Received: 12 July 2022 | Accepted: 2 November 2022

DOI: 10.1002/ppul.26229

ORIGINAL ARTICLE

PEDIATRIC PULMONOLOGY WILEY

Tidal volume optimization and heart rate response during stabilization of very preterm infants

Francesco Cavigioli MD[1] | Ilia Bresesti MD[1,2] | Antonio Di Peri MD[1] | Francesco Cerritelli MD, PhD[3] | Diego Gazzolo MD, PhD[4] | Antonio W. D. Gavilanes MD, PhD[5] | Boris Kramer MD, PhD[5] | Arjan te Pas MD, PhD[6] | Gianluca Lista MD, PhD[1]

[1]NICU "V. Buzzi" Children's Hospital, ASST-FBF-Sacco, Milan, Italy

[2]Department of Medicine and Surgery, University of Insubria, Varese, Italy

[3]Foundation COME Collaboration, Pescara, Italy

[4]Neonatal Intensive Care Unit, "G. D'Annunzio" University, Chieti, Italy

[5]Department of Pediatrics, School for Oncology and Developmental Biology (GROW), Maastricht University Medical Center, Maastricht, The Netherlands

[6]Division of Neonatology, Leiden University Medical Centre, Leiden, The Netherlands

Correspondence

Ilia Bresesti, MD, Department of Woman and Child, "Filippo del Ponte" Hospital, Via F. del Ponte 19, 21100 Varese, Italy.
Email: ilia.bresesti@uninsubria.it

Abstract

Aim: To verify the added value of respiratory function monitor (RFM) to assess ventilation and the heart rate (HR) changes during stabilization of preterm infants.

Methods: Preterm infants <32 weeks' gestation, bradycardic at birth and in need for positive pressure ventilation (PPV) were included. The first 15 min of stabilization was monitored with RFM. Three time points were identified according to HR values (T0 the start of mask PPV; T1 the HR rise >100 bpm; T2 the delivery of the last PPV). For each inflation, PIP, PEEP, MAP, expired tidal volume/kg (Vte/kg), and mean dynamic compliance (Cdyn) were analyzed.

Results: PIP and MAP values were significantly higher at T1 (27.09 ± 5.37 and 17.47 ± 3.85 cmH_2O) and at T2 (24.7 ± 3.86 and 15.2 ± 3.78 cmH_2O) compared to T0 (24.05 ± 2.27 and 15.85 ± 2.77 cmH_2O). PEEP at T1 was significantly higher (6.27 ± 2.17 cmH_2O) compared to T2 (5.61 ± 1.50 cmH_2O). Vte/kg showed significantly lower T0 values (3.57 ± 2.14 ml/kg) compared to T1 (6.18 ± 2.51 ml/kg) and T2 (6.89 ± 2.40 ml/kg). There was a significant effect of time on Cdyn.

Conclusions: A clear correspondence between HR rise and adequate Vte/kg during stabilization of very preterm infants was highlighted. RFM might be useful to tailor ventilation, following real-time changes of lung compliance.

KEYWORDS

bradycardia, positive pressure ventilation, preterm infants, respiratory function monitor, stabilization

1 | INTRODUCTION

During the fetal-neonatal transition of preterm infants, achieving adequate lung aeration and effective functional residual capacity (FRC) is crucial to promote stable heart rate (HR) rise, circulation recovery, and proper tissue oxygenation.[1] The latest recommendations for respiratory support at birth in preterm infants advocate continuous positive airway pressure (CPAP) in those showing effective spontaneous respiratory drive.[2] In case of absence or inadequate respiratory effort and/or persistent bradycardia, an initial

Abbreviations: Cdyn, dynamic compliance; CPAP, continuous positive airway pressure; DR, delivery room; FRC, functional residual capacity; GA, gestational age; HR, heart rate; MAP, mean airway pressure; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; PPV, positive pressure ventilation; RFM, respiratory function monitor; SpO_2, peripheral oxygen saturation; Vte, expired tidal volume.

Francesco Cavigioli and Ilia Bresesti contributed equally to this study.

attempt with mask positive pressure ventilation (PPV) is recommended before endotracheal intubation.[2] Although the widespread use of antenatal steroids to promote lung maturation in babies at risk for preterm birth,[3] the gestational age (GA) and the birth weight are inversely proportional to the need for respiratory support immediately after birth.[4] Noteworthy, the more the prematurity, the more the vulnerability to inappropriate pressure and volume provision.[5,6] Avoiding prolonged bradycardia at birth and providing adequate tidal volume delivery seems crucial for a safe neonatal transition to extra-uterine life.[7–9]

Monitoring the fetal-neonatal transition has been performed through different devices, analyzing the various changes characterizing this phase.[10,11] Among these tools, respiratory function monitor (RFM) can measure almost in real time, calculate and display inflation pressures, flow, and tidal volumes delivered during resuscitation. To date, there is a lack of robust evidence supporting the routine use of RFM in the delivery room (DR).[11] However, it has been suggested as an additional tool to optimize interventions at birth.[12–14] We therefore hypothesized that RFM can be used to assess ventilation and to associate HR changes to test the added value of RFM over standard resuscitation guidelines.

2 | METHODS

This is a retrospective, cross-sectional study conducted at the tertiary neonatal unit "V. Buzzi" Children's Hospital, Milan, Italy. We analyzed inborn infants <32 weeks' GA who were bradycardic at birth, received mask PPV during initial DR stabilization, and had complete video and RFM files (Figure 1). Infants with major congenital anomalies, intubated in the DR, or receiving surfactant during resuscitation were excluded. Those babies enrolled in the MONITOR trial (NCT 03256578) and randomized to RFM not visible were excluded from the analysis as well. The sample size was the one available, being this study a secondary analysis of previous cohorts. All resuscitations were recorded by a standard video recording setup. All DR resuscitations analyzed in this study were led by an attending neonatologist and recordings of the RFM were available to the resuscitation team. The use of RFM during resuscitation was

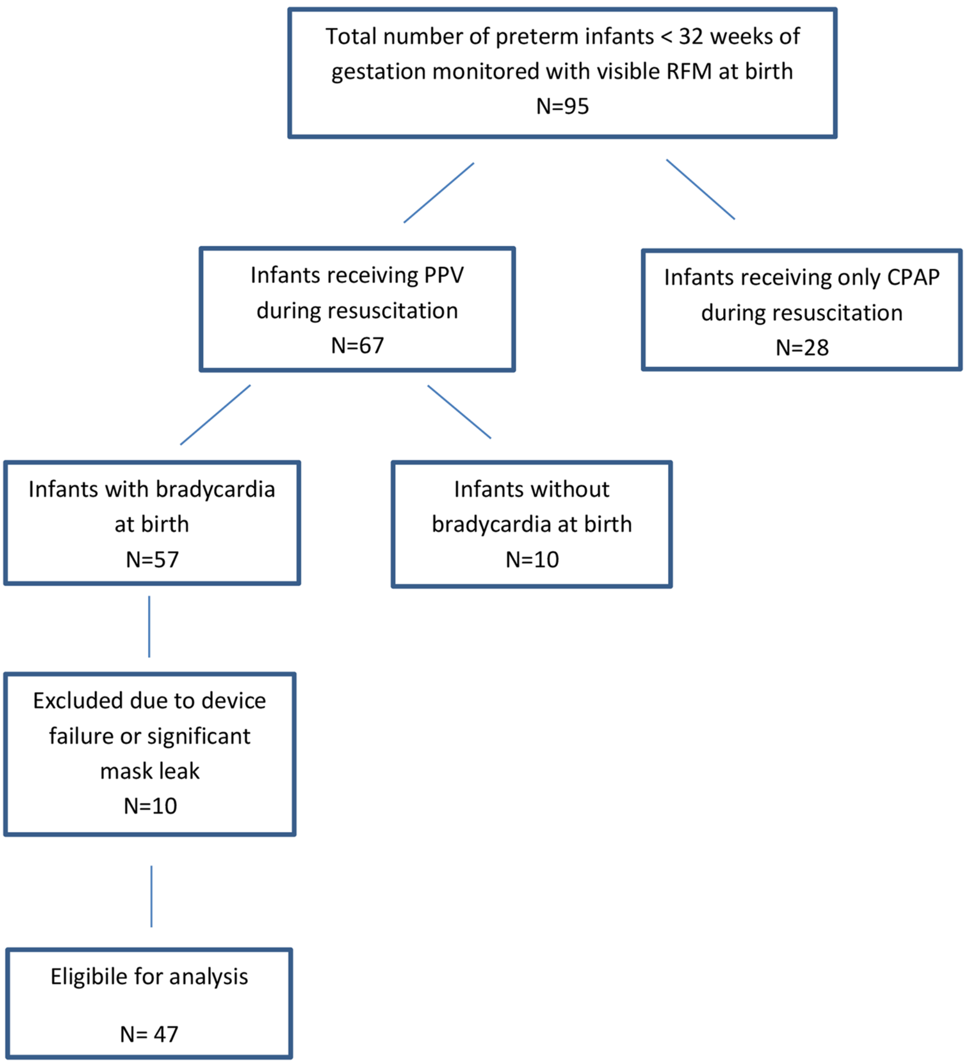

FIGURE 1 Flow-chart for patients' selection process

approved by our local IRB and consent was obtained for the analysis of RFM traces, recordings, and videos for research purposes.

As per contemporary ERC guidelines, the initial fraction of inspired oxygen (FiO_2) was set at 0.21 and then titrated to maintain peripheral oxygen saturation (SpO_2) between 25° and 50° percentile of standard ranges.[15] PEEP was set at 5–6 cmH_2O and initial PIP at 25 mmHg. During resuscitation, PIP was adjusted according to Vt, to maintain it within 4–8 ml/kg. When Vt was <4 ml/kg, PIP was increased by 2 cmH_2O every 30 s. On the other side, if Vt was >8 ml/kg, PIP was decreased with the same criteria. For DR respiratory support, a T-piece resuscitator (Neo Puff, Fisher & Paykel) was used and connected to a face mask (Hudson RCI, 40 mm neonatal air cushion). The flow and pressure sensors (AveaVaerflex flow transducer; CareFusion) of the RFM (New Life Box; Neo-RSD; Advanced Life diagnostics UG) were placed between the T-piece and the face mask. Peripheral oxygen saturation and HR were measured by a Masimo Radical 7 Pulse-Oximeter (Masimo Corporation). The pulse oximeter sensor was positioned on the baby's right wrist immediately after placement on the resuscitation table. Bradycardia was initially assessed using the stethoscope and later confirmed by the values of the pulse oximeter. FiO_2 delivered was measured by Teledyne AX 300 oximeter (Teledyne Technologies Company) and recorded. Recordings were retrospectively analyzed using Pulmochart® software (Applied Biosignal GmbH). Video recordings were reviewed by trained physicians matching respective ventilatory traces. The first 15 min after birth were analyzed. Three different time points were identified based on the resuscitation procedures and clinical response, as shown in Figure 2. T0 was defined by the start of mask PPV administration; T1 marked the time point of HR rise to stable values >100 bpm; T2 identified when the last PPV was delivered, immediately before CPAP initiation in infants showing good spontaneous respiratory effort or until the end of the recording in infants still requiring PPV after 15 min after birth. At each time point (T0, T1, and T2), 10 mask inflations per patient were analyzed. For each inflation, Peak Inspiratory Pressure (PIP), Positive End Expiratory Pressure (PEEP), Mean Airway Pressure (MAP), and expired tidal volume/kg (Vte/kg) were analyzed.

Leak (%) was calculated using the formula ([Vti − Vte]/Vti) × 100, and we included in the analysis only breaths where leak = 0. Mean dynamic compliance (Cdyn) for each period was also calculated based on Δ pressures and Vte administered.

2.1 | Statistical analysis

Data were analyzed using the R statistical program V 3.5.3 (R Foundation) and described using mean, median, standard deviation (SD), interquartile range (IQR), frequency, percentage, and range. One-way repeated measure ANOVA (rmANOVA) was used to explore differences among time points (T0–T1–T2). Tukey post hoc test was used to explore any possible difference resulted from rmANOVA. A p-value < 0.05 was considered statistically significant.

3 | RESULTS

Ninety-five infants <32 weeks of GA were recorded with visible RFM during DR stabilization. Forty-eight were excluded from the analysis due to equipment failure, no bradycardia, or no need for PPV. A total of 47 neonates were included in the final analysis (Figure 1).

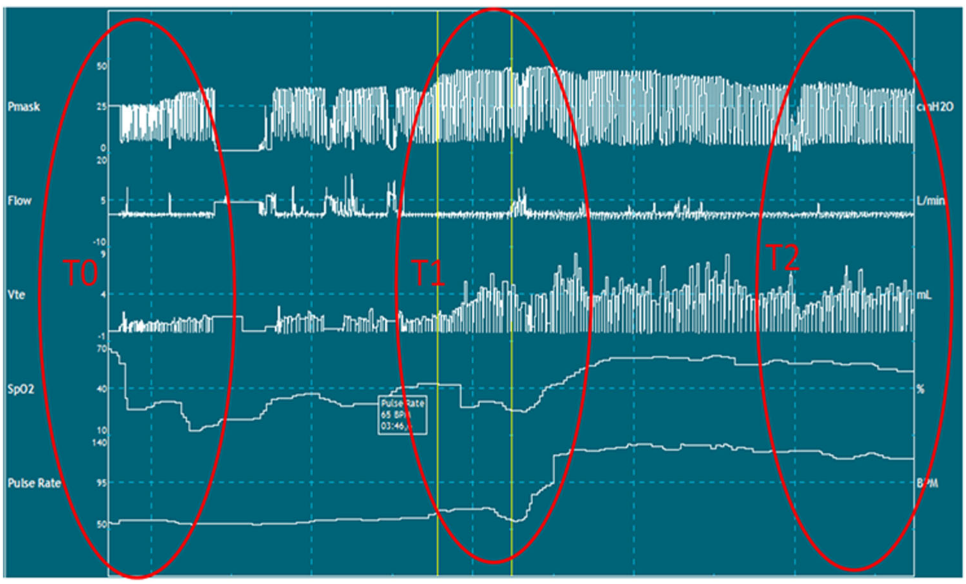

FIGURE 2 Representative monitor screenshot. Signals recorded by RFM during DR stabilization of a preterm infant: Pmask is the signal of pressures delivered during mask PPV; flow signal, expired tidal volume calculation (Vte), peripheral oxygen saturation (SpO_2), and heart rate (HR) were simultaneously recorded. The HR and SpO_2 rise in this figure were clearly correlated with PIP (T1) increase during mask PPV, with subsequent increase in Vte (original figure created by authors from the unit's RFM recordings). DR, delivery room; PIP, peak inspiratory pressure; PPV, positive pressure ventilation; RFM, respiratory function monitor; SpO2, peripheral oxygen saturation.

Mean GA (SD) was 27^{+3} weeks ±11 days, and mean weight (SD) was 894.9 ± 108.4 g. Sixteen (34%) were female. Thirty-nine infants (82%) were born via cesarean section, and 44 (93%) received antenatal steroids. Nine infants (19%) were intubated in the DR, 15 (31%) received mechanical ventilation within 72 h after birth. Surfactant replacement therapy (200 mg/kg, Curosurf® Chiesi Farmaceutici) was administered in NICU in 32 neonates (68%). No adverse events like air leak syndrome or IVH > grade 2 within 48 h after birth were reported.

Characteristics of main parameters and time points are described in Table 1.

A total of 1410 inflations were individually analyzed.

There was a significant effect of time on PIP ($F_{(2,42)}$: 9.53, $p < 0.001$) and on MAP ($F_{(2,42)}$: 10.39, $p < 0.001$). As shown in Table 2 and Figure 2, the cohort of preterm infants showed an increase in both parameters when HR reached 100 bpm onward (T1), and then they witnessed a progressive reduction until the PPV was discontinued (T2).

To further explore the detected intra-group differences among the specific time points, Tukey post hoc analyses were performed. As illustrated in Table 2, there were significant differences between the individual time points ($p < 0.01$). Indeed, PIP and MAP values were significantly higher at T1 than at T0 (PIP: $t_{(46)}$: 4.225, $p < 0.01$; MAP: $t_{(46)}$: 3.169, $p < 0.01$) and T2 (PIP: $t_{(46)}$: 3.119, $p < 0.001$; MAP: $t_{(46)}$: 4.387, $p < 0.001$). PEEP showed significant changes in the three periods ($F_{(2,42)}$: 3.40, $p < 0.05$). Post hoc comparisons, however, showed that only values at T1 were significantly higher compared to T2 (PIP: $t_{(46)}$: 2.532, $p < 0.05$). Vte/kg showed significant effect of time ($F_{(2,42)}$: 30.84, $p < 0.001$) and post hoc single t-tests revealed lower values at birth as compared to T1 ($t_{(46)}$: 5.844, $p < 0.001$) and T2 ($t_{(46)}$: 7.467, $p < 0.001$). On the other hand, no significant difference was found between T1 and T2 ($t_{(46)}$: 1.624, $p = 0.23$). Finally, there was a significant effect of time on Cdyn ($F_{(2,42)}$: 30.76, $p < 0.001$). Further post hoc analysis demonstrated statistically significant differences among the three different periods (T1 vs. T0: $t_{(46)}$: 4.969, $p < 0.001$; T2 vs. T0: $t_{(46)}$: 7.836, $p < 0.001$; T2 vs. T1: $t_{(46)}$: 2.867, $p = 0.01$).

TABLE 1 Characteristics of main parameters and time points are expressed as mean ± SD

	Mean ± SD
HR detection time (s)	58.5 ± 16.3
HR at first detection (bpm)	71.2 ± 24.1
SpO_2 at first measurement (%)	49.1 ± 20.8
T0–T1 (s)	176 ± 60
T1– T2 (s)	301 ± 70

Abbreviations: HR, heart rate; SpO2, peripheral oxygen saturation.

4 | DISCUSSION

Our study showed the close association between PPV, Vte, and HR during resuscitation of very and extremely premature infants at birth.

To date, respiratory support in the DR is the least controlled form of ventilation for preterm infants. Upon admission to NICU and during their hospital stay, clinicians have means of closely monitoring Vte, the PIP, the PEEP, and the amount of oxygen given.[16,17] On the other side, Vte during neonatal resuscitation is not routinely measured, and although mask PPV is commonly used in the DR, available data demonstrating its effectiveness remain scarce.[18] Currently, evaluation of the efficacy of PPV during resuscitation, and then of the administration of adequate Vte, is mainly based on the clinical assessment of the infant's chest wall movements. However, evidence has shown how frequently this leads to misinterpretation of the success of ventilation.[19,20] Achieving a stable HR > 100 bpm is commonly considered an indirect clinical parameter of delivering effective respiratory support.[21] In the present study, we confirmed that HR can be considered a reliable parameter to evaluate the efficacy of ventilation in the DR and that it is strictly related to the onset of physiological Vte and adequate lung recruitment.

In very premature infants, representing the majority of our study population, the respiratory drive is usually ineffective. Therefore, achieving an adequate FRC needs to be facilitated with additional applied pressure to overcome the respiratory muscles' weakness and the high resistance of the liquid-filled airways and lung tissue.

TABLE 2 Main ventilatory parameters during resuscitation at the three different time points

	T0	T1	T2	Post hoc test*
PIP (cmH_2O)	24.05 ± 2.27	27.09 ± 5.37	24.7 ± 3.86	a,c
MAP (cmH_2O)	15.85 ± 2.77	17.47 ± 3.85	15.2 ± 3.78	a,c
PEEP (cmH_2O)	5.82 ± 1.30	6.27 ± 2.17	5.61 ± 1.50	c
Vte (ml/kg)	3.57 ± 2.14	6.18 ± 2.51	6.89 ± 2.40	a,b
Cdyn ($ml/cmH_2O/kg$)	0.20 ± 0.11	0.31 ± 0.13	0.38 ± 0.12	a,b,c

Note: Data are expressed as mean ± SD. Post hoc tests' statistical significance was considered <0.05 and indicated with *: (a) T0 versus T1; (b) T0 versus T2; (c) T1 versus T2.

Abbreviations: Cdyn, dynamic compliance; MAP, mean airway pressure; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; Vte, expired tidal volume.

The current recommendations advocate the use of 25 cmH_2O of PIP,[2] since higher values have been shown to be harmful, increasing the risk of air leak syndromes, lung damage, and brain injuries.[22,23] However, there is evidence that mask leaks, airway obstruction and interpersonal differences lead to a high degree of uncontrolled variations in the pressure and volume delivery during neonatal resuscitation.[18,24,25] In our study, resuscitation was performed with RFM, and then changes in PIPs were done according to the real-time information it provided, trying to keep Vte/kg within the physiologic range (4–8 ml/kg)[26] and avoiding uncontrolled variations.

It is reasonable that the low Vte values we observed at T0 are indicators of ineffective ventilation related to glottis obstruction, undetected mask leak, or high resistance of the liquid-filled airways, which could be the reason why these infants showed persistent bradycardia at birth. Recently, the relevance of bradycardia exposure during stabilization in the DR has been highlighted. Kapadia et al. showed that preterm infants <32 weeks' GA who experienced prolonged bradycardia during resuscitation are at increased risk for death and intraventricular hemorrhage.[9] In a recent study, Bresesti et al. showed that the degree of bradycardia exposure during the first 15 min after birth, when associated with peripheral hypoxemia, significantly impacts cerebral oxygenation parameters of preterm infants receiving respiratory support.[8] For these reasons, providing proper adjustments of face mask position and then of the PIP values in real time allows a more effective early lung recruitment and avoids prolonged bradycardia exposure.

In our study, after having overcome bradycardia, we observed that despite the lower pressures administered the Vte remained within range values. Also, we observed a constant progressive rise of Cdyn lung compliance over the first minutes of life. These findings demonstrated that once the lungs have begun their recruitment and initial FRC was achieved, a closely monitored decrease in PIP avoided alveolar recruitment loss and inappropriately high volumes administration. If ventilation with high pressures had been maintained after the lung recruitment establishment, Vte would likely have become dangerously high, increasing the risk of early volutrauma.[27] Interestingly, we did not report air leak syndromes nor IVH > grade 2 within 48 h after birth in any patient, supporting the safety of higher PIP level changes when guided by the RFM monitoring of Vte. Of note, the majority of our patients received prenatal steroids for lung maturation.

Our study has some limitations. First, it is an observational study with small sample size and a high cesarean section rate. The lack of a control group prevented us from drawing broad conclusions about the real value of RFM in the DR. In addition, we have analyzed only short-term outcomes. Of note, in our unit, the use of PPV during resuscitation in infants below 32 weeks of GA seemed quite high, around 70%. Upon a retrospective analysis of the recordings, we concluded that a minority of the infants without bradycardia might have been supported with CPAP alone. Also, the mean time needed to reach a stable HR ≥ 100 bpm was 176 s, and we hypothesized that it could have been lower if the PIP increase had been faster. The device provides the measurement with a delay, since the sampling is averaged over an interval. This is an inherent pitfall of the device. These aspects suggest that the efficacy of RFM monitoring is strictly dependent on individual skills of reading and interpreting real-time information. Therefore, the implementation of good clinical practice seems necessary to maximize this tool's utility in future clinical trials.

RFM may promote earlier attainment of adequate Vte and presumably stabilization of the HR, potentially avoiding some intubations. However, further research is needed to confirm these speculations. A recently published multi-center trial (NCT 03256578) showed that the use of visible RFM during resuscitation of preterm infants <28 weeks GA is able to reduce the incidence of cerebral injuries, although it did not increase the percentage of inflations in a predefined Vte target range.[28]

5 | CONCLUSION

The present study highlighted a clear correspondence between stable HR rise over 100 bpm and adequate Vte administration during DR stabilization of very preterm infants with initial bradycardia. Our findings showed that HR is a reliable clinical sign of adequate early lung aeration and recruitment. Moreover, it seemed that RFM might be safely used for tailored ventilation in the DR, following the real-time lung compliance changes during the immediate neonatal transition.

For their potential implications in routine clinical practice, these findings warrant further large-scale studies.

AUTHOR CONTRIBUTIONS

Francesco Cavigioli: Conceptualization; investigation; methodology; formal analysis; writing – review and editing. **Ilia Bresesti**: Conceptualization; writing – original draft; methodology; investigation; formal analysis. **Antonio Peri**: Formal analysis; investigation; writing – review and editing. **Francesco Cerritelli**: Data curation; writing – review and editing. **Diego Gazzolo**: Writing – review and editing; supervision. **Antonio W. D. Gavilanes**: Writing – review and editing; supervision. **Boris Kramer**: Supervision; writing – review and editing. **Arjan te Pas**: Writing – review and editing; methodology. **Gianluca Lista**: Supervision; writing – review and editing; conceptualization.

ACKNOWLEDGMENTS

The authors are grateful to all the NICU staff members for their cooperation in this study.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES

1. Lista G, Maturana A, Moya FR. Achieving and maintaining lung volume in the preterm infant: from the first breath to the NICU. *Eur J Pediatr*. 2017;176:1287-1293.
2. Madar J, Roehr CC, Ainsworth S, et al. European Resuscitation Council Guidelines 2021: newborn resuscitation and support of transition of infants at birth. *Resuscitation*. 2021;161:291-326.
3. Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev*. 2017;3(3):CD004454.
4. Stenson BJ, Boyle DW, Szyld EG. Initial ventilation strategies during newborn resuscitation. *Clin Perinatol*. 2006;33(1):65-82.
5. Smith LJ, McKay KO, van Asperen PP, Selvadurai H, Fitzgerald DA. Normal development of the lung and premature birth. *Paediatr Respir Rev*. 2010;11(3):135-142.
6. Bresesti I, Agosti M, Lakshminrusimha S, Lista G. Synchronized invasive mechanical ventilation. *Clin Perinatol*. 2021;48(4):813-824.
7. Polglase GR, Miller SL, Barton SK, et al. Initiation of resuscitation with high tidal volumes causes cerebral hemodynamic disturbance, brain inflammation and injury in preterm lambs. *PLoS One*. 2012; 7(6):e39535.
8. Bresesti I, Avian A, Bruckner M, et al. Impact of bradycardia and hypoxemia on oxygenation in preterm infants requiring respiratory support at birth. *Resuscitation*. 2021;164:62-69.
9. Kapadia VOJ, Saugstad O, Rabi Y, et al. BRADYPREM study: is heart rate the most vital of all vital signs during preterm resuscitation? In selected abstracts of the 2nd Congress of joint European Neonatal Societies (jENS); Venice (Italy); October 31-November 4 2017; Session Neonatal Pulmonology, Neonatal respiratory support, Resuscitation. *J Pediatr Neonat Individual Med*. 2017;6(2):e060236. doi:10.7363/060236
10. Bresesti I, Bruckner M, Mattersberger C, et al. Feasibilty of transcutaneous pCO(2) monitoring during immediate transition after birth—a prospective observational study. *Front Pediatr*. 2020;8:11.
11. Foglia EE, Te Pas AB. Effective ventilation: the most critical intervention for successful delivery room resuscitation. *Semin Fetal Neonatal Med*. 2018;23(5):340-346.
12. Schmölzer GM, Morley CJ, Wong C, et al. Respiratory function monitor guidance of mask ventilation in the delivery room: a feasibility study. *J Pediatr*. 2012;160(3):377-381.
13. Verbeek C, van Zanten HA, van Vonderen JJ, Kitchen MJ, Hooper SB, te Pas AB. Accuracy of currently available neonatal respiratory function monitors for neonatal resuscitation. *Eur J Pediatr*. 2016;175(8):1065-1070.
14. Lista G, Cavigioli F, La Verde PA, Castoldi F, Bresesti I, Morley CJ. Effects of breathing and apnoea during sustained inflations in resuscitation of preterm infants. *Neonatology*. 2017;111(4):360-366.
15. Wyllie J, Perlman JM, Kattwinkel J, et al. Part 7: neonatal resuscitation: 2015 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. *Resuscitation*. 2015;95:e169-e201.
16. Tracy M. How safe is intermittent positive pressure ventilation in preterm babies ventilated from delivery to newborn intensive care unit? *Arch Dis Child Fetal Neonatal Ed*. 2004;89(1):84F-87F.
17. Klimek J, Morley CJ, Lau R, Davis PG. Does measuring respiratory function improve neonatal ventilation? *J Paediatr Child Health*. 2006; 42(3):140-142.
18. Schmolzer GM, Kamlin OCOF, O'Donnell CPF, Dawson JA, Morley CJ, Davis PG. Assessment of tidal volume and gas leak during mask ventilation of preterm infants in the delivery room. *Arch Dis Child Fetal Neonatal Ed*. 2010;95(6):F393-F397.
19. Poulton DA, Schmölzer GM, Morley CJ, Davis PG. Assessment of chest rise during mask ventilation of preterm infants in the delivery room. *Resuscitation*. 2011;82(2):175-179.
20. Schmolzer GM, Dawson JA, Kamlin COF, O'Donnell CP, Morley CJ, Davis PG. Airway obstruction and gas leak during mask ventilation of preterm infants in the delivery room. *Arch Dis Child Fetal Neonatal Ed*. 2011;96(4):F254-F257.
21. Linde JE, Schulz J, Perlman JM, et al. The relation between given volume and heart rate during newborn resuscitation. *Resuscitation*. 2017;117:80-86.
22. Jobe AH, Ikegami M. Mechanisms initiating lung injury in the preterm. *Early Hum Dev*. 1998;53(1):81-94.
23. Dammann O, Leviton A, Bartels DB, Dammann CEL. Lung and brain damage in preterm newborns. *Neonatology*. 2004;85(4):305-313.
24. Finer NN, Rich W, Wang C, Leone T. Airway obstruction during mask ventilation of very low birth weight infants during neonatal resuscitation. *Pediatrics*. 2009;123(3):865-869.
25. Murthy V, Creagh N, Peacock JL, et al. Inflation times during resuscitation of preterm infants. *Eur J Pediatr*. 2012;171(5):843-846.
26. Vyas H, Field D, Milner AD, Hopkin IE. Determinants of the first inspiratory volume and functional residual capacity at birth. *Pediatr Pulmonol*. 1986;2(4):189-193.
27. Attar MA, Donn SM. Mechanisms of ventilator-induced lung injury in premature infants. *Semin Neonatol*. 2002;7(5):353-360.
28. van Zanten HA, Kuypers LAM, van Zwet EKW, et al. A multi-centre randomised controlled trial of respiratory function monitoring during stabilisation of very preterm infants at birth. *Resuscitation*. 2021; 167:317-325.

How to cite this article: Cavigioli F, Bresesti I, Di Peri A, et al. Tidal volume optimization and heart rate response during stabilization of very preterm infants. *Pediatric Pulmonology*. 2023;58:550-555. doi:10.1002/ppul.26229