Predictors and Outcomes of Extubation Failure in Preterm Neonates: A Systematic Review

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abstract

CONTEXT: Extubation failure (EF) is common in preterm neonates and may be associated with adverse outcomes.

OBJECTIVE: To systematically review and meta-analyze the existing literature on predictors and outcomes of EF in preterm neonates.

DATA SOURCES: MEDLINE, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Embase (OvidSP), CINAHL (EBSCOHost), and Cochrane Library (Wiley) from 1995 onward. The search strategy was developed by a reference librarian.

STUDY SELECTION: Experimental or observational studies reporting on predictors and/or outcomes related to EF (defined as reintubation within 7 days) in preterm neonates less than 37 weeks were eligible. Predictors included machine learning (ML) algorithms and lung ultrasound (LUS). Main outcome of interest was association of EF with mortality and/or bronchopulmonary dysplasia (BPD).

DATA EXTRACTION: Studies identified by the search strategy were screened based on title and abstract. Data from included studies were extracted independently by 2 authors, along with adjudication of risk of bias. RevMan Web was used to conduct meta-analyses.

RESULTS: Out of 8336 studies screened, 120 were included. Neonates with lower gestational age at birth, birthweight, postmenstrual age, and weight at extubation were more likely to experience EF. Higher level of pre-extubation respiratory support, indicated by lower pre-extubation pH and higher pre-extubation mean airway pressure, fraction of inspired oxygen, and P_{CO_2} were associated with EF risk. ML models showed variable accuracy and lower external validity. LUS may be a promising predictor, though scoring systems varied. EF was associated with higher odds of mortality and/or BPD (pooled odds ratio [OR], 4.7; 95% CI, 2.84–7.76) as well as the individual components of the composite: mortality (pooled OR, 3.87; 95% CI, 2.35–6.36) and BPD (pooled OR, 3.27; 95% CI, 2.54–4.21).

LIMITATIONS: Associations were derived from unadjusted data, precluding a definitive causal relationship between EF and predictors/outcomes.

CONCLUSIONS: Lower gestational and chronological age and higher levels of pre-extubation ventilation support were associated with EF. ML models and LUS scores require further validation in larger studies. EF was associated with mortality and/or BPD.

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INTRODUCTION

Preterm birth, defined as delivery occurring before 37 weeks of gestation, accounts for approximately 10% of all births.[1] Among the challenges faced by preterm newborns, respiratory distress syndrome (RDS) is a frequent comorbidity. Although noninvasive ventilation techniques have become the preferable option in RDS management,[2] invasive mechanical ventilation (IMV) remains a life-supporting strategy. Notably, the need for IMV inversely correlates with gestational age (GA), and a recent Canadian study showed that approximately 75% of preterm babies born before 29 weeks of GA will require IMV during initial hospitalization.[3] Despite the life-saving nature of IMV, its prolonged cumulative use may be a risk factor for morbidities, including ventilator-associated injury, bronchopulmonary dysplasia (BPD), and neurodevelopmental impairment.[4–6] Consequently, there is a growing emphasis on extubation as soon as possible.[2]

Despite the recognition of the importance of early extubation, practices surrounding ventilator weaning in preterm neonates remain heterogeneous across clinical settings. The absence of standardized guidelines further exacerbates this variability, leading to inconsistencies in periextubation practices, including extubation timing, postextubation respiratory support, and criteria for reintubation. Another challenge lies in the fact that, depending on the population being evaluated, between 12% and 50% of preterm neonates experience extubation failure (EF), requiring reintubation shortly after transitioning to noninvasive support.[7–10] Given the potential consequences associated with EF and consequent prolonged IMV, it is imperative to identify predictors of EF. Considering these challenges, this systematic review and meta-analysis aims to consolidate existing evidence on predictors and outcomes of EF in preterm newborns. By synthesizing available data, this review seeks to provide an up-to-date landscape of current medical literature, aid clinical decision-making, and identify knowledge gaps for future research.

METHODS

We conducted this systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[11] The study protocol was registered on PROSPERO (registration number CRD42023395729).

Search Strategy and Study Selection

A comprehensive systematic literature search was conducted on November 18, 2022, and updated on December 26, 2023, across multiple databases: MEDLINE, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Embase (OvidSP), CINAHL (EBSCOHost), and Cochrane Library (Wiley). The search included articles published in English from 1995 onwards. Detailed search strategies for each database are provided in the Supplementary Material (Supplemental Appendix 1).

Articles included for analyses consisted of observational (cohort and case-control studies) and randomized controlled trials (RCTs) reporting clinical predictors or outcomes related to EF in English-language, peer-reviewed journals. Studies without a control group were included but were not eligible for meta-analysis due to lack of comparative data. Trials that randomized participants based on a predictor of interest were meta analyzed separately from observational studies. On the other hand, many RCTs randomized participants based on an intervention that was not a predictor of interest for our review; however, if the data provided allowed for an ascertainment of a predictor's relationship with EF, the study population was treated as a cohort and included in meta-analyses with other observational studies. Exclusion criteria composed of studies exclusively analyzing spontaneous breathing trials or related ventilator maneuvers/parameters pre-extubation, as this has been the subject of a recent systematic review.[12] Similarly, studies that provided data only on postextubation practices to prevent EF, including comparison of various noninvasive modes, were excluded, as these targeted practices have been the subject of other recent systematic reviews.[13–16] Narrative reviews, dissertations, case reports, letters to the editor, conference abstracts, and cross-sectional studies were excluded.

Participant Characteristics

We included studies reporting on preterm infants born at less than 37 weeks GA, with data on pre-extubation clinical predictors and/or outcomes related to EF. Studies involving participants who were intubated for short-term procedures such as surgeries were excluded. In studies including both term and preterm neonates, we included the entire cohort if more than 80% of patients were known to be preterm. If separate data for preterm infants were available in the paper or obtained by contacting the authors, we included only the preterm data.

EF Definition

Extubation failure was defined as the need for reintubation within 7 days after a planned extubation.[17] In cases in which studies lacked a clear definition of EF, authors were contacted to ascertain criteria for reintubation within the prespecified time frame. Studies that included unplanned extubations were included only if these accounted for less than 20% of the total events. In studies involving Intubation-Surfactant-Extubation (INSURE) procedure, EF was defined as the need for IMV within 7 days after the INSURE attempt but excluded instances in which the reintubation was only for a repeat INSURE for additional surfactant.

Predictors and Outcomes

Key predictors were determined a priori and included the following pre-extubation variables: birth weight (BW), GA at birth, 5-minute Apgar score, presurfactant fraction of inspired oxygen (Fio_2), postmenstrual age at extubation, weight at extubation, pre-extubation Fio_2, mean airway pressure (MAP) prior to extubation, Pco_2, and pH. We converted blood gas parameters from kPa to mmHg when needed using the National Institute of Standards and Technology guidelines.[18] Additional predictors encompassed clinical (eg, antenatal steroids, maternal comorbidities), laboratory (eg, blood gas parameters), and ventilation parameters (eg, mode of ventilation, peak inspiratory pressure [PIP], positive end-expiratory pressure [PEEP]). We also examined lung ultrasound (LUS) and artificial intelligence models as predictors. For this review, we have chosen to use the term "Machine Learning" (ML) when referring to studies that utilized artificial intelligence models. Postextubation respiratory support modes and related interventions were considered beyond the scope of this review, as they have been the focus of several recent reviews.[13–16]

The main outcome of interest was the composite endpoint of mortality and/or BPD. Other key outcomes of interest were mortality, BPD, moderate-to-severe BPD, and composite of mortality and/or moderate-to-severe BPD. Additional outcomes of interest encompassed a range of complications such as retinopathy of prematurity (ROP) stage 3 or higher, necrotizing enterocolitis (NEC), ventilator-associated pneumonia (VAP), intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), pneumothorax/pulmonary air leak, need for tracheostomy, length of hospital stay, duration of positive pressure respiratory support, duration of invasive respiratory support, and duration of supplemental oxygen therapy. Definitions for individual outcomes were as defined by authors, which were checked for clinical heterogeneity prior to meta-analyses. For a reported outcome to be eligible for inclusion in this review, the original study must have specifically indicated that the outcome occurred after EF.

Data Extraction

Literature searches were conducted by L.H.C. with assistance from a reference librarian, using a reference management software (Covidence systematic review software, Veritas Health Innovation, available at http://www.covidence.org). Screening of titles and abstracts was performed by L.H.C., C.R., and M.G., with final eligibility determined based on predefined criteria. Data extraction was conducted by L.H.C. and M.G. using a standardized data collection form. No blinding strategies were employed, nor were any assessment of concordance of data extraction between the 2 authors using Kappa.

Methodological quality of included studies was independently assessed by L.H.C. and M.G. using a modified Newcastle-Ottawa Scale for observational studies and the Cochrane Collaboration ROB tool (version 2) for experimental studies (Supplemental Appendices 2 and 3). Studies were categorized as high (3 or more domains deemed to have high/unclear risk of bias), moderate (2 domains deemed to have high/unclear risk of bias), or low risk of bias (maximum of 1 domain considered high/unclear risk of bias).

Statistical Analysis

Data synthesis and analysis were performed using RevMan Web (version 8.1.1, Cochrane Collaboration, available at https://revman.cochrane.org/info). For dichotomous outcomes, Mantel-Haenszel method with random-effects model was utilized, presenting results as pooled odds ratios (ORs) with 95% CIs. Continuous outcomes were analyzed using inverse variance with random-effects model, presenting weighted mean differences with 95% CIs. Conversion of median and IQR or range data to mean and SD was performed using Wan's method.[19]

Heterogeneity was assessed using χ^2 test (X^2) and I-squared statistic (I^2), with I^2 values greater than 75% indicating significant heterogeneity. Qualitative assessment of study design, participants, predictors, and outcomes informed evaluation of clinical and methodological heterogeneity.

Subgroup Analyses

Subgroup analyses were conducted only for key predictors, the main outcome of interest and key outcomes of interest associated with EF. We conducted the following sets of subgroup analyses: (1) including studies focusing on extreme prematurity (<28 weeks GA, BW <1000 g), (2) studies categorized as low risk of bias, and (3) studies published from 2010 onward (reflecting the period when noninvasive respiratory support became increasingly utilized).

RESULTS

Search Strategy and Study Selection

The results of the database search and subsequent study selection are delineated in Figure 1. The initial search yielded 8336 references and following removal of duplicates and screening of titles/abstracts, 828 studies were deemed relevant for full-text review. Ultimately, 120 studies were included.[7–10,20–135] Of these, 13 focused on predictors and/or outcomes of the INSURE technique, 18 reported on the use of ML, and 5 examined LUS as a predictor. The remaining studies covered a range of topics: 4 focused on outcomes, 46 on predictors, and 34 on a combination of predictors and outcomes. Detailed characteristics of the included studies, along with the risk of bias assessment, are provided in Supplemental Table 1 of the Supplementary Material. Among the included studies, 61 (51%) were adjudicated to exhibit a low risk of bias, whereas 37 (31%) and 22 (18%) had a moderate and high risk of bias, respectively.

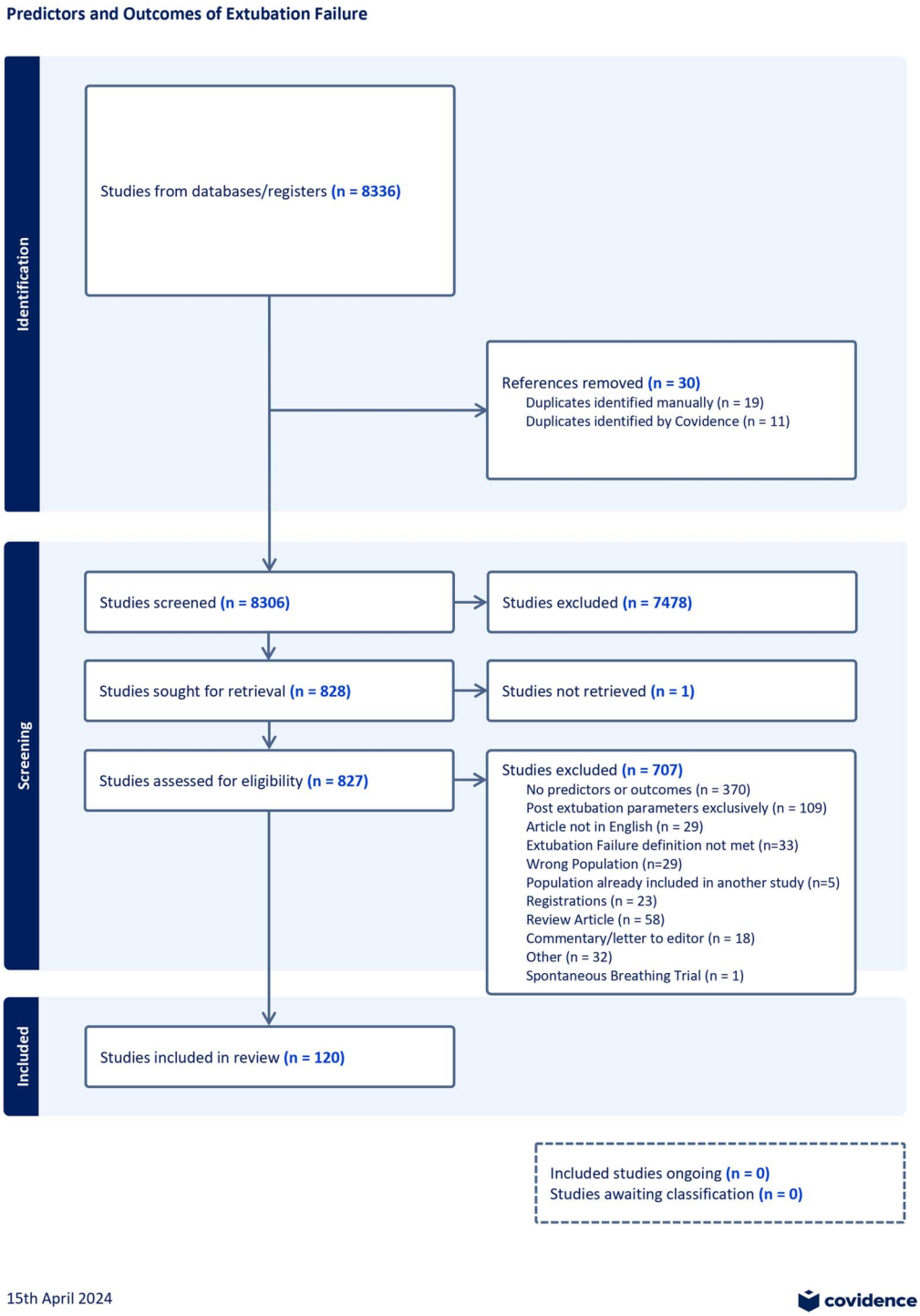

FIGURE 1.
PRISMA flow diagram of included studies.

Predictors of EF

Table 1 includes a comprehensive summary of pooled estimates of all predictors of EF in preterm neonates based on meta-analyses of included studies.

Clinical Predictors

Preterm infants who experienced EF exhibited greater immaturity at birth and at time of extubation (lower BW and GA, lower postmenstrual age and weight at extubation).

TABLE 1. Predictors of Extubation Failure

Predictor	Number of Studies	Number of Patients	OR or MD (95% CI)	Heterogeneity I^2, %
Antenatal and maternal characteristics				
Antenatal steroids	41	6742	OR 1.02 (0.92–1.12)	8
Multiple pregnancy	10	1656	OR 0.88 (0.67–1.15)	10
Pregnancy induced hypertension	9	1488	OR 1.07 (0.76–1.51)	17
Maternal age at delivery	4	656	MD 0.69 (−0.79 to 2.17)	23
Maternal chorioamnionitis	19	2787	OR 1.11 (0.85–1.45)	25
Positive maternal GBS status	4	583	OR 2.30 (0.9–5.93)	26
Prolonged ROM	13	2077	OR 0.83 (0.6–1.16)	51
Delivery characteristics				
C-section	26	3536	OR 0.9 (0.67–1.22)	63
Birth weight	64	10 037	MD −164 (−202.7 to −125.3)	93
Birth weight <1000 g	6	1105	OR 2.82 (1.38–5.74)	64
GA at birth	64	9620	MD −1.33 (−1.54 to −1.12)	91
SGA/IUGR	20	4277	OR 1.21 (0.91–1.62)	28
Male	53	9470	OR 1.54 (1.15–1.55)	44
5-min Apgar	31	5071	MD −0.47 (−0.77 to −0.17)	80
Chest compressions on DR	2	1141	OR 2.47 (1.46–4.18)	0
Epinephrine on DR	3	1269	OR 1.9 (0.99–3.66)	0
Intubation on DR	15	2124	OR 1.68 (1.21–2.32)	41
CRIB	2	483	MD 0.55 (−0.03 to 1.12)	0
Severe RDS	2	150	OR 3.09 (0.68–13.97)	67
Characteristics of hospital course				
Inotropic support first 7 days of life	3	632	OR 2.14 (1.64–2.79)	70
Surfactant	25	3359	OR 1.44 (1.12–1.84)	1
Number of surfactant doses	4	1535	MD 0.49 (0.37–0.61)	0
More than 1 surfactant	5	904	OR 4.26 (2.93–6.19)	0
Presurfactant Fio_2	1	108	MD 0.08 (0.04–0.12)	—
Highest Fio_2 (first 24 hours)	4	1369	MD 0.02 (−0.04 to 0.08)	76
PDA treatment	5	517	OR 1.71 (1.07–2.72)	44
A/a ratio	2	112	MD −0.02 (−0.1 to 0.06)	53
Early onset sepsis	6	1047	OR 1.94 (1.28–2.93)	0
Late-onset sepsis	1	905	1.59 (1.21–2.09)	—
Any methylxanthine	29	5242	OR 1.41 (0.89–2.22)	77
Doxapram	2	82	OR 0.51 (0.14–1.85)	0
Early caffeine	1	83	OR 1.03 (0.35–3.07)	—
Higher dose of caffeine	3	439	OR 0.31 (0.18–0.53)	0
Permissive hypercapnia	1	49	OR 0.59 (0.15–2.29)	—
Characteristics from extubation day				
Postmenstrual age at extubation	31	5555	MD −0.99 (−1.27 to −0.71)	72
Age at extubation	46	7407	MD +1.54 (0.68–2.4)	83
Weight at extubation	32	3304	MD −147.1 (−186.1 to −108.2)	65
Overnight extubation[a]	1	379	OR 1.07 (0.6–1.92)	—
Duration of intubation	23	4388	MD 1.83 (0.26–3.40)	88
Early extubation	1	86	OR 0.84 (0.35–2.01)	—
Physiotherapy postextubation	1	120	OR 0.59 (0.10–3.67)	—
RSS	8	1172	MD 0.19 (−0.04 to 0.43)	86
Unplanned extubation	3	681	OR 4.65 (2.25–9.63)	0
Postnatal steroids	14	1661	OR 1.91 (1.22–3.00)	80
Blood gas pre extubation				
pH	30	5275	MD −0.03 (−0.04 to −0.01)	79
Pco_2	32	5193	MD 3.13 (1.88–4.37)	39
Bicarbonate	10	914	MD −0.08 (−0.95 to 0.8)	
Base excess	12	1596	MD −0.5 (−1.33 to 0.33)	68
PO2	7	1369	MD −5.17 (−9.41 to −0.92)	62

(Continued on next page)

TABLE 1. Predictors of Extubation Failure (Continued)

Predictor	Number of Studies	Number of Patients	OR or MD (95% CI)	Heterogeneity I^2, %
Pre-extubation ventilation settings				
Fio_2	40	5968	MD 0.02 (0.01–0.03)	85
MAP	29	4326	MD 0.31 (0.15–0.46)	57
PIP	27	2684	MD 0.31 (0.01–0.61)	63
Tidal volume	13	911	MD −0.39 (−0.6 to −0.18)	52
PEEP	21	2369	MD 0.14 (0.02–0.26)	74
Ti	4	637	MD −0.02 (−0.03 to −0.01)	0
Rate	22	2869	MD 0.69 (−0.05 to 1.43)	49
High-frequency ventilation (vs conventional)	3	590	OR 1.85 (0.45–7.63)	53
NAVA ventilation (vs any), RCT	1	53	OR 0.08 (0–1.47)	—

Abbreviations: A/a ratio, alveolar-arterial gradient; CRIB, clinical risk index for babies; DR, delivery room; Fio_2, fraction of inspired oxygen; GA, gestational age; GBS, group B streptococcus; IUGR, intrauterine growth restriction; MAP, mean airway pressure; MD, mean difference; NAVA, neurally adjusted ventilatory assist; OR, odds ratio; PDA, patent ductus arteriosus; PEEP, positive end-expiratory pressure; PO2, partial pressure of oxygen; Prolonged ROM, rupture of membranes for more than 18 hours prior to delivery; RCT, randomized controlled trial; RDS, respiratory distress syndrome; ROM, rupture of membranes; RSS, respiratory severity score; SGA, small for gestational age; Ti, inspiratory time.

[a] Guy et al studied association of time of day and extubation failure/success, dividing extubation events into "overnight extubation" and "day extubation."

Additionally, this group was more likely to received extensive resuscitation at birth (lower 5-minute Apgar scores, more frequent chest compressions and intubation in the delivery room). Male sex was more prevalent among those with EF, as were occurrences of early and late-onset sepsis, along with longer duration of intubation. The EF group also more frequently received surfactant (including higher doses) and exhibited higher presurfactant Fio_2. Additional significant clinical characteristics of patients with EF included unplanned extubation, patent ductus arteriosus (PDA) requiring treatment, and exposure to postnatal steroids to facilitate extubation.

Ventilation-Related Predictors

Pre-extubation blood gas parameters revealed that respiratory acidosis, higher Pco_2, and lower Po_2 were significantly associated with EF. With respect to pre-extubation ventilatory settings, preterm neonates who experienced EF received more intensive respiratory support prior to extubation (as indicated by higher Fio_2, MAP, PIP, PEEP). Additionally, neonates in the EF group received lower tidal volume and shorter inspiratory time. Notably, there were no discernible differences regarding the use of conventional ventilation when compared with high-frequency ventilation [33,35,79] or neurally adjusted ventilatory assist.[50]

Machine Learning to Predict EF

The studies employing ML to predict EF are summarized in Table 2. Broadly, these studies encompass a range of combinations of baseline characteristics, including GA, BW, postmenstrual age, and weight at extubation. Additionally, they incorporate pre-extubation ventilatory settings and blood gas parameters. Some studies correlate these clinical predictors with automatic monitoring analysis tools such as AUREA, Heart Rate Characteristics Index, and Pneumotachograph measurements. Internal validation of these predictive models ranged from 0.65 to 0.92, indicating moderate to high levels of accuracy within the datasets used for model development. External validation generally demonstrated lower accuracy levels (area under the curve [AUC] 0.607–0.836).

Lung and Diaphragm Ultrasound to Predict EF

Five studies presented data from lung or diaphragm ultrasound aimed at predicting EF, with detailed findings summarized in Supplemental Table 2 of the Supplementary Material. There was considerable variability regarding the LUS scoring systems employed; in general utilizing between 3 to 7 zones bilaterally, and scoring according to the local ultrasound pattern, with a range from 0 to 4 to 6 points in each zone. All systems demonstrated significant differences between the EF and extubation success (ES) groups. The scoring systems and associated cutoffs yielded sensitivity levels as high as 100% and specificity levels reaching 93.8%. Notably, scoring systems encompassing a greater number of chest zones yielded higher overall accuracy. Of the included studies, only 2 incorporated measurements of diaphragm thickness and excursion[28,94]; they presented variable techniques as well as scoring systems, and demonstrated conflicting results in their ability to predict EF.

Outcomes Associated With EF

Forest plots illustrating the impact of EF on the main as well as key outcomes of interest are depicted in Figure 2, with comprehensive details provided in Table 3. EF was notably associated with the main outcome of mortality and/or BPD, as well as the key outcomes of mortality, occurrence of BPD, moderate-severe BPD, and mortality and/or moderate-severe BPD. Additionally, EF prolonged the duration of respiratory support, hospital stay, duration of IMV, duration of oxygen requirement, and the overall cost of hospitalization.

TABLE 2. Summary of Studies Evaluating Machine Learning to Predict Extubation Failure

Author, Year, Country	N Training Set	N Validation Set	Predictors Included	Models Examined	Internal Validation – AUC and 95% CI	External Validation – AUC and 95% CI
Chakraborty, 2020, UK	397	180	HRCi, BW, PMA at extubation, antibiotic	MLR	0.72 (0.71–0.74)	0.68 (0.59–0.77)
Chen, 2023, China	432	183	BW, 5-minute Apgar, PMA at extubation, P02 and Pco_2 before extubation, NIV mode after extubation	Nomogram, MLR	0.744 (0.69–0.80)	0.826 (0.79–0.93)
Cheng, 2021, China	128	58	5-minute Apgar, EOS, pH, HgB before extubation, caffeine	Nomogram, MLR	0.824 (0.748–0.90)	0.797
Dryer, 2022, USA	—	177	GA at birth, age at extubation, weight at extubation, pre-extubation Fio2, pre-extubation pH, highest RSS in the first 6 hours of age (Gupta et al)	Predicted probabilities, based on available extubation success calculator	—	0.72 (0.65–0.80)
Goel, 2017, UK	96	—	BW, HRCi baseline epoch score, blood culture results, duration of ventilation, PMA	Hierarchical mixed model regression analysis	Estimated 14.0824, SE, 6.6088; *P*, 0.0331	—
Gourdeau, 2015, Canada and USA	—	—	BW, bicarbonate, base excess, Pco_2, weight at extubation, PMA	Mutual information, synthetic minority oversampling technique, SVM	0.76	—
Gupta, 2019, USA	312	—	GA at birth, age at extubation, weight at extubation, pre-extubation Fio2, pre-extubation pH, highest RSS in the first 6 hours of age	MLR	0.77	—
Hoffman, 2022, USA	89	—	α1 (marker of sympathetic tone from EKG continuous recording), GA, pre-extubation tidal volume and Fio_2	Spectral analysis, MLR	0.81 (0.7–0.93)	—
Kanbar, 2018, Canada	—	—	BW, GA, cardiorespiratory metrics, patterns and variability (AUREA)	RF, BRF, CD-BRF	RF 0.65 BRF 0.66 CD-BRF 0.7	—
Kanbar, 2022, Canada	241	—	Clinical data and cardiorespiratory metrics, patterns and variability (AUREA)	Principal component features, CD-BRF	Clinical classifier AUC, 0.67 Cardiorespiratory classifier AUC, 0.67 Clinical and cardiorespiratory classifier AUC, 0.75	—
Mikhno, 2012, USA	179	—	Fio_2, monocytes, rapid shallow breathing index, heart rate, Pao_2/Fio_2 index, work of breathing	MLR	0.87	—
Mueller, 2013, USA	486	—	54 input variables (demographic and clinical characteristics, maternal and newborn medication, ventilator settings)	ANN, SVM, CNB, boosted DT, and MLR	ANN 0.921 MLR 0.853 CNB 0.769	ANN 0.682 MLR 0.776 CNB 0.607
Mueller, 2004, USA Mueller, 2006, USA	130	53	13 variables combined, from 51 variables analyzed (pH, Spo_2, gestational age, PEEP, sex, pulse, mode of ventilation, $Pcco_2$, MAP, PIP, I:E ratio, tidal volume)	ANN, MLR	AAN 0.81 MLR 0.81	ANN 0.87 MLR 0.75
Natarajan, 2023, USA	1348	—	20 variables included: demographics, medications, vital signs and respiratory support readings	MLR, XGB	XGBoost 0.82 MLR 0.81	—
Precup, 2012, Canada and USA	53	—	Respiratory pattern from RIP and EEG signals, analyzed with AUREA	SVM, MLR	Accuracy: Failure class: 85.4% Success class: 89.7%	Accuracy: Failure class: 83.2% Success class: 73.6%
Song, 2023, Korea[a]	481	Internal validation n = 197 External validation n = 802	NExt-Predictor: vital signs, clinical characteristics (GA, BW, PMA at the time of extubation, sex, pre-extubation pH and Pco_2), ventilator settings (Fio_2, PEEP, MAP, frequency), respiratory indices	LOCF, MLR, RF, GBM, DT, SGD, CNB, XGB	MLR 0.783 (0.780–0.795) RF 0.883 (0.881–0.884)	Internal validation MLR 0.892 (0.890–0.895) RF 0.836 (0.833–0.839) External validation MLR 0.766 (0.765–0.768) RF 0.720 (0.718–0.721)

Abbreviations: ANN, artificial neural networks; AUC, area under the curve; BRF, balanced random forest; BW, birth weight; CD-BRF, clinical decision – balanced random forest; DT, decision tree; EEG, electroencephalogram; EKG, electrocardiogram; EOS, early onset sepsis; Fio_2, fraction of inspired oxygen; GA, gestational age; GBM, gradient boosting model; HgB, hemoglobin; HRCi, heart rate characteristics index; I:E, inspiratory to expiratory ratio; LOCF, last observation carried forward; MAP, mean airway pressure; MLR, multivariable logistic regression; NIV, noninvasive ventilation; Pao_2, partial pressure of oxygen; $Pcco_2$, partial pressure of carbon-dioxide; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; PMA, postmenstrual age; Po_2, partial pressure of oxygen; RF, random forest; RSS, respiratory severity score; SE, standard error; SGD, stochastic gradient descent classifier; Spo_2, oxygen saturation; SVM, support vector machine; XGB, extreme gradient boosting.

[a] Partial results presented in order to summarize the data.

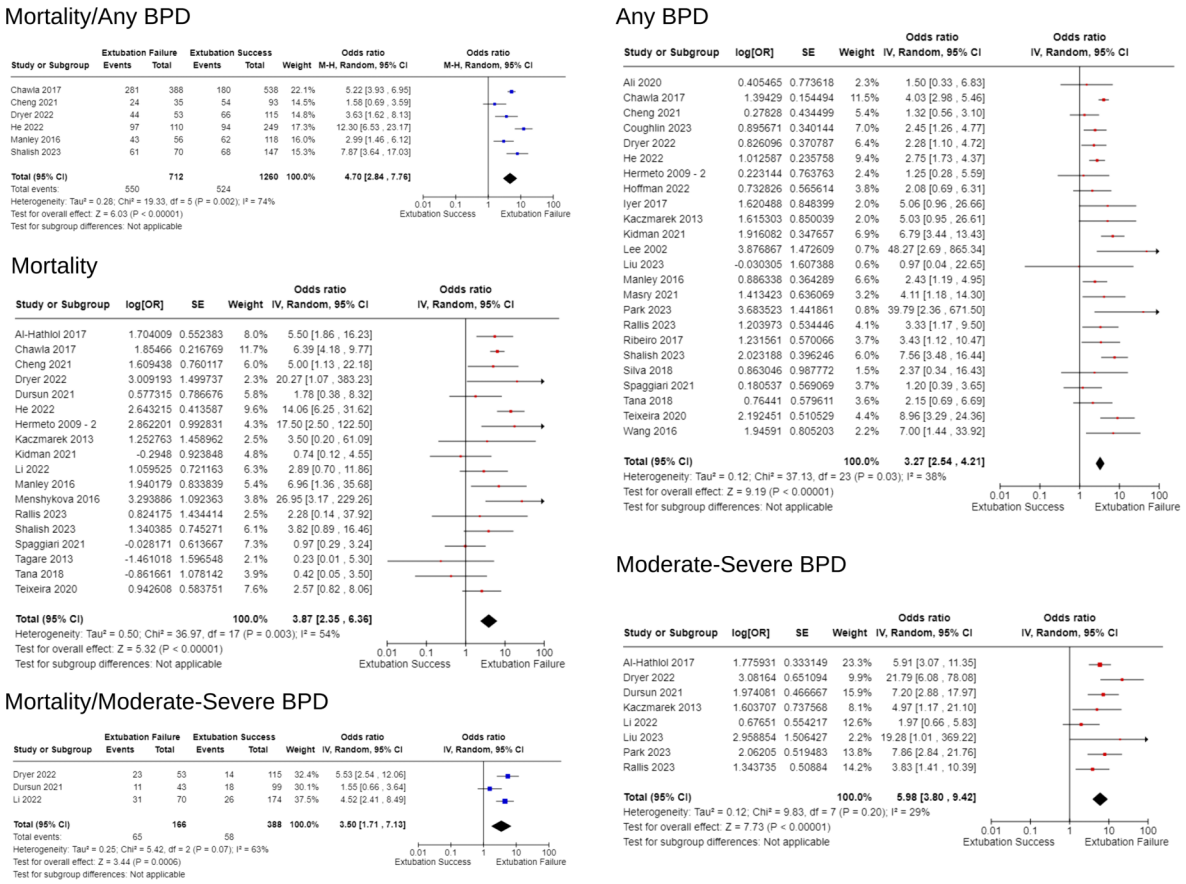

FIGURE 2.
Forest plots of the main outcome and key outcomes of interest following EF (vs no EF).
Abbreviations: BPD, bronchopulmonary dysplasia; IV, inverse variance; M-H, Mantel-Haenszel method; OR, odds ratio; SE, standard error.

Furthermore, EF was correlated with various other adverse outcomes, including abnormal findings on head ultrasound (IVH, IVH grades 3–4, composite of IVH grades 3–4 and PVL), occurrence of ROP and ROP grades 3 or higher, as well as PDA ligation, VAP, and pneumothorax.

Notably, there was no observed association between EF and tracheostomy; however, it is important to note that only one study included this outcome in its analysis.

INSURE and EF: Predictors and Outcomes

Thirteen studies investigated predictors and outcomes of INSURE failure, with detailed data presented in Supplemental Table 3 of the Supplementary Material. Significant predictors identified among the studies included lower GA at birth, reduced A/a ratio, elevated pre-extubation pCO2, lower pre-extubation pH, higher presurfactant Fio_2, increased RSS, and severe RDS. Regarding outcomes, INSURE failure was associated with the following: increase in mortality rate, mortality and/or moderate-severe BPD, grade 3–4 IVH, prolonged duration of IMV, extended duration of oxygen requirement, NEC, PDA and pneumothorax.

Subgroup Analys: Studies With Low Risk of Bias

We conducted a subgroup analysis of 61 studies identified as having a low risk of bias (Supplemental Table 4). The results were consistent with the primary analysis, linking EF to immaturity, increased need for delivery room resuscitation, pre-extubation respiratory acidosis, and higher levels of respiratory support prior to extubation. In this subgroup, EF remained significantly associated with the main outcome of mortality and/or BPD, as well as the individual components of the main outcome.

Subgroup Analysis: Preterm Less Than 28 Weeks GA or Less Than 1000 g

We conducted a subgroup analysis in 17 studies focusing on preterm infants with GA of less than 28 weeks or BW below 1000g. These findings, summarized in Table 4, were comparable to the main analysis, with predictors such as increased immaturity, higher presurfactant Fio_2, and lower pre-extubation pH associated with EF. However, EF was not linked to weight at extubation, pre-extubation MAP, or pre-extubation Pco_2. In this highly immature sub-population, EF

TABLE 3. Outcomes of Extubation Failure

Outcomes	Number of Studies	Number of Patients	OR or MD (95% CI)	Heterogeneity I^2, %
Any IVH	12	1279	OR 1.72 (1.31–2.26)	0
IVH 3–4	17	2814	OR 3.28 (2.48–4.13)	0
IVH 3–4 + PVL	1	65	OR 4.61 (2.33–9.13)	—
PVL	4	556	OR 2.43 (0.77–7.67)	27
Any ROP	8	851	OR 2.07 (1.3–3.3)	25
ROP 3 or higher	12	2200	OR 3.3 (2.28–4.77)	28
Ligation of PDA	3	580	OR 4.05 (2.01–8.16)	0
NEC 2–3	16	2293	OR 1.44 (0.91–2.3)	39
VAP	4	285	OR 4.93 (1.1–22.16)	48
Pneumothorax	7	1103	OR 3.71 (1.96–7.0)	0
Any BPD	24	3510	OR 3.27 (2.54–4.21)	38
Moderate-severe BPD	8	1254	OR 5.98 (3.8–9.42)	29
Tracheostomy	1	43	OR 2.49 (0.1–64.62)	—
Mortality	18	3560	OR 3.87 (2.35–6.36)	54
Mortality + any BPD	6	1972	OR 4.7 (2.84–7.76)	74
Mortality + moderate-to-severe BPD	3	554	OR 3.5 (1.71–7.13)	63
Cost of hospital stay	1	128	MD 122.86 (33.6–212.1)	—
Length of respiratory support	3	331	MD 18.06 (8.55–27.58)	11
Length of hospital stay	16	2896	MD 20.44 (14.1–26.8)	75
Length of invasive mechanical ventilation	17	2882	MD 15.04 (10.42–19.67)	97
Length of noninvasive respiratory support	3	430	MD 2.5 (−2.83 to 7.84)	64
Duration of oxygen requirement	9	1986	MD 21.26 (8.26–34.27)	93

Abbreviations: BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; MD, mean difference; NEC, necrotizing enterocolitis; OR, odds ratio; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity; PVL, periventricular leukomalacia; VAP, ventilator-associated pneumonia.

TABLE 4. Subgroup Analysis of Studies Including Only Preterm Neonates <28 Weeks GA at Birth and/or BW <1000 g

	Number of Studies	Number of Patients	Odds Ratio or Mean Difference [95% CI]	Heterogeneity I^2, %
Predictor				
BW	11	2266	MD −70.39 [−100.1 to −40.6]	69
GA at birth	11	2266	MD −0.7 [−0.84 to −0.56]	59
5-minute Apgar	8	1841	MD −0.29 [−1 to 0.41]	91
Presurfactant Fio_2	1	108	MD 0.08 [0.04–0.12]	—
PMA at extubation	6	1688	MD −0.55 [−0.87 to −0.23]	56
Weight at extubation	4	523	MD 70.34 [−84.5 to 225.2]	91
Pre-extubation Fio_2	8	2006	MD 0.03 [0.00–0.05]	95
Pre-extubation MAP	5	754	MD 0.21 [−0.28 to 0.70]	82
Pre-extubation Pco_2	9	2095	MD 2.98 [−0.01 to 5.98]	88
Pre-extubation pH	8	2050	MD −0.03 [−0.06 to −0.01]	88
Outcome				
Mortality + any BPD	3	1208	OR 3.28 [1.66–6.49]	70
BPD	9	1774	OR 3.26 [2.2–4.83]	49
Mortality	5	1492	OR 1.97 [0.6–6.52]	77

Abbreviations: BPD, bronchopulmonary dysplasia; BW, birth weight; GA, gestational age; Fio_2, fraction of inspired oxygen; MAP, mean airway pressure; PMA, postmenstrual age.

was associated with combined outcome of mortality and/or BPD as well as BPD, but not with mortality alone.

Subgroup Analysis: Studies From 2010 Onwards

We also analyzed separately 94 studies published from 2010 onwards, and the results are summarized in Supplemental Table 5. The findings were consistent with the overall previous results, showing that EF was associated with more immature infants, lower 5-minute Apgar scores, and higher levels of pre-extubation respiratory support (including Fio_2, MAP, Pco_2, and lower pH). In this subgroup, EF continued to be associated with mortality and/or BPD, as well as BPD (both overall and moderate-to-severe forms) and mortality.

DISCUSSION

This systematic review and meta-analysis aimed to consolidate current evidence on the predictors and outcomes of EF in preterm newborns, toward providing clinicians with a comprehensive summary of the available evidence as well as highlighting areas in need of further research. Results of our review and analyses revealed that more immature infants, characterized by lower GA, BW, and postmenstrual age, were at heightened risk for EF. Pre-extubation blood gas parameters and ventilatory settings representative of higher level of respiratory support requirements prior to extubation were also associated with EF. Newer tools such as ML and LUS hold promise as tools for predicting EF, each offering distinct advantages. Finally, EF was consistently linked with adverse outcomes, including increased odds of mortality and/or BPD, as well as prolonged requirements for respiratory support and hospitalization.

The association between younger gestational and chronological ages with EF may indicate relative pulmonary immaturity, as these lungs may have yet underdeveloped gas-exchange units. This finding may also be indicative of a lower ability to maintain functional residual capacity, due to lack of strength of the chest wall and inability to generate and maintain intrinsic PEEP. Similarly, the association of surrogates of higher ventilation requirement and EF is likely indicative of the relatively lower level of the work of breathing being generated by the infant, which may be potentially unsustainable following extubation. Nevertheless, clinical characteristics, pre-extubation ventilatory and blood gas parameters may suggest an increase chance of EF, although should not be the sole guide for this decision-making. In isolation, no single parameter is likely to predict EF. However, identification of EF predictors may help guide clinicians into anticipating the high-risk extubations, while optimizing peri-extubation strategies, potentially mitigating risks associated with EF and prolonged mechanical ventilation.

While advanced ML models have demonstrated moderate to high accuracy in predicting EF based on a range of clinical and ventilatory parameters, variability in external validation suggests ongoing refinement is necessary. Beyond that, advanced monitoring utilized in some models (such as AUREA and HRCi) are costly and not universally available at bedside in NICUs. In contrast, LUS, being widely available with a relatively simple technique, has shown promising accuracy in predicting EF, surpassing the use of individual clinical parameters alone. While methods and scoring systems utilized for LUS were highly variable, they generally had high sensitivity and specificity. Larger studies with more unified criteria for scoring systems as predictors of EF may help enhance uptake of this tool at the bedside.

Failure of extubation was associated with adverse outcomes, as described throughout the results. While the procedure of reintubation is known to carry inherent risks including hemodynamic perturbations and altered intracranial pressure and blood flow, the associations noted in our review may in part be related to the consequent longer duration of intubation and mechanical ventilation following EF. In addition, EF may simply be a marker of a more immature and/or sicker neonate as well as more severe lung disease, all of which may be important confounders. Unfortunately, as elaborated upon further below in limitations, our review constituted pooled odds ratios from unadjusted analyses and we are thus unable to fully account for these potential confounding variables. However, irrespective of these issues, a clinician may note that an EF may portend worse clinical outcomes in a preterm neonate.

To our knowledge, ours is the first systematic review that comprehensively evaluate predictors and outcomes of EF. Shalish et al performed a systematic review specifically targeting pre-extubation bedside tests, such as spontaneous breathing trials and highlighted their variable nature and limitations toward clinical practice implementation.[12] Ferguson et al evaluated postextubation strategies to improve ES,[13] while recent/upcoming Cochrane reviews examine the impact of various postextubation noninvasive respiratory support strategies.[14,136–138] All of these realms were outside the scope of this current review, especially considering the knowledge that these topics have already been covered.

There are recent reviews on ML and LUS with respect to EF. In comparison to existing literature, our study's findings on ML predictors of EF align with a recent narrative review by Jenkinson et al.[139] We observed comparable high variability in the AUC among ML models, reflecting inconsistent predictive performance. Notably, a higher proportion of studies in our review included an external validation cohort, though those in general demonstrated lower accuracy compared with the internal validation. As highlighted by Jenkinson et al., the methodologies and variables incorporated across these studies vary widely, reinforcing the current limitations in establishing an ML model superior to clinical predictors or expert opinion in predicting EF. Regarding LUS, our findings are in line with a recent systematic review by Mohsen et al[140], whose population comprehended newborns born both term and preterm. Similar to their observations, we found that LUS demonstrates good sensitivity and accuracy in predicting EF.

Strengths and Limitations

Our review has several strengths. We conducted a comprehensive literature review that encompassed a diverse array of predictors associated with EF. Our analysis included a subgroup specifically focusing on infants born at less than 28 weeks' GA and/or BW less than 1000g, providing valuable insights into this particularly vulnerable population. However, certain limitations should be acknowledged.

The studies included in our review exhibited considerable heterogeneity, particularly in methodologies and definitions and durations of EF (latter ranging from 24 hours following extubation up to 7 days). Such heterogeneity precluded a meta-analysis for studies involving ML and LUS, which can limit the clinical impact of our analysis. Additionally, there are inherent risks of bias associated with observational study designs, including referral bias as patients are only assessed when a clinical deems them ready for extubation. In addition, all our pooled analyses data come from unadjusted data from these original studies, potentially not accounting for confounders and precluding firm causal associations.

CONCLUSIONS AND FUTURE DIRECTIONS

In conclusion, EF in preterm infants is influenced by a complex array of predictors. While no single clinical characteristic, blood gas parameter, or ventilator setting can reliably predict outcomes, knowledge of potential predictors can alert clinicians to the possibility of EF. In addition, our study provides key clinical variables that should be incorporated into future models to enhance accuracy and clinical utility in neonatal intensive care. Future research should focus on validating predictive models using LUS and/or ML associated with clinical predictors to prevent EF. Finally, EF was found to be associated with increased mortality and/or BPD, although whether it indicates severe lung disease or is an independent risk factor remains unclear.

ABBREVIATIONS

AUC: area under the curve
BPD: bronchopulmonary dysplasia
EF: extubation failure
Fio_2: fraction of inspired oxygen
GA: gestational age
IMV: invasive mechanical ventilation
INSURE: Intubation-Surfactant-Extubation
IVH: intraventricular hemorrhage
LUS: lung ultrasound
MAP: mean airway pressure
ML: machine learning
NAVA: neurally adjusted ventilatory assist
NEC: Necrotizing Enterocolitis
Pco_2: partial pressure of carbon dioxide
PDA: patent ductus arteriosus
PEEP: positive end-expiratory pressure
PIP: peak inspiratory pressure
PVL: periventricular leukomalacia
RDS: respiratory distress syndrome
ROP: retinopathy of prematurity
RSS: respiratory severity score
Ti: inspiratory time
VAP: ventilator-associated pneumonia

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REFERENCES

1. Chawanpaiboon S, Vogel JP, Moller AB, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *Lancet Glob Health.* 2019;7(1):e37–e46. doi: 10.1016/S2214-109X(18)30451-0
2. Ho JJ, Subramaniam P, Davis PG. Continuous positive airway pressure (CPAP) for respiratory distress in preterm infants. *Cochrane Database Syst Rev.* 2020;15;10(10):CD002271. doi: 10.1002/14651858.CD002271.pub3
3. Beltempo M, Shah P, Yoon EW, et al. *The Canadian Neonatal Network Annual Report 2020.* Canadian Neonatal Network; 2020.
4. Walsh MC, Morris BH, Wrage LA, et al; National Institutes of Child Health and Human Development Neonatal Research Network. Extremely low birthweight neonates with protracted ventilation:

mortality and 18-month neurodevelopmental outcomes. *J Pediatr.* 2005;146(6):798–804. doi: 10.1016/j.jpeds.2005.01.047

5. Choi YB, Lee J, Park J, Jun YH. Impact of prolonged mechanical ventilation in very low birth weight infants: results from a national cohort study. *J Pediatr.* 2018;194:34–39.e3. doi: 10.1016/j.jpeds.2017.10.042
6. Jensen EA, DeMauro SB, Kornhauser M, Aghai ZH, Greenspan JS, Dysart KC. Effects of multiple ventilation courses and duration of mechanical ventilation on respiratory outcomes in extremely low-birth-weight infants. *JAMA Pediatr.* 2015;169(11):1011–1017. doi: 10.1001/jamapediatrics.2015.2401
7. Hermeto F, Martins BM, Ramos JR Jr, Bhering CA, Sant'Anna GM. Incidence and main risk factors associated with extubation failure in newborns with birth weight <1,250 grams. Article in Portuguese. *J Pediatr (Rio J).* 2009;85(5):397–402. doi: 10.1590/S0021-75572009000500005
8. Al-Hathlol K, Bin Saleem N, Khawaji M, et al. Early extubation failure in very low birth weight infants: clinical outcomes and predictive factors. *J Neonatal Perinatal Med.* 2017;10(2):163–169. doi: 10.3233/NPM-171647
9. Chakraborty M, Watkins WJ, Tansey K, King WE, Banerjee S. Predicting extubation outcomes using the Heart Rate Characteristics index in preterm infants: a cohort study. *Eur Respir J.* 2020;56(4):1901755. doi: 10.1183/13993003.01755-2019
10. Kidman AM, Manley BJ, Boland RA, Davis PG, Bhatia R. Predictors and outcomes of extubation failure in extremely preterm infants. *J Paediatr Child Health.* 2021;57(6):913–919. doi: 10.1111/jpc.15356
11. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev.* 2021;10(1):89. doi: 10.1186/s13643-021-01626-4
12. Shalish W, Latremouille S, Papenburg J, Sant'Anna GM. Predictors of extubation readiness in preterm infants: a systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed.* 2019;104(1):F89–F97. doi: 10.1136/archdischild-2017-313878
13. Ferguson KN, Roberts CT, Manley BJ, Davis PG. Interventions to improve rates of successful extubation in preterm infants: a systematic review and meta-analysis. *JAMA Pediatr.* 2017;171(2):165–174. doi: 10.1001/jamapediatrics.2016.3015
14. Lemyre B, Deguise MO, Benson P, Kirpalani H, De Paoli AG, Davis PG. Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation. *Cochrane Database Syst Rev.* 2023;2023;7(7):CD003212. doi: 10.1002/14651858.CD003212.pub4
15. Lemyre B, Deguise MO, Benson P, Kirpalani H, Ekhaguere OA, Davis PG. Early nasal intermittent positive pressure ventilation (NIPPV) versus early nasal continuous positive airway pressure (NCPAP) for preterm infants. *Cochrane Database Syst Rev.* 2023;2023;7(7):CD005384. doi: 10.1002/14651858.CD005384.pub3
16. Teixeira RF, Carvalho ACA, de Araujo RD, Veloso FCS, Kassar SB, Medeiros AMC. Spontaneous breathing trials in preterm infants: systematic review and meta-analysis. *Respir Care.* 2021;66(1):129–137. doi: 10.4187/respcare.07928
17. Shalish W, Kanbar L, Keszler M, et al. Patterns of reintubation in extremely preterm infants: a longitudinal cohort study. *Pediatr Res.* 2018;83(5):969–975. doi: 10.1038/pr.2017.330
18. National Institute of Standards and Technology (NIST). The International System of Units (SI). *NIST Special Publication.* 2008;811.
19. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol.* 2014;14(135):135. doi: 10.1186/1471-2288-14-135
20. Abu Jawdeh EG, Pant A, Gabrani A, Cunningham MD, Raffay TM, Westgate PM. Extubation readiness in preterm infants: evaluating the role of monitoring intermittent hypoxemia. *Children (Basel).* 2021;8(3):237. doi: 10.3390/children8030237
21. Ahmed WO, AbuSaif lSH, Salaheldin SA, et al. Noninvasive high frequency oscillatory ventilation versus noninvasive positive pressure ventilation in preterm neonates after extubation: a randomized controlled trial. *J Neonatal Perinatal Med.* 2023;16(3):393–402. doi: 10.3233/NPM-221199
22. Alarcon-Martinez T, Latremouille S, Kovacs L, Kearney RE, Sant'Anna GM, Shalish W. Clinical usefulness of reintubation criteria in extremely preterm infants: a cohort study. *Arch Dis Child Fetal Neonatal Ed.* 2023;108(6):643–648. doi: 10.1136/archdischild-2022-325245
23. Ali YAH, Seshia MM, Ali E, Alvaro R. Noninvasive high-frequency oscillatory ventilation: a retrospective chart review. *Am J Perinatol.* 2022;39(6):666–670. doi: 10.1055/s-0040-1718738
24. Alonzo CJ, Fairchild KD. Dexamethasone effect on heart rate variability in preterm infants on mechanical ventilation. *J Neonatal Perinatal Med.* 2017;10(4):425–430. doi: 10.3233/NPM-16157
25. Amaro CM, Bello JA, Jain D, et al. Early caffeine and weaning from mechanical ventilation in preterm infants: a randomized, placebo-controlled trial. *J Pediatr.* 2018;196:52–57. doi: 10.1016/j.jpeds.2018.01.010
26. Azzabi O, Selmi I, Bellali H, et al. Intubation-surfactant-extubation strategy in a medical resource-limited department: a prospective study. *J Trop Pediatr.* 2016;62(2):169–170. doi: 10.1093/tropej/fmv074
27. Bagley CE, Gray PH, Tudehope DI, Flenady V, Shearman AD, Lamont A. Routine neonatal postextubation chest physiotherapy: a randomized controlled trial. *J Paediatr Child Health.* 2005;41(11):592:597. doi: 10.1111/j.1440-1754.2005.00728.x
28. Bahgat E, El-Halaby H, Abdelrahman A, Nasef N, Abdel-Hady H. Sonographic evaluation of diaphragmatic thickness and excursion as a predictor for successful extubation in mechanically ventilated preterm infants. *Eur J Pediatr.* 2021;180(3):899–908. doi: 10.1007/s00431-020-03805-2
29. Barrington KJ, Muttitt SC. Randomized, controlled, blinded trial of doxapram for extubation of the very low birthweight infant. *Acta Paediatr.* 1998;87(2):191–194. doi: 10.1080/08035259850157651
30. Bastos de Souza Júnior NW, Rosa TR, Cerântola JCK, Ferrari LSL, Probst VS, Felcar JM. Predictive factors for extubation success in very low and extremely low birth weight preterm infants. *Can J Respir Ther.* 2023;59:204–213. doi: 10.29390/001c.87789

31. Brix N, Sellmer A, Jensen MS, Pedersen LV, Henriksen TB. Predictors for an unsuccessful INtubation-SURfactant-Extubation procedure: a cohort study. *BMC Pediatr*. 2014;14(155):155. doi: 10.1186/1471-2431-14-155

32. Chawla S, Natarajan G, Shankaran S, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Markers of successful extubation in extremely preterm infants, and morbidity after failed extubation. *J Pediatr*. 2017;189:113–119.e2. doi: 10.1016/j.jpeds.2017.04.050

33. Chen F, Chen Y, Wu Y, Zhu X, Shi Y. A nomogram for predicting extubation failure in preterm infants with gestational age less than 29 weeks. *Neonatology*. 2023;120(4):424–433. doi: 10.1159/000530759

34. Chen YH, Lin HL, Sung YH, Hsu JF, Chu SM. Analysis of predictive parameters for extubation in very low birth weight preterm infants. *Pediatr Neonatol*. 2023;64(3):274–279. doi: 10.1016/j.pedneo.2022.08.007

35. Cheng Z, Dong Z, Zhao Q, et al. A prediction model of extubation failure risk in preterm infants. *Front Pediatr*. 2021;9(693320):693320. doi: 10.3389/fped.2021.693320

36. Cherif A, Hachani C, Khrouf N. Risk factors of the failure of surfactant treatment by transient intubation during nasal continuous positive airway pressure in preterm infants. *Am J Perinatol*. 2008;25(10):647–652. doi: 10.1055/s-0028-1090590

37. Coughlin K, Jen P, Katheria A. Characteristics and outcomes in preterm infants with extubation failure in the first week of life. *Am J Perinatol*. 2024;41(S 01):e1675–e1680. doi: 10.1055/s-0043-1768245

38. Currie A, Patel DS, Rafferty GF, Greenough A. Prediction of extubation outcome in infants using the tension time index. *Arch Dis Child Fetal Neonatal Ed*. 2011;96(4):F265–F269. doi: 10.1136/adc.2010.191015

39. Danan C, Durrmeyer X, Brochard L, Decobert F, Benani M, Dassieu G. A randomized trial of delayed extubation for the reduction of reintubation in extremely preterm infants. *Pediatr Pulmonol*. 2008;43(2):117–124. doi: 10.1002/ppul.20726

40. Dani C, Corsini I, Bertini G, Fontanelli G, Pratesi S, Rubaltelli FF. The INSURE method in preterm infants of less than 30 weeks' gestation. *J Matern Fetal Neonatal Med*. 2010;23(9):1024–1029. doi: 10.3109/14767050903572174

41. Dassios T, Kaltsogianni O, Greenough A. Relaxation rate of the respiratory muscles and prediction of extubation outcome in prematurely born infants. *Neonatology*. 2017;112(3):251–257. doi: 10.1159/000477233

42. Dassios T, Williams E, Ambulkar H, Shetty S, Hickey A, Greenough A. Tidal volumes and outcome of extubation in mechanically ventilated premature infants. *Am J Perinatol*. 2020;37(2):204–209. doi: 10.1055/s-0039-1696714

43. Dehdashtian M, Malakian A, Aramesh MR, et al. Effectiveness of intratracheal salbutamol in addition to surfactant on the clinical course of newborns with respiratory distress syndrome: a clinical trial. *Ital J Pediatr*. 2016;42(6):6. doi: 10.1186/s13052-016-0215-1

44. Dimitriou G, Fouzas S, Vervenioti A, Tzifas S, Mantagos S. Prediction of extubation outcome in preterm infants by composite extubation indices. *Pediatr Crit Care Med*. 2011;12(6):e242–e249. doi: 10.1097/PCC.0b013e3181fe3431

45. Dimitriou G, Greenough A, Endo A, Cherian S, Rafferty GF. Prediction of extubation failure in preterm infants. *Arch Dis Child Fetal Neonatal Ed*. 2002;86(1):F32–F35. doi: 10.1136/fn.86.1.F32

46. Dimitriou G, Greenough A, Laubscher B. Lung volume measurements immediately after extubation by prediction of "extubation failure" in premature infants. *Pediatr Pulmonol*. 1996;21(4):250–254. doi: 10.1002/(SICI)1099-0496(199604)21:4<250:AID-PPUL9>3.0.CO;2-S

47. Dryer RA, Salem A, Saroha V, et al. Evaluation and validation of a prediction model for extubation success in very preterm infants. *J Perinatol*. 2022;42(12):1674–1679. doi: 10.1038/s41372-022-01517-z

48. Dursun M, U ZA, Bulbul A. Relationship between the respiratory severity score and extubation failure in very-low-birth-weight premature infants. *Sisli Etfal Hastan Tip Bul*. 2021;55(3):382–390. doi: 10.14744/SEMB.2021.92693

49. El-Farrash RA, DiBlasi RM, AbdEL-Aziz EA, et al. Postextubation noninvasive ventilation in respiratory distress syndrome: a randomized controlled trial. *Am J Perinatol*. 2022;29(14):1577–1585. doi: 10.1055/s-0041-1723999

50. Fang SJ, Su CH, Liao DL, et al. Neurally adjusted ventilatory assist for rapid weaning in preterm infants. *Pediatr Int*. 2023;65(1):e15360. doi: 10.1111/ped.15360

51. Gharehbaghi MM, Peirovifar A, Ghojazadeh M. Risk factors contributing to the failure of surfactant administration with INSURE method. *J Pioneer Med Sci*. 2014;4(2):55–59.

52. Gillespie LM, White SD, Sinha SK, Donn SM. Usefulness of the minute ventilation test in predicting successful extubation in newborn infants: a randomized controlled trial. *J Perinatol*. 2003;23(3):205–207. doi: 10.1038/sj.jp.7210886

53. Goel N, Chakraborty M, Watkins WJ, Banerjee S. Predicting extubation outcomes-a model incorporating heart rate characteristics index. *J Pediatr*. 2018;195:53–58.e1. doi: 10.1016/j.jpeds.2017.11.037

54. Goudarzi RM, Badiee Z, Sadeghnia A, Barekatain B. Evaluation of intratracheal salbutamol effects in addition to surfactant in the clinical course of premature neonates with respiratory distress syndrome. *J Res Med Sci*. 2023;28:53. doi: 10.4103/jrms.jrms_548_22

55. Gourdeau P, Kanbar L, Shalish W, Sant'Anna G, Kearney R, Precup D. Feature selection and oversampling in analysis of clinical data for extubation readiness in extreme preterm infants. *Annu Int Conf IEEE Eng Med Biol Soc*. 2015;2015:4427–4430. doi: 10.1109/EMBC.2015.7319377

56. Gupta D, Greenberg RG, Natarajan G, et al. Respiratory setback associated with extubation failure in extremely preterm infants. *Pediatr Pulmonol*. 2021;56(7):2081–2086. doi: 10.1002/ppul.25387

57. Gupta D, Greenberg RG, Sharma A, et al. A predictive model for extubation readiness in extremely preterm infants. *J Perinatol*. 2019;39(12):1663–1669. doi: 10.1038/s41372-019-0475-x

58. Gupta D, Greenberg RG, Natarajan G, et al. Association of patent ductus arteriosus with extubation failure among preterm infants. *Pediatr Pulmonol.* 2023;58(7):1977–1981. doi: 10.1002/ppul.26420

59. Guy B, Dye ME, Richards L, Guthrie SO, Hatch LD III. Association of time of day and extubation success in very low birthweight infants: a multicenter cohort study. *J Perinatol.* 2021; 41(10):2532–2536. doi: 10.1038/s41372-021-01168-6

60. He F, Wu D, Sun Y, Lin Y, Wen X, Cheng ASK. Predictors of extubation outcomes among extremely and very preterm infants: a retrospective cohort study. *J Pediatr (Rio J).* 2022;98(6):648–654. doi: 10.1016/j.jped.2022.04.001

61. Hermeto F, Bottino MN, Vaillancourt K, Sant'Anna GM. Implementation of a respiratory therapist-driven protocol for neonatal ventilation: impact on the premature population. *Pediatrics.* 2009;123(5):e907–e916. doi: 10.1542/peds.2008-1647

62. Hoffman SB, Govindan RB, Johnston EK, Williams J, Schlatterer SD, du Plessis AJ. Autonomic markers of extubation readiness in premature infants. *Pediatr Res.* 2023;93(4):911–917. doi: 10.1038/s41390-022-02397-x

63. Hunt KA, Hunt I, Ali K, Dassios T, Greenough A. Prediction of extubation success using the diaphragmatic electromyograph results in ventilated neonates. *J Perinat Med.* 2020;48(6):609–614. doi: 10.1515/jpm-2020-0129

64. Huon C, Rey E, Mussat P, Parat S, Moriette G. Low-dose doxapram for treatment of apnoea following early weaning in very low birthweight infants: a randomized, double-blind study. *Acta Paediatr.* 1998;87(11):1180–1184. doi: 10.1111/j.1651-2227.1998.tb00927.x

65. Iyer NP, Dickson J, Ruiz ME, et al. Neural breathing pattern in newborn infants pre- and postextubation. *Acta Paediatr.* 2017; 106(12):1928–1933. doi: 10.1111/apa.14040

66. Janjindamai W, Pasee S, Thatrimontrichai A. The optimal predictors of readiness for extubation in low birth weight infants. *J Med Assoc Thai.* 2017;100(4):427–434.

67. Jiang QX, Shi LJ, Shen LY, et al. Application value of a new lung ultrasound scoring method in neonatal respiratory distress syndrome treatment. *Ultrasound Med Biol.* 2022;48(2):275–282. doi: 10.1016/j.ultrasmedbio.2021.10.009

68. Kaczmarek J, Chawla S, Marchica C, Dwaihy M, Grundy L, Sant'Anna GM. Heart rate variability and extubation readiness in extremely preterm infants. *Neonatology.* 2013;104(1):42–48. doi: 10.1159/000347101

69. Kaczmarek J, Kamlin CO, Morley CJ, Davis PG, Sant'anna GM. Variability of respiratory parameters and extubation readiness in ventilated neonates. *Arch Dis Child Fetal Neonatal Ed.* 2013;98(1):F70–F73. doi: 10.1136/fetalneonatal-2011-301340

70. Kadivar M, Mosayebi Z, Razi N, Nariman S, Sangsari R. High flow nasal cannulae versus nasal continuous positive airway pressure in neonates with respiratory distress syndrome managed with INSURE method: a randomized clinical trial. *Iran J Med Sci.* 2016;41(6):494–500.

71. Kamlin CO, Davis PG, Morley CJ. Predicting successful extubation of very low birthweight infants. *Arch Dis Child Fetal Neonatal Ed.* 2006;91(3):F180–F183. doi: 10.1136/adc.2005.081083

72. Kanbar LJ, Onu CC, Shalish W, et al. Undersampling and bagging of decision trees in the analysis of cardiorespiratory behavior for the prediction of extubation readiness in extremely preterm infants. *Annu Int Conf IEEE Eng Med Biol Soc.* 2018;2018:4940–4944. doi: 10.1109/EMBC.2018.8513194

73. Kanbar LJ, Shalish W, Onu CC. Automated prediction of extubation success in extremely preterm infants: the APEX multicenter study. *Pediatr Res.* 2023;93(4):1041–1049. doi: 10.1038/s41390-022-02210-9

74. Khorana M, Paradeevisut H, Sangtawesin V, Kanjanapatanakul W, Chotigeat U, Ayutthaya JK. A randomized trial of non-synchronized Nasopharyngeal Intermittent Mandatory Ventilation (nsNIMV) vs. Nasal Continuous Positive Airway Pressure (NCPAP) in the prevention of extubation failure in pre-term < 1,500 grams. *J Med Assoc Thai.* 2008;91(suppl 3):S136–S142.

75. Koh JW, Kim JW, Chang YP. Transient intubation for surfactant administration in the treatment of respiratory distress syndrome in extremely premature infants. *Korean J Pediatr.* 2018; 61(10):315–321. doi: 10.3345/kjp.2018.06296

76. Shivakumar MS, Najih M, Bhat YR, et al. Prophylactic methylxanthines for preventing extubation failure in the preterm neonates with the gestational age of ≤30 weeks: a randomized controlled trial. *Iran J Neonatol.* 2017;8(3). doi: 10.22038/ijn.2017.23031.1281

77. Lakkundi A, Wright I, de Waal K. Transitional hemodynamics in preterm infants with a respiratory management strategy directed at avoidance of mechanical ventilation. *Early Hum Dev.* 2014; 90(8):409–412. doi: 10.1016/j.earlhumdev.2014.04.017

78. Latremouille S, Al-Jabri A, Lamer P, et al. Heart rate variability in extremely preterm infants receiving nasal CPAP and non-synchronized noninvasive ventilation immediately after extubation. *Respir Care.* 2018;63(1):62–69. doi: 10.4187/respcare.05672

79. Latremouille S, Shalish W, Kanbar L, et al. The effects of nasal continuous positive airway pressure and high flow nasal cannula on heart rate variability in extremely preterm infants after extubation: a randomized crossover trial. *Pediatr Pulmonol.* 2019; 54(6):788–796. doi: 10.1002/ppul.24284

80. Latremouille S, Bhuller M, Shalish W, Sant'Anna G. Cardiorespiratory measures shortly after extubation and extubation outcomes in extremely preterm infants. *Pediatr Res.* 2023; 93(6):1687–1693. doi: 10.1038/s41390-022-02284-5

81. Lee CY, Su BH, Lin TW, Lin HC, Li TC, Wang NP. Risk factors of extubation failure in extremely low birth weight infants: a five year retrospective analysis. *Acta Paediatr Taiwan.* 2002;43(6):319–325.

82. Li J, Zhang J, Hao Q, et al. The impact of time interval between first extubation and reintubation on bronchopulmonary dysplasia or death in very low birth weight infants. *Front Pediatr.* 2022; 10(867767):867767. doi: 10.3389/fped.2022.867767

83. Liang Z, Meng Q, You C, Wu B, Li X, Wu Q. Roles of lung ultrasound score in the extubation failure from mechanical ventilation among premature infants with neonatal respiratory distress syndrome. *Front Pediatr.* 2021;9(709160):709160. doi: 10.3389/fped.2021.709160

84. Liu YC, Yeh CY, Yang ST, et al. Feasibility of endotracheal extubation evaluation form in predicting successful extubation in neonatal

intensive care units: a retrospective study. *Children (Basel)*. 2023;10(6):1053. doi: 10.3390/children10061053

85. Magalhães P, Leme Silva P, Almeida L. Positive pressure ventilation in the weaning of preterm newborns. *Minerva Pediatr (Torino)*. 2023;75(6):817–821. doi: 10.23736/S2724-5276.20.05677-7

86. Mandhari HA, Al Riyami B, Khan A, Nonoyama M, Rizvi SGA. Risk factors of extubation failure in intubated preterm infants at a tertiary care hospital in Oman. *Sultan Qaboos Univ Med J*. 2022;22(2):247–252. doi: 10.18295/squmj.8.2021.122

87. Manley BJ, Doyle LW, Owen LS, Davis PG. Extubating extremely preterm infants: predictors of success and outcomes following failure. *J Pediatr*. 2016;173:45–49. doi: 10.1016/j.jpeds.2016.02.016

88. Mariani G, Cifuentes J, Carlo WA. Randomized trial of permissive hypercapnia in preterm infants. *Pediatrics*. 1999;104(5 Pt 1):1082–1088. doi: 10.1542/peds.104.5.1082

89. Masry A, Nimeri NAMA, Koobar O, et al. Reintubation rates after extubation to different non-invasive ventilation modes in preterm infants. *BMC Pediatr*. 2021;21(1):281. doi: 10.1186/s12887-021-02760-7

90. Menshykova A, Dobryanskyy D. Risk factors associated with extubation failure in preterm infants with very low birth weight. *Pediatria. Pediatr Pol*. 2017;92(1):22–27. doi: 10.1016/j.pepo.2016.10.005

91. Mhanna MJ, Iyer NP, Piraino S, Jain M. Respiratory severity score and extubation readiness in very low birth weight infants. *Pediatr Neonatol*. 2017;58(6):523–528. doi: 10.1016/j.pedneo.2016.12.006

92. Mikhno A, Ennett CM. Prediction of extubation failure for neonates with respiratory distress syndrome using the MIMIC-II clinical database. *Annu Int Conf IEEE Eng Med Biol Soc*. 2012;2012:5094–5097. doi: 10.1109/EMBC.2012.6347139

93. Mohammed S, Nour I, Shabaan AE, Shouman B, Abdel-Hady H, Nasef N. High versus low-dose caffeine for apnea of prematurity: a randomized controlled trial. *Eur J Pediatr*. 2015;174(7):949–956. doi: 10.1007/s00431-015-2494-8

94. Mohsen N, Nasef N, Ghanem M, et al. Accuracy of lung and diaphragm ultrasound in predicting successful extubation in extremely preterm infants: a prospective observational study. *Pediatr Pulmonol*. 2023;58(2):530–539. doi: 10.1002/ppul.26223

95. Mueller M, Almeida JS, Stanislaus R, Wagner CL. Can machine learning methods predict extubation outcome in premature infants as well as clinicians? *J Neonatal Biol*. 2013;2:1000118. doi: 10.4172/2167-0897.1000118

96. Mueller M, Wagner CC, Stanislaus R, Almeida JS. Machine learning to predict extubation outcome in premature infants. *Proc Int Jt Conf Neural Netw*. 2013:1–6. doi: 10.1109/IJCNN.2013.6707058

97. Mueller M, Wagner CL, Annibale DJ, Hulsey TC, Knapp RG, Almeida JS. Predicting extubation outcome in preterm newborns: a comparison of neural networks with clinical expertise and statistical modeling. *Pediatr Res*. 2004;56(1):11–18. doi: 10.1203/01.PDR.0000129658.55746.3C

98. Mueller M, Wagner CL, Annibale DJ, Knapp RG, Hulsey TC, Almeida JS. Parameter selection for and implementation of a web-based decision-support tool to predict extubation outcome in premature infants. *BMC Med Inform Decis Mak*. 2006;6(11):11. doi: 10.1186/1472-6947-6-11

99. Mukerji A, Razak A, Aggarwal A, et al. Early versus delayed extubation in extremely preterm neonates: a retrospective cohort study. *J Perinatol*. 2020;40(1):118–123. doi: 10.1038/s41372-019-0495-6

100. Najafian B, Fakhraie SH, Afjeh SA, Kazemian M, Shohrati M, Saburi A. Early surfactant therapy with nasal continuous positive airway pressure or continued mechanical ventilation in very low birth weight neonates with respiratory distress syndrome. *Iran Red Crescent Med J*. 2014;16(4):e12206. doi: 10.5812/ircmj.12206

101. Naseh A, Yekta BG. INSURE method (INtubation-SURfactant-Extubation) in early and late premature neonates with respiratory distress: factors affecting the outcome and survival rate. *Turk J Pediatr*. 2014;56(3):232–237.

102. Natarajan A, Lam G, Liu J, Beam AL, Beam KS, Levin JC. Prediction of extubation failure among low birthweight neonates using machine learning. *J Perinatol*. 2023;43(2):209–214. doi: 10.1038/s41372-022-01591-3

103. O'Brien K, Campbell C, Brown L, Wenger L, Shah V. Infant flow biphasic nasal continuous positive airway pressure (BP-NCPAP) vs. infant flow NCPAP for the facilitation of extubation in infants' ≤ 1,250 grams: a randomized controlled trial. *BMC Pediatr*. 2012;12:43. doi: 10.1186/1471-2431-12-43

104. Ognean ML, Stoicescu SM, Boant O, N stase L, Gliga C, Cucerea M.Intubation-surfactant: extubation on continuous positive pressure ventilation. Who are the best candidates? *J Crit Care Med (Targu Mures)*. 2016;2(2):73–79. doi: 10.1515/jccm-2016-0010

105. Ohnstad MO, Stensvold HJ, Pripp AH, et al; Norwegian Neonatal Network. Predictors of extubation success: a population-based study of neonates below a gestational age of 26 weeks. *BMJ Paediatr Open*. 2022;6(1):e001542. doi: 10.1136/bmjpo-2022-001542

106. Ohnstad MO, Stensvold HJ, Pripp AH, et al. Associations between unit workloads and outcomes of first extubation attempts in extremely premature infants below a gestational age of 26 weeks. *Front Pediatr*. 2023;11(1090701):1090701. doi: 10.3389/fped.2023.1090701

107. Okur N, Buyuktiryaki M, Sari FN, Dizdar EA, Oguz SS. Ventilator-delivered nasal intermittent positive pressure ventilation versus nasal biphasic positive airway pressure following extubation in infants ≤1250 g birth weight: a randomized trial. *J Matern Fetal Neonatal Med*. 2022;35(4):752–758. doi: 10.1080/14767058.2020.1731462

108. Park SJ, Bae MH, Jeong MH, et al. Risk factors and clinical outcomes of extubation failure in very early preterm infants: a single-center cohort study. *BMC Pediatr*. 2023;23(1):36. doi: 10.1186/s12887-023-03833-5

109. Pholanun N, Srisatidnarakul B, Longo J. Development and validation of extubation readiness assessment tool and accuracy to predict successful extubation in preterm infants. *Int J Afr Nurs Sci*. 2023;19:100599. doi: 10.1016/j.ijans.2023.100599

110. Precup D, Robles-Rubio CA, Brown KA, et al. Prediction of extubation readiness in extreme preterm infants based on measures of

cardiorespiratory variability. *Annu Int Conf IEEE Eng Med Biol Soc.* 2012;2012:5630–5633. doi: 10.1109/EMBC.2012.6347271

111. Rallis D, Ben-David D, Woo K. Predictors of successful extubation from volume-targeted ventilation in extremely preterm neonates. *J Perinatol.* 2024;44(2):250–256. doi: 10.1038/s41372-023-01849-4

112. Ribeiro SNS, Fontes MJF, Bhandari V, Resende CB, Johnston C. Noninvasive ventilation in newborns ≤ 1,500 g after tracheal extubation: randomized clinical trial. *Am J Perinatol.* 2017; 34(12):1190–1198. doi: 10.1055/s-0037-1602141

113. Robles-Rubio CA, Kaczmarek J, Chawla S, et al. Automated analysis of respiratory behavior in extremely preterm infants and extubation readiness. *Pediatr Pulmonol.* 2015;50(5):479–486. doi: 10.1002/ppul.23151

114. Shalish W, Kanbar L, Kovacs L, et al. The impact of time interval between extubation and reintubation on death or bronchopulmonary dysplasia in extremely preterm infants. *J Pediatr.* 2019;205:70–76.e2. doi: 10.1016/j.jpeds.2018.09.062

115. Shalish W, Keszler M, Kovacs L. Age at first extubation attempt and death or respiratory morbidities in extremely preterm infants. *J Pediatr.* 2023;252:124–130.e3. doi: 10.1016/j.jpeds.2022.08.025

116. Silva MGF, Gregório ML, de Godoy MF. Does heart rate variability improve prediction of failed extubation in preterm infants? *J Perinat Med.* 2019;47(2):252–257. doi: 10.1515/jpm-2017-0375

117. Singh N, McNally MJ, Darnall RA. Does diaphragmatic electrical activity in preterm infants predict extubation success? *Respir Care.* 2018;63(2):203–207. doi: 10.4187/respcare.05539

118. Smith J, Pieper CH, Maree D, Gie RP. Compliance of the respiratory system as a predictor for successful extubation in very-low-birth-weight infants recovering from respiratory distress syndrome. *S Afr Med J.* 1999;89(10):1097–1102.

119. Song W, Hwa Jung Y, Cho J, Baek H, Won Choi C, Yoo S. Development and validation of a prediction model for evaluating extubation readiness in preterm infants. *Int J Med Inform.* 2023; 178(105192):105192. doi: 10.1016/j.ijmedinf.2023.105192

120. Spaggiari E, Amato M, Ricca OA, et al. Can fraction of inspired oxygen predict extubation failure in preterm infants? *Children (Basel).* 2022;9(1):30. doi: 10.3390/children9010030

121. Spasojevic S, Doronjski A. Risk factors associated with failure of extubation in very-low-birth-weight newborns. *J Matern Fetal Neonatal Med.* 2018;31(3):300–304. doi: 10.1080/14767058.2017.1285884

122. Steer P, Flenady V, Shearman A, et al; Caffeine Collaborative Study Group Steering Group. High dose caffeine citrate for extubation of preterm infants: a randomised controlled trial. *Arch Dis Child Fetal Neonatal Ed.* 2004;89(6):F499–F503. doi: 10.1136/adc.2002.023432

123. Steer PA, Flenady VJ, Shearman A, Lee TC, Tudehope DI, Charles BG. Periextubation caffeine in preterm neonates: a randomized dose response trial. *J Paediatr Child Health.* 2003;39(7):511–515. doi: 10.1046/j.1440-1754.2003.00207.x

124. Stefanescu BM, Murphy WP, Hansell BJ, Fuloria M, Morgan TM, Aschner JL. A randomized, controlled trial comparing two different continuous positive airway pressure systems for the successful extubation of extremely low birth weight infants. *Pediatrics.* 2003;112(5):1031–1038. doi: 10.1542/peds.112.5.1031

125. Szymankiewicz M, Vidyasagar D, Gadzinowski J. Predictors of successful extubation of preterm low-birth-weight infants with respiratory distress syndrome. *Pediatr Crit Care Med.* 2005;6(1): 44–49. doi: 10.1097/01.PCC.0000149136.28598.14

126. Tagare A, Kadam S, Vaidya U, Pandit A. Outcome of intubate surfactant rapidly extubate (InSuRE): an Indian experience. *Indian J Pediatr.* 2014;81(1):20–23. doi: 10.1007/s12098-013-1090-z

127. Tana M, Lio A, Tirone C, et al. Extubation from high-frequency oscillatory ventilation in extremely low birth weight infants: a prospective observational study. *BMJ Paediatr Open.* 2018;2(1):e000350. doi: 10.1136/bmjpo-2018-000350

128. Teixeira RF, Costa CM, Maria de Abreu C, et al. Factors associated with extubation failure in very low birth weight infants: a cohort study in the northeast Brazil. *J Perinat Med.* 2020;49(4):506–513. doi: 10.1515/jpm-2020-0313

129. Thatrimontrichai A, Techato C, Dissaneevate S, et al. Risk factors and outcomes of carbapenem-resistant Acinetobacter baumannii ventilator-associated pneumonia in the neonate: A case-case-control study. *J Infect Chemother.* 2016;22(7):444–449. doi: 10.1016/j.jiac.2016.03.013

130. Tooley J, Dyke M. Randomized study of nasal continuous positive airway pressure in the preterm infant with respiratory distress syndrome. *Acta Paediatr.* 2003;92(10):1170–1174. doi: 10.1111/j.1651-2227.2003.tb02479.x

131. van Velzen A, De Jaegere A, van der Lee J, van Kaam A. Feasibility of weaning and direct extubation from open lung high-frequency ventilation in preterm infants. *Pediatr Crit Care Med.* 2009;10(1): 71–75. doi: 10.1097/PCC.0b013e3181936fbe

132. Vento G, Tortorolo L, Zecca E, et al. Spontaneous minute ventilation is a predictor of extubation failure in extremely-low-birth-weight infants. *J Matern Fetal Neonatal Med.* 2004;15(3):147–154. doi: 10.1080/14767050410001668239

133. Wang SH, Liou JY, Chen CY, Chou HC, Hsieh WS, Tsao PN. Risk factors for extubation failure in extremely low birth weight infants. *Pediatr Neonatol.* 2017;58(2):145–150. doi: 10.1016/j.pedneo.2016.01.006

134. Wilson BJ Jr, Becker MA, Linton ME, Donn SM. Spontaneous minute ventilation predicts readiness for extubation in mechanically ventilated preterm infants. *J Perinatol.* 1998;18(6 Pt 1):436–439.

135. Yang Y, Yan W, Ruan M, et al. Lung recruitment improves the efficacy of intubation-surfactant-extubation treatment for respiratory distress syndrome in preterm neonates, a randomized controlled trial. *BMC Pediatr.* 2022;22(1):14. doi: 10.1186/s12887-021-03096-y

136. Razak A, Shah PS, Ye XY, Mukerji A. Post-extubation use of non-invasive respiratory support in preterm infants: a network meta-analysis. *Cochrane Libr.* 2021;10:1465–1858. doi: 10.1002/14651858.CD014509

137. Mukerji A, Shah PS, Ye XY, Razak A. Non-invasive respiratory support in preterm infants as primary mode: a network meta-analysis. *Cochrane Database of Systematic Reviews.* 2021;11:CD014895. doi: 10.1002/14651858.CD014895

138. Junior JC, de Azevedo R, Araujo O, de Carvalho WB. High-flow nasal cannula as a post-extubation respiratory support strategy in preterm infants: a systematic review and meta-analysis. *J Pediatr (Rio J)*. 2020;96(4):422–431. doi: 10.1016/j.jped.2019.11.004

139. Jenkinson A, Dassios T, Greenough A. Artificial intelligence in the NICU to predict extubation success in prematurely born infants. *J Perinat Med*. 2023;52(2):119–125. doi: 10.1515/jpm-2023-0454

140. Mohsen N, Solis-Garcia G, Jasani B, Nasef N, Mohamed A. Accuracy of lung ultrasound in predicting extubation failure in neonates: a systematic review and meta-analysis. *Pediatr Pulmonol*. 2023;58(10):2846–2856. doi: 10.1002/ppul.26598