Predictors of extubation success: a population-based study of neonates below a gestational age of 26 weeks

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ABSTRACT

Objective The aim of the study was to investigate first extubation attempts among extremely premature (EP) infants and to explore factors that may increase the quality of clinical judgement of extubation readiness.

Design and method A population-based study was conducted to explore first extubation attempts for EP infants born before a gestational age (GA) of 26 weeks in Norway between 1 January 2013 and 31 December 2018. Eligible infants were identified via the Norwegian Neonatal Network database. The primary outcome was successful extubation, defined as no reintubation within 72 hours after extubation.

Results Among 482 eligible infants, 316 first extubation attempts were identified. Overall, 173 (55%) infants were successfully extubated, whereas the first attempt failed in 143 (45%) infants. A total of 261 (83%) infants were successfully extubated, whereas the first attempt failed in 143 (45%) infants. A total of 261 (83%) infants were extubated from conventional ventilation (CV), and 55 (17%) infants were extubated from high-frequency oscillatory ventilation (HFOV). In extubation from CV, pre-extubation fraction of inspired oxygen (FiO2) ≤0.35, higher Apgar score, higher GA, female sex and higher postnatal age were important predictors of successful extubation. In extubation from HFOV, a pre-extubation FiO2 level ≤0.35 was a relevant predictor of successful extubation.

Conclusions The correct timing of extubation in EP infants is important. In this national cohort, 55% of the first extubation attempts were successful. Our results suggest that additional emphasis on oxygen requirement, sex and general condition at birth may further increase extubation success when clinicians are about to extubate EP infants for the first time.

INTRODUCTION

Most extremely premature (EP) infants born before a gestational age (GA) of 26 weeks receive mechanical ventilation (MV).1,2 Although MV may be life-saving, ventilator-induced lung injury increases the risk of chronic respiratory morbidity.3,4 Therefore, clinicians strive for extubation as soon as possible. Extubation failure is common, and associated with longer duration of MV, increased length of hospital stay and increased risk of nosocomial infections and death.3,9 Clinical assessment of the ideal timing of extubation for EP infants is complex, including identification of optimal pre-extubation, perextubation and postextubation management.10 Consequently, studies that can help predict successful extubation in EP infants are warranted and of clinical importance.11 Several studies have investigated extubation readiness in premature infants.12-14 A systematic review and meta-analysis of predictors of extubation readiness found insufficient...
evidence to support the use of any predictors over clinical judgement alone. Although various prediction models have been developed, none have been widely accepted in clinical practice. Gupta et al developed a prediction model for extubation success and proposed an extubation calculator for use in clinical practice. A recent study conducted at two tertiary perinatal centres in Australia suggested that the extubation outcome is associated with the mean airway pressure (MAP) and GA. However, these previous studies have examined populations of EP infants with a mean GA of 26–27 weeks, potentially limiting the applicability to the most immature infants. Hence, the primary aim of our study was to investigate infant characteristics and ventilation parameters at first extubation attempt in a national cohort of EP infants below 26 weeks GA, and second to explore factors that may increase the quality of clinical judgement of extubation readiness.

METHODS
We conducted an analysis of prospectively registered data from the Norwegian Neonatal Network (NNN), supplemented by data extracted from patient records, to explore the first extubation events among premature infants <26 weeks GA born in Norway between 1 January 2013 and 31 December 2018. Eligible infants were identified in the NNN database. An information letter describing the purpose of the study was distributed to the infants’ mothers, including an opt-out alternative. Infants were automatically enrolled in the study if the mother did not respond to the letter within 4 weeks to decline participation.

Demographic and clinical factors with a potential predictive effect on extubation success were determined by the study investigators and were based on clinical experience and prior research in the field. Data regarding MV settings and blood gas samples related to the extubation events were extracted from patients’ medical records at the 10 neonatal intensive care units (NICUs) where the infants had been treated. A senior clinician at each participating NICU reported the unit’s clinical extubation strategy during the study period.

Variables and definitions
The primary outcome was a successful first extubation attempt, defined as no reintubation event within 72 hours. We also explored success rates within 7 days with no reintubation. Prenatal variables included antenatal steroids, mode of delivery and plurality. Demographic variables included GA, sex, birth weight (BW) and weight for GA. Apgar score at 5 min and Clinical Risk Index for Babies (CRIB II) score were included as variables describing general condition at birth and illness severity score. Delivery room variables included endotracheal intubation and surfactant administration.

Pre-extubation variables extracted from medical records included the last registered ventilator mode prior to extubation. For infants extubated from conventional ventilation (CV), we extracted fraction of inspired oxygen (FiO₂), peak inflation pressure (PIP; set for infants receiving pressure-limited ventilation measured for those receiving volume-targeted ventilation-VTV), MAP and the ventilator set rate. For infants extubated from high-frequency oscillatory ventilation (HFOV), FiO₂ and MAP values were extracted. For all variables, both the last registered value and mean values for the last 6 hours prior to the extubation attempt were extracted.

For all included infants, weight at extubation and blood gas variables measured a maximum of 12 hours prior to extubation were extracted. The Ventilation Index (VI) and Respiratory Severity Score (RSS) were calculated and applied as objective measures of respiratory illness. VI was calculated as partial pressure of carbon dioxide (pCO₂) in arterial, venous or capillary blood multiplied by the ventilator set rate multiplied by the difference between PIP and positive end expiratory pressure, all divided by 1000. RSS was calculated as a product of MAP and FiO₂. Growth throughout the MV course was calculated based on the difference between the infants’ weight on the day of intubation and the day of extubation. Information regarding caffeine and postnatal corticosteroid therapy on the day of extubation was recorded. Postextubation variables included the mode of non-invasive respiratory support delivered immediately after extubation. Accidental extubation events were identified by screening of notes written by the physician and nurses in charge on the day of extubation.

Statistical analyses
Demographic data were expressed as numbers with proportions (%), means with SD, or medians with 25th and 75th percentiles (IQR). We compared the perinatal and peri-extubation characteristics of infants successfully extubated at the first attempt with those who failed. Extubations from CV and HFOV were explored separately.

Categorical variables were compared between successful and failed extubations by using the χ² test or Fisher’s exact test when appropriate. Continuous variables were analysed using a Wilcoxon rank-sum test. The pre-extubation variables, FiO₂, and RSS were examined for cut-off points at the 95th percentiles for successfully extubated infants.

Logistic regression modelling to identify variables predicting extubation success was applied separately for the extubations from CV and HFOV. Relevant variables based on clinical significance were included in the logistic regression models. All multivariable logistic regression models were internally validated by bootstrapping, using 1000 bootstrap samples to assess overfitting and provide shrinkage factors for adjusting regression coefficients. We assessed the model performance in terms of the Nagelkerke R-squared (R²) from logistic regression, calibration slope and area under the curve before and after internal validation with optimism corrected estimates, please
Premature infants born <26 weeks gestational age between 1 Jan 2013 and 31 Dec 2018 in Norway n = 482

Unavailable for inclusion n = 22
Opt-out solution n = 21
Never intubated n = 10
Died prior extubation n = 101
Accidental extubation n = 11

First extubation attempts included in final analysis n = 316

Successful extubation n = 173 (55%)
Extubation failure n = 143 (45%)

Figure 1 Flowchart of infants in the study.

see22 23 for a through statistical explanation of internal validation with bootstrapping.

The threshold for statistical significance was set at p<0.05. Initial summary statistics and comparison tests were performed using Stata/MP V.16.1 and internal validation was conducted using the R package rms.24

RESULTS
During the 6-year study period, 482 EP infants of <26 weeks GA received treatment in Norwegian NICUs (figure 1).

Of these, 43 (9%) infants were excluded because the mothers’ address could not be verified or the mother chose to opt out. There were no statistical differences in GA, BW or mortality before discharge between infants who were included versus excluded (data not shown).

Furthermore, 10 (2%) infants were included because they only received non-invasive respiratory support, 102 (21%) died prior to the first extubation attempt and 11 (2%) infants had an identified accidental extubation. In the final analysis, 316 infants with first extubation attempts were included, 173 (55%) were successfully extubated and 143 (45%) failed. While exploring success rates using the 7-day definition, 138 (44%) infants were successfully extubated.

Clinical extubation criteria and ventilator mode at extubation
Similar extubation criteria were reported in all participating units. Infants treated with CV were generally considered ready for extubation with a sufficient respiratory drive, PIP <20 cm H_2O and FiO_2 <0.3–0.4. Two NICUs reported clinical considerations for extubation readiness in infants treated with HFOV, that is, MAP at 7–8 cm H_2O and a FiO_2 requirement <0.3–0.4.

Overall, a total of 261 (83%) and 55 (17%) infants were extubated from the CV and HFOV, respectively.

Characteristics at birth
Characteristics at birth in infants with successful and failed first extubation attempts are presented in table 1. Antenatal steroids were given to 298 (94%) infants, and 185 (61%) infants received a complete course. There was no association between receiving antenatal steroids and extubation outcomes.

Successful extubation from CV was associated with GA, BW, delivery method, sex, 5 min Apgar score and CRIB II score. For the infants extubated from HFOV, there was no significant difference in characteristics at birth between those with successful and unsuccessful attempts.

Extubation characteristics
Extubation characteristics of infants with successful or failed first extubation attempts are presented in table 2. Among extubations from CV, 11 (4%) infants received synchronised intermitted mandatory ventilation, 230 (89%) received synchronised positive pressure ventilation or pressure support ventilation and 18 (7%) infants received neurally adjusted ventilatory assist prior to the extubation attempt. A total of 123 (47%) infants received NTV.

Unadjusted analyses showed significantly higher weight, higher pH, lower oxygen and lower mean RSS before extubation but no other differences in objective measures of respiratory illness or medical treatment between successfully extubated infants and those who failed. All infants received either bilevel positive airway pressure or nasal continuous positive airway pressure (NCPAP) immediately after extubation, with NCPAP as the foremost chosen respiratory support.

Adjusted analyses
In a multivariable analysis of extubation from CV, pre-extubation FiO_2 ≤0.35, 5 min Apgar score >5, higher GA, female sex and higher postnatal age at the extubation day remained predictive of successful extubation (table 3). The OR of successful extubation was 6.3 (95% CI 2.5 to 16.0) if the received pre-extubation FiO_2 ≤0.35 prior to the attempt. In multivariable analysis of extubation from HFOV, pre-extubation FiO_2 ≤0.35 remained predictive of successful extubation.

The predictors of successful extubation were combined in a model to construct a receiver operating characteristic curve for the two prediction models. Internal validation of the model for extubation from CV showed the optimism corrected (a measure of model performance after internal validation) R^2 at 0.28, corrected area under the curve at 0.77 and calibration slope at 0.89. The internal validation of the model for extubation from HFOV identified large model overfitting (R^2=0.23, area under the curve=0.76, calibration slope=0.76). Multivariable analyses performed separately for female and male infants, as well as for infants with late first extubation attempt (>14 days postnatal age) are shown in online supplemental tables 1 and 2, respectively.
DISCUSSION

In this population-based study of EP infants clinically judged ready for extubation, we found that successful extubation from CV was associated with pre-extubation FiO\textsubscript{2} ≤0.35, a 5 min Apgar score >5, higher GA, female sex and higher postnatal age. Successful extubation from HFOV was associated with pre-extubation FiO\textsubscript{2} ≤0.35. It is important to note that associations between these factors and the results of extubation attempts may be an addition to, not replacement for, clinical judgement.

Our results align with Gupta et al, with a higher GA, higher postnatal age, and lower pre-extubation FiO\textsubscript{2} being predictive of successful extubation. Apre-extubation pH, weight at extubation and RSS at birth did not independently predict extubation success in our cohort. The differences in the findings may be related to differences in the populations explored. Our population only included EP infants <26 weeks GA in a national cohort, whereas the Gupta study was not population based and included more mature infants. In contrast to the results of Kidman et al, we did not identify associations with successful extubation and MAP, a finding that probably reflects the clinical evaluation prior to the extubation attempt because all the participating units reported PIP (to achieve normal tidal volume) and oxygen requirement as clinical considerations for extubation readiness.

In several previous studies, low pre-extubation FiO\textsubscript{2} has been reported as predictive of extubation success.\textsuperscript{9,14,25} We suggest that a cut-off for pre-extubation FiO\textsubscript{2} at ≥0.35 is a clinically relevant predictor indicating a high risk for extubation failure. In addition to oxygen requirement, clinicians consider blood gas measurements including pCO\textsubscript{2} prior to extubation. Earlier studies have identified lower pre-extubation pCO\textsubscript{2} as an important predictor of successful extubation,\textsuperscript{8,2} as hypercapnia could be an indication of insufficient respiratory drive or low lung compliance. In this study, the pre-extubation pCO\textsubscript{2} was not significantly lower in infants with extubation success compared with those who failed. These results may indicate that clinicians attempt extubation when infants’ blood gas measurements are within the normal range.

Similar to previous studies, a 5 min Apgar score >5 was associated with extubation success in the present research.\textsuperscript{9,26} The value of the Apgar score in EP infants has been questioned because the frequency of low Apgar scores increases with decreasing GA and may reflect immaturity in general.\textsuperscript{25} The relevance of the Apgar score in clinical practice regarding the evaluation of extubation readiness is also questionable. We find the association

| Table 1 Characteristics at birth of infants extubated from conventional ventilation and high-frequency ventilation at first extubation attempt, n=316 |
|---------------------------------------------------------------|
| Variable                                             | Extubated from CV | Extubated from HFOV |
|                                                    | Successful, n=140 | Failed, n=121       | Successful, n=33 | Failed, n=22       | P value |
| GA, weeks, median (IQR)                               | 25.1 (24.4–25.5) | 24.4 (23.5–25.1) | <0.001*         | 24.4 (23.5–25.1)  | 24.1 (23.5–24.4) | 0.13* |
| Birth weight g, mean (SD)                             | 695 (147)        | 651 (124)        | 0.01*          | 641 (127)        | 628 (118)       | 0.69  |
| Complete ANS course†, n (%)                           | 84/133 (63)      | 69/116 (59)      | 0.60           | 20/31 (65)       | 10/20(50)       | 0.39  |
| Vaginal delivery, n (%)                               | 86 (61)          | 91 (75)          | 0.02*          | 20 (61)          | 16 (73)         | 0.40* |
| Male sex, n (%)                                       | 64 (46)          | 77 (64)          | 0.004*         | 9 (27)           | 10 (45)         | 0.25* |
| Female sex, n (%)                                     | 76 (54)          | 44 (36)          |               | 24 (73)          | 12 (55)         |       |
| Multiple birth, n (%)                                 | 32 (23)          | 33 (27)          | 0.48           | 10 (30)          | 6 (27)          | 1.0   |
| SGA, n (%)                                            | 29 (21)          | 21 (17)          | 0.35*          | 6 (18)           | 4 (18)          | 1.0   |
| RSS at birth‡, median (IQR)                           | 2.1 (1.7–2.9)    | 2.3 (1.9–2.9)    | 0.14           | 2.6 (1.9–4.0)    | 3.1 (2.0–4.6)   | 0.39  |
| Apgar <5 at 5 min, n (%)                              | 15 (11)          | 29 (24)          | 0.01*          | 9 (27)           | 7 (32)          | 0.77* |
| CRIB II>14, n (%)                                     | 64 (48)          | 74 (64)          | 0.02*          | 20 (61)          | 14 (67)         | 0.78* |
| Surfactant <first 30 min of life, n (%)               | 137/139 (99)    | 119/120 (99)     | 1.0            | 31 (94)          | 22 (100)        | 0.51  |
| LISA, n (%)                                           | 19 (14)          | 9 (7)            | 0.16           | 0 (0)            | 2 (9)           | 0.16  |

*Variables included in multivariable analysis.
†A complete ANS course was defined as when the first dose was administered at least 24 hours before birth. Time of first dose was not registered in 16 (4.9%) infants.
‡RSS was calculated as a product of MAP and fraction of inspired oxygen. Mean RSS at birth was calculated for each infant’s first 6 hour of life.
ANS, antenatal steroids; CRIB, Clinical Risk Index for Babies; CV, conventional ventilation; GA, gestational age; HFOV, high frequency oscillatory ventilation; LISA, less invasive surfactant administration; MAP, mean airway pressure; RSS, Respiratory Severity Score; SGA, small for gestational age.
between Apgar score and the lack of association between CRIB II and extubation outcome surprising. Notably, our findings indicate that the association between the general condition at birth and extubation outcome may be reserved for female infants.

The relationship between extubation success and increased GA is well established.1 21 26–30 A likelihood of extubation success for infants born at higher GA could be explained by advanced lung maturity with increasing GA. However, GA was not independently predictive of extubation success for infants extubated from HFOV in our study. HFOV is commonly used as a rescue treatment for infants where CV does not provide sufficient respiratory support. In our cohort, infants extubated from HFOV had a significantly higher postnatal age when clinicians first attempted extubation. In addition, the proportion of infants who received corticosteroids on the extubation day was higher among infants extubated from HFOV compared with infants extubated from CV. These findings may indicate that infants extubated from HFOV had more severe pulmonary morbidity compared with infants extubated from CV, because in Norwegian NICUs

### Table 2

| Variable | Extubated from CV | Extubated from HFOV |
|----------|-------------------|---------------------|
|          | Successful, n=140 | Failed, n=121       | Successful, n=33 | Failed, n=22 | P value |
| PNA in days, median (IQR) | 5 (2–19) | 7 (3–16) | 0.14* | 18 (9–32) | 15 (8–25) | 0.46* |
| PMA in weeks, median (IQR) | 25.9 (25.4–27.1) | 25.6 (24–26.7) | 0.004 | 27.3 (25.8–28.2) | 25.9 (25.1–28.0) | 0.13 |
| Weight g, median (IQR) | 740 (620–864) | 675 (607–780) | 0.02 | 792 (653–924) | 800 (653–1000) | 0.97 |
| Growth course g†, median (IQR) | 0 (-41–129) | 1 (-31–112) | 0.87* | 118 (37–305) | 148 (43–300) | 0.87* |
| Pre-extubation Vi‡, median (IQR) | 1.9 (1.2–2.4) | 1.9 (1.3–2.7) | 0.32 | NA | NA | NA |
| Pre-extubation pH§, median (IQR) | 7.30 (7.26–7.34) | 7.28 (7.23–7.33) | 0.04 | 7.27 (7.19–7.35) | 7.26 (7.20–7.33) | 0.73 |
| Pre-extubation pCO₂§¶ median (IQR) | 6.2 (5.5–7.0) | 6.3 (5.7–7.5) | 0.06 | 6.6 (6.3–7.5) | 6.6 (5.4–8.0) | 0.67 |
| Pre-extubation BE‡, median (IQR) | −3.6 (−6.3 to −1.1) | −5.1 (−6.8 to −1.6) | 0.18 | −2.5 (−7.0 to −1.5) | −2.6 (−8.2 to −0.6) | 0.51 |
| Pre-extubation FiO₂, median (IQR) | 0.23 (0.21–0.28) | 0.25 (0.21–0.33) | 0.006* | 0.28 (0.24–0.31) | 0.33 (0.29–0.44) | 0.001* |
| Pre-extubation RSS**, median (IQR) | 1.9 (1.7–2.3) | 2.1 (1.7–2.9) | 0.005 | 2.8 (2.2–3.4) | 3.3 (2.8–4.0) | 0.02 |
| Pre-extubation set ventilation rate, median (IQR) | 35 (30–40) | 35 (30–45) | 0.03 | NA | NA | NA |
| Pre-extubation MAP††, mean (SD) | 8.1 (0.13) | 8.4 (0.11) | 0.07* | 9.7 (0.30) | 10.2 (0.44) | 0.40* |
| Pre-extubation PIP‡‡, median (IQR) | 15 (12–17) | 15 (13–16) | 0.95 | NA | NA | NA |
| Caffein administration at the day of extubation, n (%) | 137 (98) | 120 (99) | 0.63 | 32 (97) | 22 (100) | 1.0 |
| Caffein mg/kg/day, median (IQR), | 9.3 (6.0–10.8) | 9.8 (7.1–12.4) | 0.10 | 7.5 (6.2–9.8) | 8.5 (5.9–16.3) | 0.42 |
| Steroid administration at the day of extubation, n (%) | 37 (26) | 30 (25) | 0.78 | 21 (64) | 11 (50) | 0.41 |

*Variables included in multivariable analysis.
†Growth course is the calculated difference between weight at the intubation day and the day of extubation.
‡VI was calculated as partial pressure of carbon dioxide (pCO₂) in arterial, venous or capillary blood multiplied by the ventilator set rate multiplied by the difference between PIP and positive end expiratory pressure, all divided by 1000.
§Measured in arterial, capillary or venous blood samples.
¶The pCO₂ values are given in kilopascal (multiplication by 7.50062 provide values in millimetres of mercury).
**RSS was calculated as a product of MAP and FiO₂. Pre-extubation RSS was calculated based on the last 6 hours before extubation.
††Presented as mean MAP last 6 hours before extubation, missing values in 4 (7%) infants extubated from HFOV.
‡‡PIP derived by a set pressure for infants on pressure limited ventilation, and measured PIP for infants on volume target ventilation.
BE, base excess; CV, conventional ventilation; FiO₂, fraction of inspired oxygen; HFOV, high-frequency oscillatory ventilation; MAP, mean airway pressure; NA, not applicable; pH, potential of hydrogen; PIP, peak inspiratory pressure; PMA, postmenstrual age; PNA, postnatal age; RSS, Respiratory Severity Score; Vi, ventilation index.
postnatal corticosteroid therapy are usually reserved infants considered in high risk of bronchopulmonary pulmonary disease and prolonged MV treatment after 10–14 days of age.

We found that females were more often successfully extubated than males. Male sex has previously been identified as a risk factor for longer hospital stay, higher postmenstrual age at discharge and lower survival. In addition, we previously reported that males had significantly longer cumulative MV compared with females.

Our study has limitations. We relied on retrospective data retrieved from medical records when infants were considered extubation ready. Some potentially useful variables (eg, blood gas values and tidal values) were missing and not included. Furthermore, information on maternal health and infant infection status at birth which could affect the respiratory trajectory and first extubation outcome were not available.

The strength of our study is the inclusion of a complete national cohort of premature infants born at <26 weeks GA we provide descriptions of extubation outcomes for infants extubated from CV and HFOV. In addition to the already established clinical evaluation of lung compliance, respiratory drive and oxygen demand, clinicians may also consider the infants’ GA, postnatal age, sex and general condition at birth in the evaluation before first extubation of the smallest EP infants.

CONCLUSION
In this population-based study exploring first extubation attempts among EP infants <26 weeks GA, 55% remained successfully extubated within the first 72 hours. Our results suggest that additional emphasis on oxygen requirement, sex and general condition at birth may further increase extubation success when clinicians are about to extubate the most immature infants for the first time.

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REFERENCES

1. Stensvold HJ, Klingenberg C, Stoen R, et al. Neonatal morbidity and 1-year survival of extremely preterm infants. Pediatrics 2017;139:e20161821.
2. Stoll BJ, Hansen N, Bell EF, et al. Trends in care practices, morbidity, and mortality of extremely preterm neonates, 1993–2012. JAMA 2015;314:1039–51.
3. Choi Y-B, Lee J, Park J, et al. Impact of prolonged mechanical ventilation in very low birth weight infants: results from a national cohort study. J Pediatr 2018;194:34–9.
4. Jensen EA, DeMauro SB, Kornhauser M, et al. Effects of multiple ventilation courses and duration of mechanical ventilation on respiratory outcomes in extremely low–birth-weight infants. JAMA Pediatr 2015;169:1011.
5. Epstein SK, Chubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. Chest 1997;112:186–92.
6. Thille AW, Harrois A, Schortgen F, et al. Outcomes of extubation failure in medical intensive care unit patients. Crit Care Med 2011;39:2612–8.
7. Baisch SD, Wheeler WB, Kurachek SC, et al. Extubation failure in pediatric intensive care incidence and outcomes. Pediatr Crit Care Med 2005;6:312–8.
8. Manley BJ, Doyle LW, Owen LS, et al. Extubating extremely preterm infants: predictors of success and outcomes following failure. J Pediatr 2016;173:45–9.
9. Chawla S, Natarajan G, Shankaran S, et al. Markers of successful extubation in extremely preterm infants, and morbidity after failed extubation. J Pediatr 2017;189:113–9.
10. Gremark A, Prendergast M. Difficult extubation in low birthweight infants. Arch Dis Child Fetal Neonatal Ed 2008;93:F242–5.
11. Sant AGM, Keizer M. Weaning from mechanical ventilation. Clin Perinatol 2012;39:543–62.
12. Janjindamai W, Pasee S, Thatrimontrichai A. The optimal predictors of readiness for extubation in low birth weight infants. J Med Assoc Thai 2017;100:327–34.
13. Kaczmarek J, Chawla S, Marchica C, et al. Heart rate variability and extubation readiness in extremely preterm infants. Neonatology 2013;104:42–8.
14. Kaczmarek J, Kamlin COF, Morley CJ, et al. Variability of respiratory parameters and extubation readiness in ventilated neonates. Arch Dis Child Fetal Neonatal Ed 2013;98:F70–4.
15. Shalish W, Latremouille S, Papenburg J, et al. Predictors of extubation readiness in preterm infants: a systematic review and meta-analysis. Arch Dis Child Fetal Neonatal Ed 2019;104:F89–97.
16. Bancalari E, Claire N. Strategies to accelerate weaning from respiratory support. Early Hum Dev 2013;89 Suppl 1:S4–6.
17. Kamlin COF, Davis PG, Morley CJ. Predicting successful extubation of very low birthweight infants. Arch Dis Child Fetal Neonatal Ed 2006:91:F180–3.
18. Gupta D, Greenberg RG, Sharma A, et al. A predictive model for extubation readiness in extremely preterm infants. J Perinatol 2019;39:1663–9.
19. Kidman AM, Manley BJ, Boland RA, et al. Predictors and outcomes of extubation failure in extremely preterm infants. J Paediatr Child Health 2021;57:913–9.
20. Bohn D, Tamura M, Perrin D, et al. Ventilatory predictors of pulmonary hypoplasia in congenital diaphragmatic hernia, confirmed by morphologic assessment. J Pediatr 1987;111:423–31.
21. Mhianna MJ, Iyer NP, Piraino S, et al. Respiratory severity score and extubation readiness in very low birth weight infants. Pediatr Neonatol 2017;58:523–8.
22. Steyberg EW. Clinical prediction models: a practical approach to development, validation, and updating. 2nd edn. Switzerland: Springer Nature, 2019.
23. Steyberg EW, Bleeker SE, Moll HA, et al. Internal and external validation of predictive models: a simulation study of bias and precision in small samples. J Clin Epidemiol 2003;56:441–7.
24. Team RC. R: a language and environment for statistical computing. 2020. Available. https://www.r-project.org/.
25. O’Connor K, Hurst EW, Bohn D, et al. Factors associated with successful extubation following the first course of systemic dexamethasone in ventilator-dependent preterm infants with or at risk of developing bronchopulmonary dysplasia. Pediatr Pulmonol 2018;53:1–11.
26. Cheng Z, Dong Z, Zhao Q, et al. A prediction model of extubation failure risk in preterm infants. Front Pediatr 2021;3:693320.
27. AMERICAN ACADEMY OF PEDIATRICS COMMITTEE ON FETUS AND NEWBORN. AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS COMMITTEE ON OBSTETRIC PRACTICE. The Apgar score. Pediatrics 2015;136:819–22.
28. Dimitriou G, Greenough A, Endo A, et al. Prediction of extubation failure in preterm infants. Arch Dis Child Fetal Neonatal Ed 2002;86:32F–5.
29. Shalish W, Kanbar L, Keszler M, et al. Patterns of reintubation in extremely preterm infants: a longitudinal cohort study. Pediatr Res 2018;83:969–75.
30. Ferguson KN, Roberts CT, Manley BJ, et al. Interventions to improve rates of successful extubation in preterm infants. JAMA Pediatr 2017;171:165–74.
31. Fröhlich M, Tissen-Diabaté T, Bührer C, et al. Sex-Specific long-term trends in length of hospital stay, postmenstrual age at discharge, and survival in very low birth weight infants. Neonatology 2021;118:416–24.
32. Ohnstad MO, Stensvold HJ, Tvedt CR, et al. Duration of mechanical ventilation and extubation success among extremely premature infants. Neonatology 2021;118:90–7.