is found with seizures: in our sample, only five babies had convulsions in the first 12 hours. Also this item is probably more useful in larger babies, where admission to NICU reflects a larger variety of causes.

For CRIB and SNAPPE-II, a possible cause of reduced discrimination is the weight given to levels of physiological derangement for some items: the fact that low Apgar score and being SGA (for SNAPPE-II) and congenital anomalies and GA (for CRIB) are highly significant and increase discrimination when added to the models implies that these factors, already present, are inadequately weighted by the scores.

For SNAPPE-II, the problem could again be because the weights were derived from samples in which VLBWI represented a minority, and for CRIB because the weights were derived a decade ago, when a different mix of risk factors (with different relative importance) probably influenced mortality.

Moreover, in CRIB some items are determined by the care team. For instance, CRIB takes into account both highest and lowest appropriate FIO2 used during the first 12 hours, and it is possible that prophylactic surfactant administration was sometimes used in VLBWI, which could explain the lower discrimination in this group.

**Table 2** Odds ratios for CRIB based logistic regression model of mortality

<table>
<thead>
<tr>
<th>Odds ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (per week)</td>
<td>0.70 (0.61 to 0.80)</td>
</tr>
<tr>
<td>Steroid prophylaxis</td>
<td>0.47 (0.22 to 0.99)</td>
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<tr>
<td>Vaginal delivery</td>
<td>2.13 (0.79 to 5.73)</td>
</tr>
<tr>
<td>Multiple birth</td>
<td>2.12 (1.27 to 3.54)</td>
</tr>
<tr>
<td>5 min Apgar &lt; 7</td>
<td>1.64 (1.01 to 2.67)</td>
</tr>
<tr>
<td>Being SGA</td>
<td>2.44 (0.98 to 6.08)</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>2.50 (1.42 to 4.42)</td>
</tr>
</tbody>
</table>

Odds ratio for CRIB (per point change): 1.352 (1.21 to 1.51), p < 0.001.
CRIB, Clinical risk index for babies; SGA, small for gestational age.

**Table 3** Odds ratios for SNAPPE-II based logistic regression model of mortality

<table>
<thead>
<tr>
<th>Odds ratio (95% CI)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (per week)</td>
<td>0.62 (0.55 to 0.71)</td>
</tr>
<tr>
<td>Steroid prophylaxis</td>
<td>0.39 (0.22 to 0.71)</td>
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<tr>
<td>Vaginal delivery</td>
<td>2.46 (1.24 to 4.90)</td>
</tr>
<tr>
<td>Multiple birth</td>
<td>2.02 (1.28 to 3.17)</td>
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<tr>
<td>5 min Apgar &lt; 7</td>
<td>1.72 (1.01 to 2.91)</td>
</tr>
<tr>
<td>Being SGA</td>
<td>3.20 (1.54 to 6.66)</td>
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<tr>
<td>Congenital anomalies</td>
<td>4.92 (1.55 to 15.55)</td>
</tr>
</tbody>
</table>

Odds ratio for SNAPPE-II (per point change): 1.036 (1.02 to 1.05), p < 0.001.
SNAPPE, score for neonatal acute physiology—perinatal extension; SGA, small for gestational age.
oblitrate this difference, and thus reduce CRIB performance. In this sample, 48.4% of the newborns received surfactant at any time, and only 12.5% of these in the delivery room. We cannot therefore comment on the performance of CRIB when a prophylactic surfactant strategy is used. However, the problem of using variables that can be arbitrarily determined by doctors, such as FIO2, was one of the main reasons for using variables that can be arbitrarily determined by doctors, such as FIO2, was one of the main reasons for developing CRIB-II, which only uses information available within one hour of admission and independent of the care provided. Our data show that the new score has a discrimination that is comparable to that of the “old” CRIB, but potentially less confounded by treatment given by the team.

A surprising finding with CRIB-II is that GA is almost significant (table 4), with death risk increasing with increasing GA. This suggests that the BW-GA-sex matrix used in CRIB-II is not well calibrated for our sample. This interpretation is strengthened by the observation that risk adjustment using all scores is imperfect, and even after accounting for “severity of illness”, other important prenatal and perinatal factors influence VLBWI survival, including antenatal steroid prophylaxis. Aggar score at five minutes, type of delivery, multiple birth, and congenital anomalies. These factors are known to influence survival in VLBWI, and a logistic model including only these variables and BW, but without CRIB, CRIB-II, or SNAPPE-II, showed excellent discrimination. CRIB-II and SNAPPE-II do not take into account congenital anomalies, but the large estimated effect on mortality (an odds ratio of 5.01 for CRIB-II and 4.92 for SNAPPE-II) when added to the model suggests that this information should be included in a severity score.62

The imperfect adjustment has been reported before.4 8 9 10 11 12 For antenatal steroid prophylaxis, Richardson et al62 argue against including it in the score, because this would excise poor obstetrical management, and “it may obscure the ill effects of improper treatment”. This line of reasoning cannot, however, be applied to other factors which do not depend on medical decisions, such as multiple birth, congenital anomalies, or being SGA. The important contribution to risk of these factors means that the use of CRIB, SNAPPE-II, or, to a lesser degree, CRIB-II alone cannot guarantee an unbiased risk adjustment, thus partly losing the reason for using these scores.

In conclusion, this study shows that CRIB and CRIB-II were superior to SNAPPE-II in VLBWI, but their goodness of fit was not good. CRIB-II appeared to be as accurate as CRIB in this sample, and was less confounded by other factors. All scores do not fully estimate the risk of death—that is, in addition to CRIB, CRIB-II, or SNAPPE-II, other perinatal factors influence survival and should be included in any analysis to improve risk adjustment.

<table>
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Odds ratio for CRIB-II (per point change): 1.853 (1.64 to 2.09); p < 0.001.

CRIB, Clinical risk index for babies; SGA, small for gestational age.

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REFERENCES


18 Hanley JA, McNeil BJ. The meaning and the use of the area under a receiver operating characteristics (ROC) curve. Radiology 1982;143:29–36.


