

Weaning from nCPAP in Preterm Infants: Current Evidence and Evolving Strategies

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18TH HOT TOPICS IN NEONATAL MEDICINE
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RITZ CARLTON, JEDDAH

I have nothing to declare

Outlines

- When to wean?
- Factors affecting weaning success
- How to wean?

Introduction

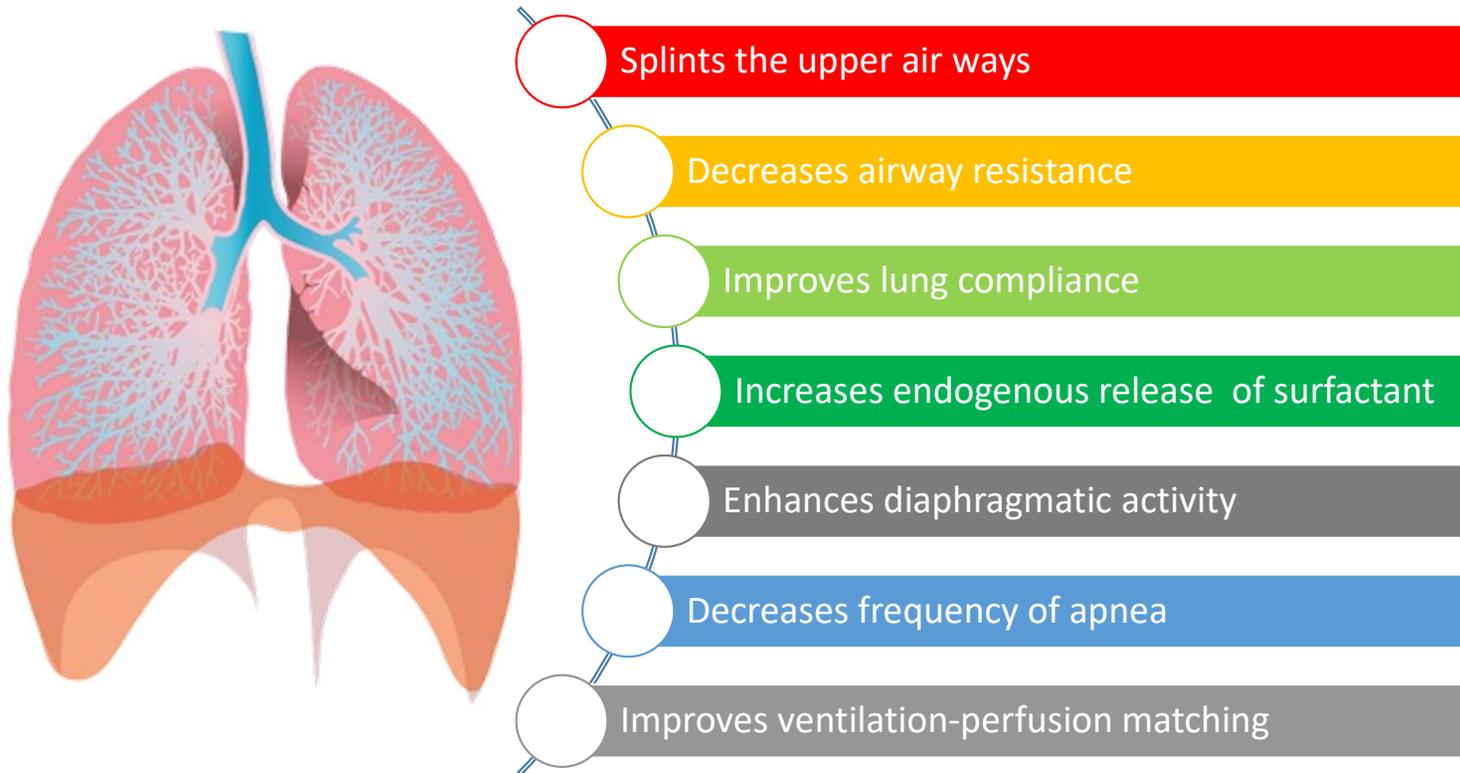
- Nasal-CPAP has become the mainstay of non-invasive respiratory support for preterm infants
- Reported benefits compared with mechanical ventilation include lower rates of combined death or CLD at 36 weeks' PMA
- Potential complications of nCPAP
 - Nasal trauma
 - Gastric distension
 - Pulmonary air leaks
 - Excessive secretions
 - Patient discomfort

• *Chowdhury O, et al. CPAP review. Eur J Pediatr 2012;171:1441-8*

• *Schmolzer GM, et al. Non-Invasive versus invasive respiratory support in preterm infants at birth: systematic review and meta-analysis. BMJ 2013;347:f5980*

• *Guimões AR, et al. Nasal CPAP complications in very low birth weight preterm infants. J Neonatal Perinatal Med 2019;13:197–206*

Physiological benefits of NCPAP



Introduction

- **Early weaning**

- Reduce these complications
- Utilization of resources
- Workload for staff

- **Too early weaning**

- Atelectrauma
- Increased frequency of apneas
- Increased work of breathing
- Increased oxygen use
- The need to put the infant back on nCPAP/ MV

- Despite the widespread use of nCPAP in NICUs, there is no consensus on when and how to wean preterm infants from nCPAP

- *Jardine LA, et al. Strategies for the withdrawal of NCPAP in preterm infants. Cochrane Database Syst Rev. 2011;(2):CD006979*
- *Abdel-Hady H, et al. Weaning preterm infants from CPAP: evidence for best practice. World J Pediatr 2015;11:212-8*

When to Wean from NCPAP ?

- It is generally considered appropriate to evaluate an infant's readiness to come off nCPAP when they are stable on a minimal end-expiratory pressure with no (or minimal) supplemental oxygen requirement
- Some neonatologists consider weaning the ELBW infants who have been on nCPAP since birth off nCPAP when they reach 32 wks PMA and at least 1200-1400 g in weight
- It is critical that a proactive weaning process is in place and followed
- The decision is often arbitrary, based on the 'judgment and experience' of the neonatologist

Criteria for Readiness-to-Wean from NCPAP

- nCPAP at a pressure of 3-6 cmH₂O for 24-48 h
- FiO₂ < 30% to keep SpO₂ ≥ 87% in the preceding 24 h
- No single apnea requiring bagging
- Not > 6 episodes of apnea requiring stimulation during the preceding 24 h
- < 3 episodes of self reverting apneas and/or desaturations in 1 h during the previous 6 h
- Respiratory rate < 60/min
- No significant chest recession
- Satisfactory arterial blood gases
- Hemodynamically stable
- Not currently treated for PDA or sepsis
- Hemoglobin level of ≥ 8 g/dl within 7 days
- Tolerates time off nCPAP during nursing cares (up to 15 min)

Criteria for readiness-to-wean from NCPAP

- Despite the use of these criteria, multiple trials have reported nCPAP-weaning failure rates exceeding 50%
- These failures to successfully wean infants from nCPAP suggest that currently used criteria to identify infants ready to wean from nCPAP are insufficient

- *Todd, D. A. et al. Methods of weaning preterm babies <30 weeks gestation off CPAP: a multicentre randomised controlled trial. ADC Child Fetal Neonatal Ed 2012;97: F236–40*
- *Rastogi, S. et al. Gradual versus sudden weaning from nasal CPAP in preterm infants: a pilot randomized controlled trial. Respir. Care 2013; 58:511–6*
- *Nair, V. et al. Effect of nCPAP cycling and continuous nCPAP on successful weaning: a randomized controlled trial. Indian J Pediatr 2015; 82:787–93*

Evolving Strategies

- Point of care lung ultrasound (POC-LUS)
- Oxygen saturation histograms
- Silverman-Andersen score
- Modified physiologic test
- Electromagnetic inductive plethysmography

Point-of-Care Lung Ultrasound (POC-LUS)

- Two studies evaluated the use of POC-LUS as a tool for weaning nCPAP in preterm infants
- A prospective study was performed to assess whether end-expiratory lung ultrasound severity score (expLUSsc) at day 3 of life, the second wk of life, and before weaning off nCPAP can predict the weaning readiness off nCPAP in preterm infants <33 weeks GA
- Also they evaluated the value of adding lung tidal recruitment (LTR) to expLUSsc to improve predictability
- A total of 148 studies were performed on 39 infants, of them 12 (31%) weaned off nCPAP from the first trial and 27 (69%) infants failed attempts off nCPAP

Point-of-Care Lung Ultrasound (POC-LUS)

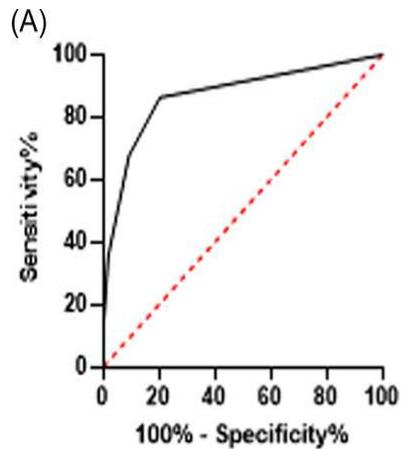
TABLE 2 Diagnostic test characteristics of expLUSsc and LTR for prediction of weaning readiness to nCPAP, at Day 3, the second week of life, and within 24 h before trial off nCPAP.

	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Day 3 of age						
expLUSsc > 6	0.38 (0.27, 0.57)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	0.63 (0.52, 0.760)	-	0.24 (0.09, 0.31)
expLUSsc > 10	0.87 (0.81, 0.95)	0.85 (0.79, 0.92)	0.81 (0.73, 0.89)	0.89 (0.84, 0.92)	4.94 (2.64, 8.83)	0.23 (0.15, 0.34)
The second week of life						
expLUSsc > 8	0.88 (0.82, 0.96)	0.90 (0.83, 0.96)	0.87 (0.78, 0.95)	0.92 (0.86, 0.98)	6.83 (2.62, 11.0)	0.10 (0.03, 0.16)
Within 24 h before trial off nCPAP trial						
expLUSsc > 8	0.88 (0.79, 0.94)	0.81 (0.72, 0.89)	0.82 (0.69, 0.86)	0.9 (0.85, 0.94)	4.33 (1.49, 5.7)	0.30 (0.15, 0.41)
expLUSsc > 8 plus LTR	0.95 (0.91, 0.97)	0.90 (0.87, 0.94)	0.88 (0.81, 0.92)	0.90 (0.84, 0.95)	5.37 (3.47, 7.79)	0.20 (0.13, 0.38)

Abbreviations: CI, confidence interval; LTR, lung tidal recruitment; nCPAP, nasal continuous positive airway pressure; expLUSsc, end-expiratory lung ultrasound severity score.

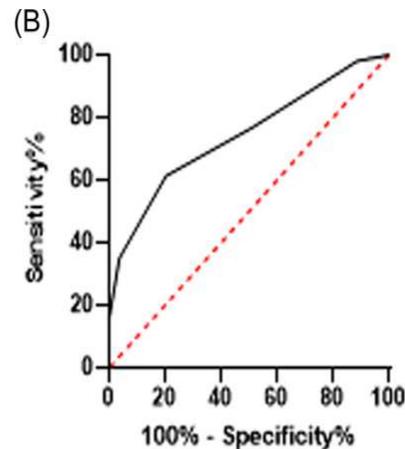
Point-of-Care Lung Ultrasound (POC-LUS)

AUC: 0.87



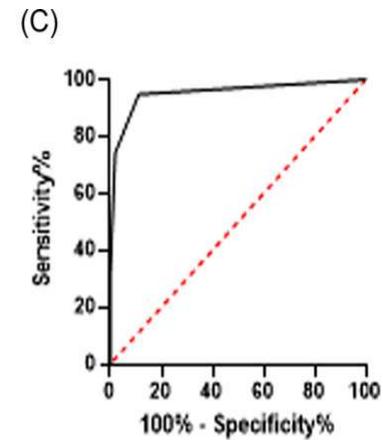
LUSsc

AUC: 0.65



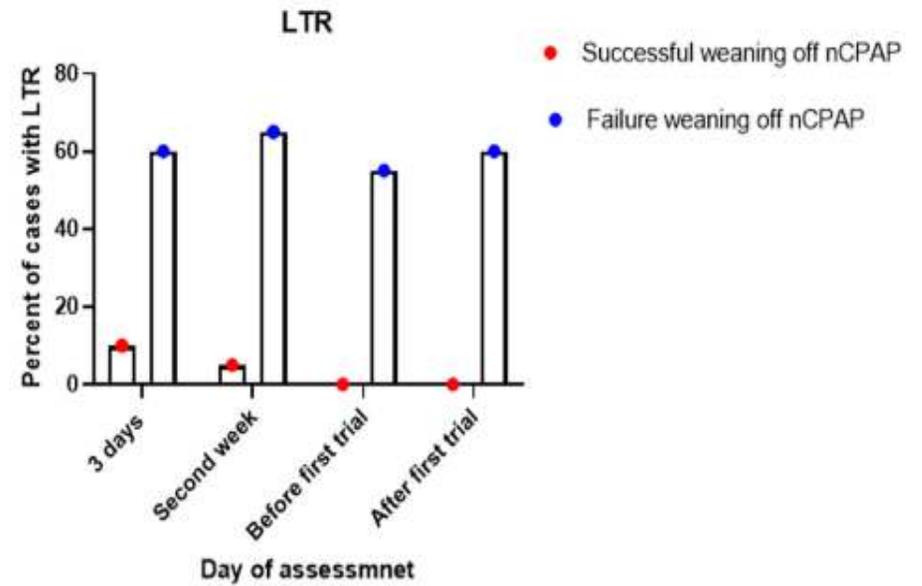
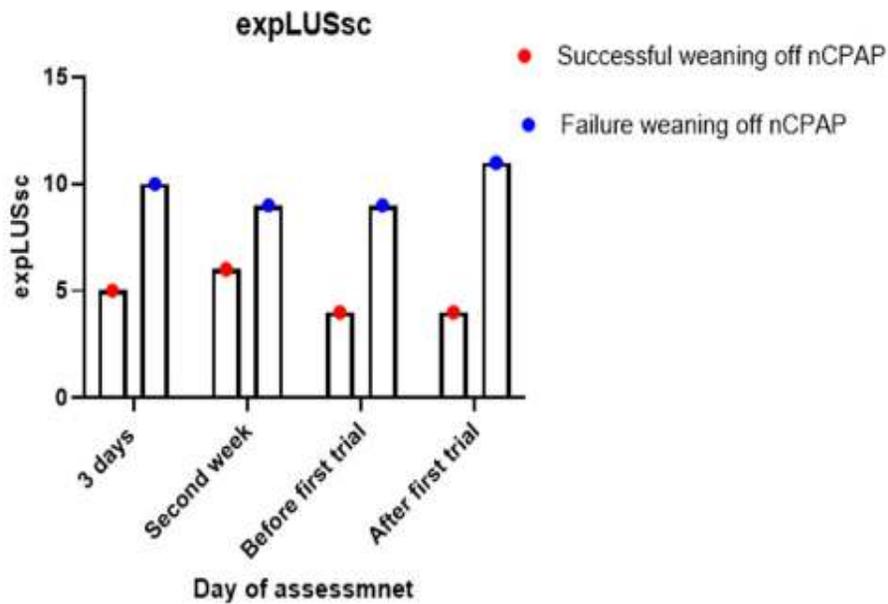
LTR

AUC: 0.95



LUSsc + LTR

Point-of-Care Lung Ultrasound (POC-LUS)



Point-of-Care Lung Ultrasound (POC-LUS)

- Our group performed a prospective cohort study on preterm infants who were considered ready for weaning off nCPAP
- Lung and diaphragm US were performed just before and 3 hs after weaning off nCPAP
- The objective was to:
 - Evaluate the accuracy of LUS and diaphragm US in predicting successful weaning from nCPAP
 - Ascertain the ability of LUS performed 3 hrs after discontinuation of nCPAP in detecting early signs of alveolar de-recruitment, as indicated by changes in LUS score, and increased diaphragmatic activity
- Out of 65 enrolled preterm infants, 30 (46.2%) were successfully weaned from nCPAP to room air

Point-of-Care Lung Ultrasound (POC-LUS)

- Full data will be available on Pediatric Pulmonology soon

Oxygen Saturation Histograms

- Two observational studies evaluated the value of oxygen saturation histogram in predicting nCPAP weaning success
- The first study included 31 infants, 24 –32 weeks gestational age
- They hypothesized that infants with > 15% of time spent with SpO₂ <86% before transitioning from CPAP or HFNC to LFNC, oxyhood, or room air are more likely to fail transitioning
- The SpO₂ histograms were downloaded daily before transition from nCPAP or HFNC to LFNC, oxyhood, or room air and continued for each infant for 1 week after transition or when the infant reached 36 wks PMA

Oxygen Saturation Histograms

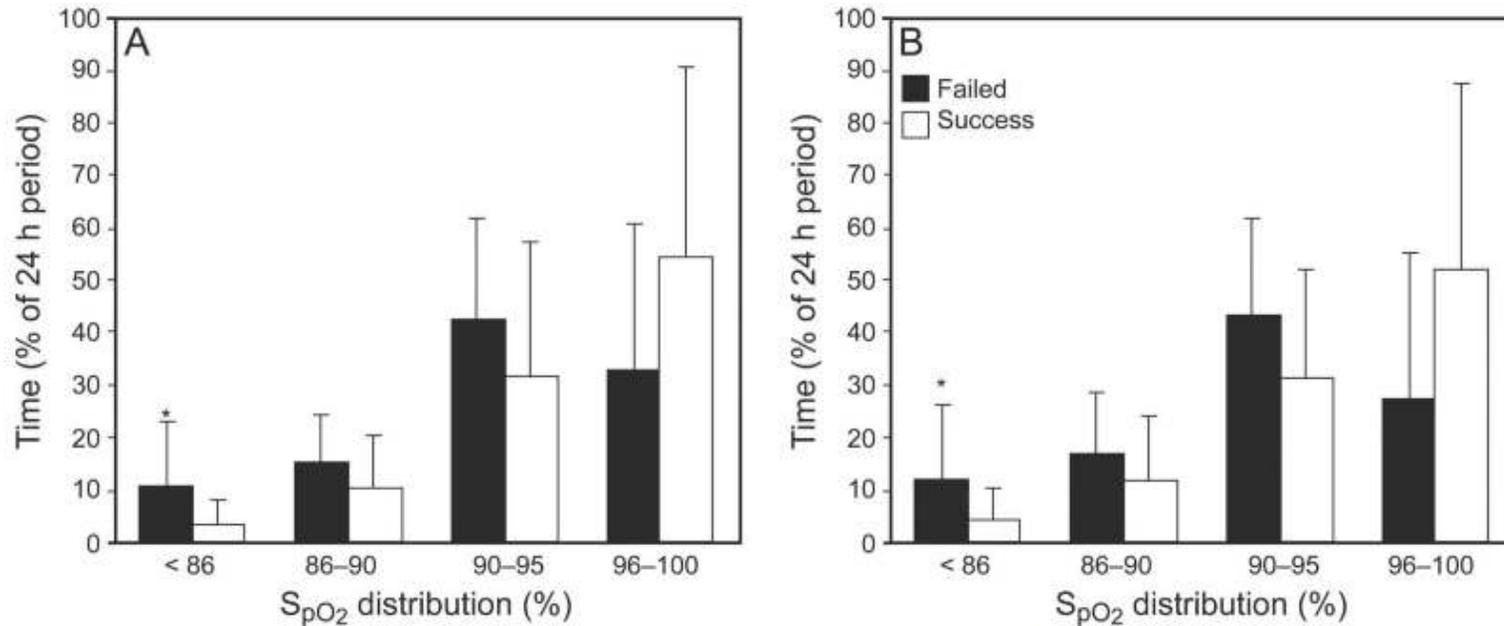


Fig. 2. Comparison of S_{pO_2} histogram distribution pre-transition (A) and post-transition (B) between successful and failed transition groups. S_{pO_2} histogram was recorded for the 24-h periods pre- and post-transition from either CPAP or high-frequency nasal cannula to low-frequency nasal cannula or room air. Data are expressed as mean \pm SD. * $P < .05$.

Oxygen Saturation Histograms

- The second study, a single-center-matched case–control study in 36 infants ≤ 30 weeks' gestation receiving $\leq 30\%$ FiO₂ weaned off CPAP during the first postnatal week
- Cases were infants placed back on CPAP within 7 days of being taken off CPAP
- Control infants remained off CPAP for 7 days following CPAP discontinuation
- Infants were matched on gestational age at birth (± 10 days)
- Prospectively collected histograms detailing the distribution of oxygen saturations prior to CPAP discontinuation were compared between cases and controls

Oxygen Saturation Histograms

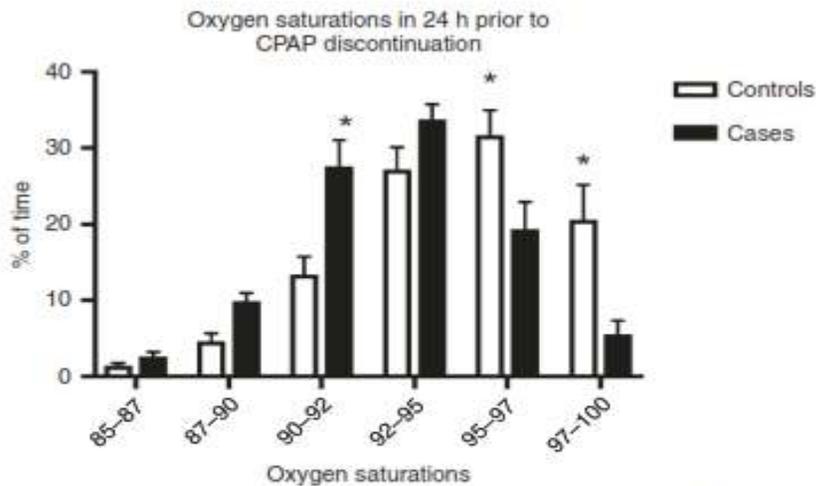


Fig. 2 Achieved oxygen saturations in cases and controls in the 24 h prior to CPAP discontinuation. Controls infants achieved saturations 95–97 and 97–100% for a greater percentage of time than cases. Data represent mean \pm standard error of mean. Analysis performed using two-way ANOVA with Sidak's multiple comparisons test.

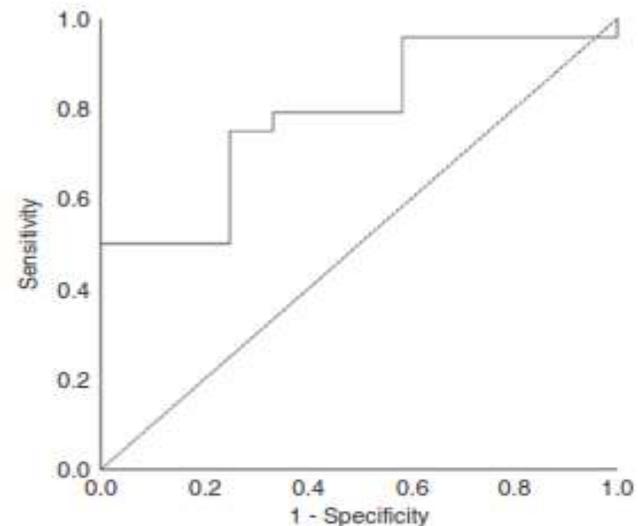


Fig. 3 The area under the curve for oxygen saturation achievement >95% was 0.79 (95% CI, 0.63–0.94). Using a value of 31.6%, the sensitivity and specificity for predicting CPAP-weaning success were 75% and 75%, respectively.

Silverman-Andersen Score (SAS)

- A recent study investigated the factors that steer weaning from NIV and whether the inclusion of the SAS would lead to more stringent weaning
- Following SAS implementation, they prospectively evaluated 33 neonates born < 32 wks GA
- Control group: age-, weight- and sex-matched infants born before routine SAS evaluation
- In 173 of 575 patient days, NIV was not weaned despite little respiratory distress (SAS ≤ 2), mainly due to bradycardias (60% of days without weaning), occurring alone (40%) or in combination with other factors such as apnea/desaturations
- “soft factors” impact on weaning decisions, whereas the SAS overall played a minor role

Modified Physiologic Test

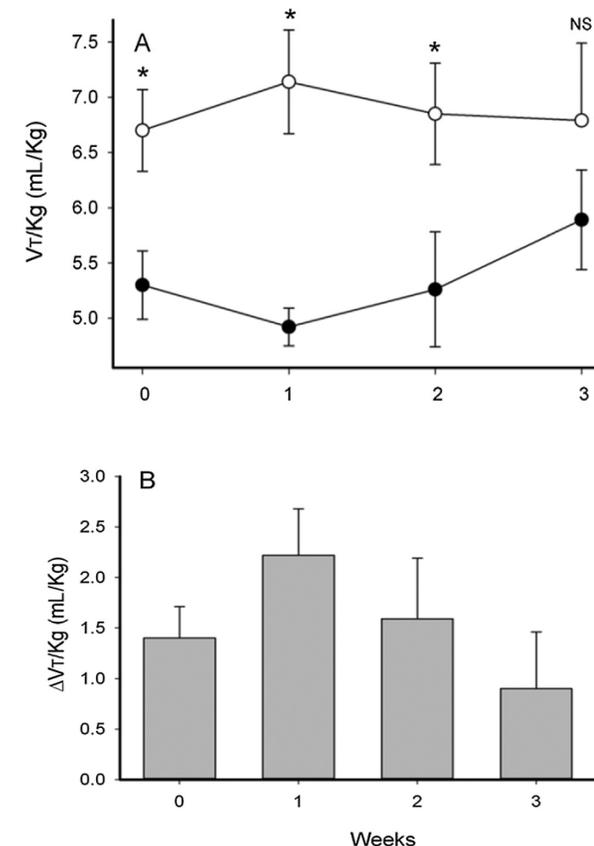
- A study was done to verify if a physiologic test, modified respect to that developed by Walsh et al. for estimating BPD rate, can be used as a clinical tool for weaning the premature babies ≤ 32 weeks GA from CPAP and/or oxygen therapy
- Six of 26% tested babies passed the challenge at 28 days of life, 40% tested babies passed the challenge at 36 weeks
- Median values of SpO₂ were significantly higher in the neonates passing the test, respect to the failing patients
- At the same time median values of TcPCO₂ were significantly higher in the failing patients

• Walsh MC, et al. *Impact of a physiologic definition on bronchopulmonary dysplasia rates. Pediatrics. 2004 ;114:1305-11*

• Vento G et al. *A modified physiologic test for BPD: a clinical tool for weaning from CPAP and/or oxygen therapy the premature babies? Ital J Pediatr 2019;45:2-7*

Electromagnetic Inductive Plethysmography “EIP”

- Tidal breathing was measured using EIP in 29 preterm infants (GA 28 ± 2 wks) receiving nCPAP
- The reduction in VT/kg and MV/kg when on nCPAP is probably due to a reduction in dead space ventilation attributable to establishment of a satisfactory FRC capacity leading to decreased work of breathing, whereas there was increased work of breathing without nCPAP
- Serial tidal breathing measurements showed decreasing difference for VT/kg over time on and off nCPAP indicating that it is useful objective tool to guide weaning from nCPAP



CPAP Weaning Failure Criteria

- Increased FiO₂ above baseline by $\geq 10\%$ - 15%
- Decreased SpO₂ <87% despite increasing FiO₂ to a maximum of 60%
- Increased oxygen requirements >25% to maintain SpO₂ >86%
- One apneic episode requiring either moderate stimulation or PPV
- > one self-correcting apneic episode/h or > 6 apnea requiring stimulation/24h
- Increased work of breathing
 - Respiratory rate >70 BPM
 - Use of accessory respiratory muscles
 - Expiratory grunting
 - A score of 6-10 on the Silverman-Anderson Respiratory Scale
- PaCO₂ > 60 mmHg, pH <7.2

Factors Influencing NCPAP weaning

Non-modifiable	Modifiable
Gestational age	Intubation
Birth weight	Caffeine
	PDA
	GERD
	Chorioamnionitis
	Anemia
	Apnea
	IVH
	Sepsis/NEC

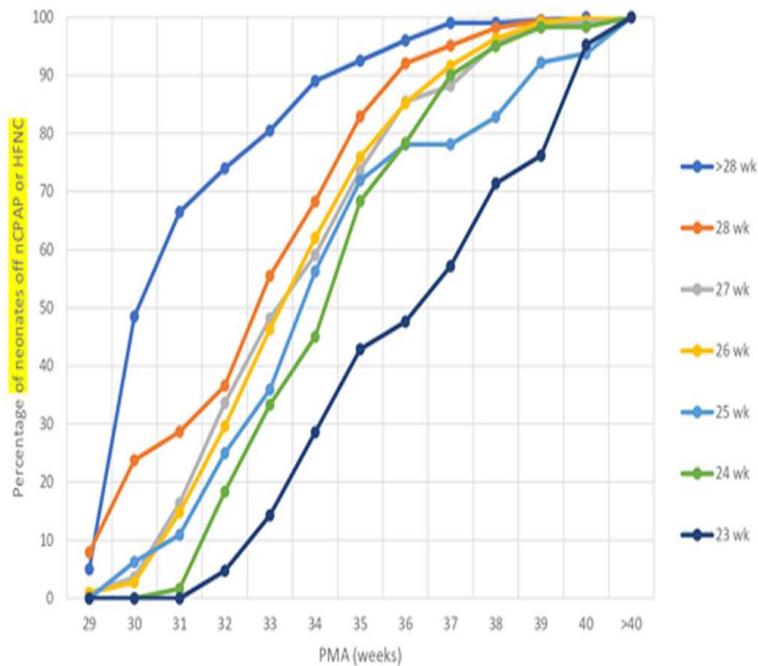
Factors Influencing NCPAP weaning

- A retrospective study to identify clinical variables that could affect successful weaning from nCPAP in very preterm infants <32 weeks
- In the univariate analysis
 - GA, birth weight, BW z-score at the time of successful nCPAP weaning, intubation, total duration of intubation, RDS grade, APGAR score at the 1 and 5 min, initial shock, anemia, BPD, number of blood transfusions, total duration of dopamine use, administration of more than two doses of surfactant, use of aminophylline, use of a diuretic, and total duration of TPN
- Multivariate analysis
 - Total duration of intubation, BPD, and administration of > 2 doses of surfactant
- A reverse association was noted between BW z-score and PMA at the time of successful nCPAP weaning

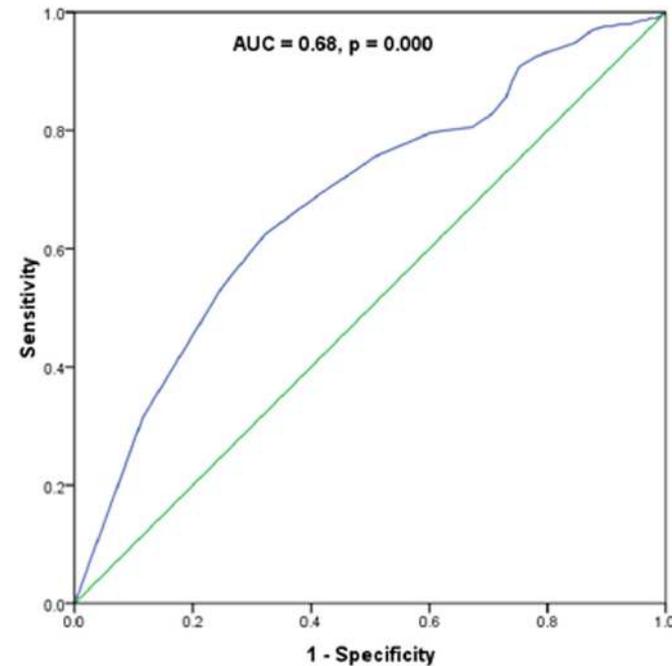
Factors Influencing NCPAP weaning

- A retrospective cohort study of 727 infants ≤ 29 weeks' gestation who required nCPAP for >24
- Infants who were successful in their first trial off nCPAP ($n = 313$) were of higher GA and BW, as well as a higher proportion of female infants
- When stratified by GA, a negative correlation was noted between GA and PMA at successful trial off nCPAP or HFNC
- Logistic regression analysis showed that GA and percentage of time spent with an oxygen saturation over 89% in the 24 h preceding the trial off nCPAP were independent predictors for successful trial off nCPAP

Factors Influencing NCPAP weaning



Proportion of neonates off nCPAP of HFNC by GA (weeks)



SpO₂ histogram for infants spent >90% of the time in a SpO₂ of >89% in the 24 h preceding the first trial off nCPAP

Mohsen N et al. Predictors of successful trial off continuous positive airway pressure and high flow nasal cannula in preterm infants <30 weeks' gestation: A retrospective study. *Peidatr Pulmonol* 2022, 57:1000-7

How to wean from NCPAP?

1. Sudden weaning of nCPAP
2. Gradual wean of nCPAP pressure
3. Graded-time-off nCPAP “nCPAP cycling”
4. Weaning to HHHFNC (nHFT)
5. Weaning to LFNC
6. Combinations of the above methods

How to wean from NCPAP?

- There is few data on the best way to wean from nCPAP
- **A survey CPAP among 857 neonatologists from the AAP Neonatal-Perinatal section¹:**
 - 69% use specific respiratory stability criteria
 - 22% a specific PMA
 - 64% did not have guidelines for nCPAP discontinuation
- **A survey of 58 NICUs in the North of England²:**
 - Lack of consensus, with only 6% having a written protocol
 - Variability in the methods:
 - The majority (66%) weaned by 'time off'
 - 4% by weaning pressure
- **A survey involving 124 neonatologists in Australia³:**
 - 71% of neonatologists reported using a graded-time-off nCPAP
 - 74% used gradually decreased airway pressure prior to coming off nCPAP
 - Substantial inter-institutional and inter-provider variability

1. Mamidi, RR, et al. Nasal continuous positive airway pressure practices in preterm infants: A survey of neonatal providers. *J Neonat-Perinat Med* 2023;16:611-7
2. Bowe L, Clarke P. Current use of nasal CPAP in neonates. *ADC Fetal Neonatal Ed* 2005;90:F92-3
3. Jardine L, Davies MW. Withdrawal of neonatal continuous positive airway pressure: current practice in Australia. *Pediatr Int* 2008;50:572-5

How to wean?

- Multiple studies showed conflicting results
- Small sample size
- Methodological issues

Pressure vs. Time weaning

- A meta-analysis including 3 RCTs concluded that graded-time-off strategy significantly increased the total time on nCPAP as well as the durations of oxygen therapy and hospital stay

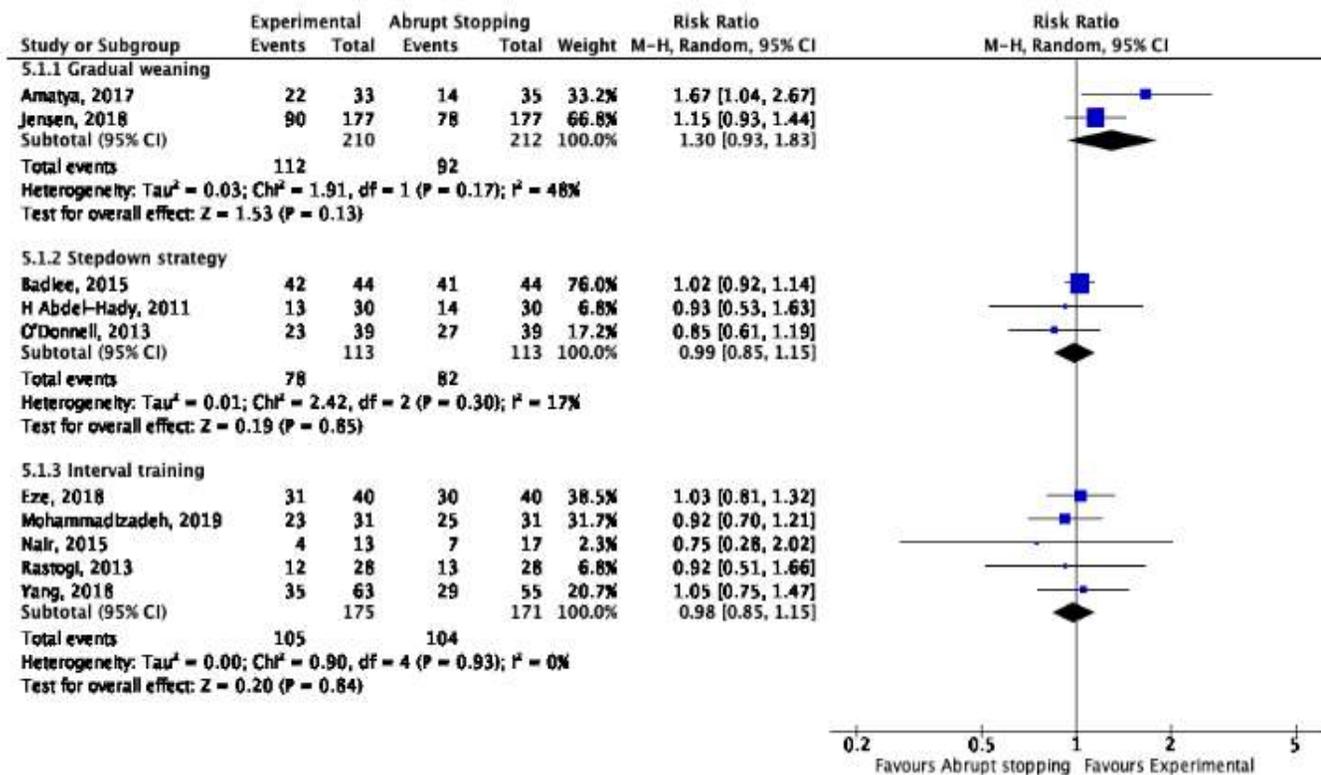


How to wean?

- A systematic review to determine the most effective strategy for weaning preterm infants from non-invasive respiratory support included 15 trials (1.547 infants)
- Gradual weaning of airway pressure might increase the chances of successful weaning
- Stepping down from CPAP to HFNC shortens the duration of CPAP treatment but is associated with a longer duration of oxygen administration
- No major benefits were found for a weaning strategy based on interval training (cycling)
- None of the weaning strategies had any effect on the development of CLD
- NICUs should make their own specific weaning protocol with prespecified readiness-to-wean criteria and provide adequate training for nursing staff

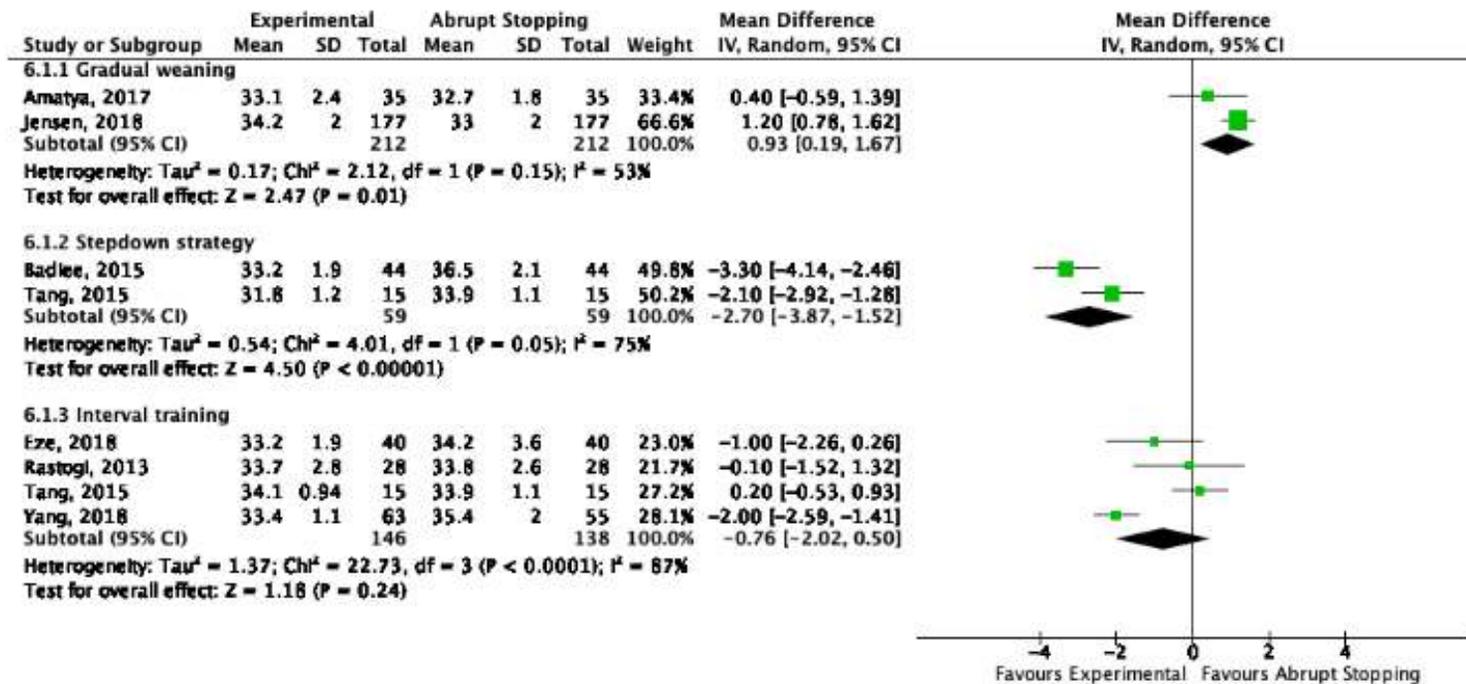
Van Delft B, et al. Weaning strategies for the withdrawal of non- invasive respiratory support applying CPAP in preterm infants: a systematic review and meta-analysis. BMJ Paediatrics Open 2020;4:e000858

Successful weaning at the first weaning trial (gradual weaning, stepdown strategy and interval training vs abrupt stopping)



van Delft B, et al. Weaning strategies for the withdrawal of non- invasive respiratory support applying CPAP in preterm infants: a systematic review and meta-analysis. *BMJ Paediatrics Open* 2020;4:e000858

PMA in weeks at the first successful weaning trial (gradual weaning, stepdown strategy and interval training vs abrupt stopping)



van Delft B, et al. Weaning strategies for the withdrawal of non-invasive respiratory support applying CPAP in preterm infants: a systematic review and meta-analysis. *BMJ Paediatrics Open* 2020;4:e000858

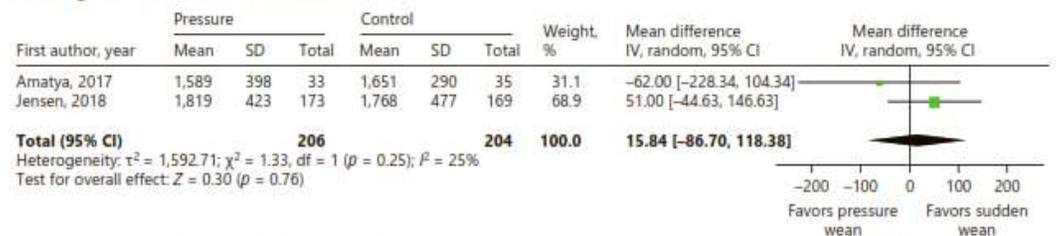
How to wean?

- A systematic review compared the success of progressive pressure wean versus sudden wean for discontinuation of nCPAP in preterm infants
- Included two RCTs (422 infants)
- Concluded that sudden wean of nCPAP was associated with:
 - A lower PMA at successful wean
 - A lower rate of successful wean at first attempt

a Postmenstrual age at successful NCPAP wean



b Weight at successful NCPAP wean



c Success of weaning strategy at first attempt



Weaning to HHHFNC (nHFT)

- Weaning preterm infants from NCPAP to HHHFNC is a common practice in many NICUs, although there is insufficient evidence to establish the safety or effectiveness of HHHFNC in preterm infants
- HHHFNC:
 - Perceived by health care givers and parents as gentler way to deliver CPAP
 - Relatively easy to apply
 - Improves patient comfort
 - Cause less nasal trauma
 - Allows greater access to the baby's face, thus improving developmental care

- *Hong H, et al. High-flow nasal cannula versus nCPAP for respiratory support in preterm infants: a meta-analysis of randomized controlled trials. J Matern Fetal Neonatal Med. 2021;34:259-66*
- *Ramaswamy VV, et al. Non-invasive ventilation in neonates: a review of current literature. Front Pediatr. 2023;11:1248836.*

Weaning to HHHFNC (nHFT)

- Several RCTs have assessed the role of nHFT, in weaning preterm infants from nCPAP, with conflicting results
- Three RCTs found that nHFT use contributed to shorter time on nCPAP without reducing the overall duration of non-invasive support¹⁻³
- One RCT found that the use of nHF 2 L/min to wean from CPAP resulted in more days on oxygen and respiratory support³
- Another study found that nHF 2 L/min reduced the duration of supplemental oxygen and hospital stay but did not increase successful weaning from CPAP⁴

1. Soonsawad S, et al. Heated humidified high-flow nasal cannula for weaning from CPAP in preterm infants: a randomized controlled trial. *Neonatology* 2016 110:204–209
2. Fernandez-Alvarez JR, et al. Heated humidified high-flow nasal cannula versus low-flow nasal cannula as weaning mode from nasal CPAP in infants >528 weeks of gestation. *Eur J Pediatr* 2014;73:93–98
3. Abdel-Hady H, et al. Early weaning from CPAP to high flow nasal cannula in preterm infants is associated with prolonged oxygen requirement: a randomized controlled trial. *Early Hum Dev* 2011;87:205–208
4. Badiie Z, et al. High flow nasal cannula as a method for rapid weaning from nasal CPAP. *Int J Prev Med* 2015;6:33

Weaning to HHHFNC (nHFT)

- **CHiPS study:** Single-centre, non-inferiority, RCT to determine whether weaning from nCPAP using nHF
- 120 preterm infants, <30 weeks' GA, stable on nCPAP for at least 48 hours
- Infants underwent stratified randomization to HF 6 L/min or bubble CPAP 6 cm water
- In both groups, stepwise weaning of their respiratory support over 96 hours according to a strict weaning protocol was carried out
- nHF weaning was non-inferior to nCPAP weaning
- There was no significant difference in time to discharge

Clements J, et al. A randomized trial comparing weaning from CPAP alone with weaning using HHHFNC in very preterm infants: the CHiPS study. Arch Dis Child Fetal Neonatal Ed 2023;108:F63–8

Weaning to HHHFNC (nHFT)

- A retrospective matched-pair case-control study of 70 infants ≤ 28 weeks GA found that Optiflow[®] and Vapotherm[®] seem to be equally effective and safe for weaning from nCPAP
- However, infants weaned to Vapotherm[®] were found to spend less time on HHHFNC and overall non-invasive respiratory support despite spending more time on nCPAP before changing to HHHFNC



Weaning to LFNC

- Many NICUs use LFNC to wean infants from nCPAP
- A RCT “*NOFLO Trial*” included 87 VLBW infants did not demonstrate any benefit in the use of LFNC air in weaning from nCPAP compared with spontaneous breathing
- Todd et al. have shown that preterm infants who were cycled off nCPAP with the use of LFNC required a prolonged duration of nCPAP compared with infants who were taken off nCPAP directly
- Fernandez-Alvarez et al. have demonstrated that weaning preterm infants to HHHFNC shortened the time on nCPAP by 50% whilst reducing the risk of nasal trauma and maintaining the same risk for BPD compared to weaning to LFNC

- *O'Donnell SM, et al. The NOFLO trial: low-flow nasal prongs therapy in weaning nasal CPAP in preterm infants. J Pediatr 2013;163:79-83*
- *Todd DA, et al. Methods of weaning preterm babies <30 weeks gestation off CPAP: a multicentre RCT. ADC Fetal Neonatal Ed 2012;97:F236-40*
- *Fernandez-Alvarez JR, et al. HHHFNC versus LFNC as weaning mode from nasal CPAP in infants ≤28 weeks of gestation. Eur J Pediatr 2014;73:93–98*

Conclusions

- Determining the optimal time and best strategy for successful weaning from nCPAP in preterm infants is crucial to reduce unwarranted complications and costs
- There is no consensus on defining the optimal timing and methods for weaning
- Readiness- to- wean should be assessed in a very consistent way
- New tools can help in decision making e.g. POC-LUS, oxygen saturation histograms

Conclusions

- Gradual weaning of airway pressure might increase the chances of successful weaning, however, it is associated with a higher PMA at successful wean compared to abrupt discontinuation
- The practice of “CPAP-cycling” has been shown to be associated with worse outcomes, and better be avoided
- Stepping down from CPAP to HFNC shortens the duration of CPAP treatment but is associated with a longer duration of oxygen administration
- There is no benefit in the use of LFNC air in weaning from nCPAP
- It is important that each NICU develops its own specific weaning protocol and invests in adequate training of nursing staff

Thank You

