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BRIEF REPORT

Thoracic electrical bioimpedance in preterm newborns with and without respiratory distress syndrome: an exploratory observational study

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Abstract

To test the hypothesis that thoracic fluid content (TFC) by thoracic electrical bioimpedance would be higher in preterm infants with respiratory distress syndrome (RDS) both at birth and in the first 48 h of life than in those without RDS and that TFC measured at birth would be associated with RDS diagnosis and need for surfactant. Cross-sectional exploratory observational study including infants ≤ 34 weeks of gestation admitted to two level three NICUs. TFC, clinical, and respiratory data were recorded at 5 timepoints: within the first 2 h of life, before surfactant therapy, and at 4, 12, 24, and 48 h of life. TFC was compared between infants with and without RDS. A ROC curve was calculated to assess the association between TFC at birth and the need for surfactant. TFC was higher in infants with RDS than in infants without RDS at all timepoints. The ROC AUC of TFC measured at birth for the need for surfactant was 0.817 (95% CI 0.64–0.93, $p < 0.001$); a TFC cut-off of 20.4 1/KOhm/Kg yielded a sensitivity of 83% and specificity of 80% for the need for surfactant.

Conclusion: TFC in the first 48 h of life was higher in preterm infants with RDS than in infants without RDS. TFC measured within the first 2 h of life had a good association with the need for surfactant.

What is known:
• *Thoracic electrical bioimpedance can be used to measure thoracic fluid content (TFC) non invasively in newborns*
What is new:
• *TFC was higher in premature newborns with respiratory distress syndrome (RDS) that in those without RDS in the first 48 h of life. A high TFC in the first 2 h was associated with the need for surfactant*

Keywords Thoracic fluid content · Respiratory distress syndrome · Prematurity

Abbreviations

AUC	Area under the curve
BPD	Bronchopulmonary dysplasia
CI	Confidence interval
CPAP	Continuous positive airway pressure
GA	Gestational age
MAP	Mean airway pressure
OSI	Oxygen saturation index
ROC	Receiver operating characteristic analysis
RDS	Respiratory distress of the newborn
SD	Standard deviation
TB	Thoracic electrical bioimpedance

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TFC Thoracic fluid content
TFI Total fluid intake
TTN Transient tachypnea of the newborn

Introduction

Electrical velocimetry is a thoracic electrical bioimpedance (TB)-based method for hemodynamic monitoring. It measures thoracic fluid content (TFC) from baseline whole TB [1].

Respiratory distress syndrome(RDS) is a common respiratory disease associated with preterm birth [2]. Its pathogenesis is complex, secondary to incomplete lung maturation, surfactant deficiency, atelectasis, inflammation, and immaturity of mechanisms of alveolar fluid reabsorption [2]. Its treatment is based on ventilatory support and exogenous surfactant [3].

Evidence about TFC monitoring in neonatal respiratory conditions is still sparse [4]. In late preterm and term infants with transient tachypnea of the newborn (TTN), TFC at birth and in the first day of life was higher than in those without TTN and decreased in the following days [5, 6]. TFC was reported to increase or, conversely, to decrease more rapidly on the second day of life in late preterm and term infants with TTN when compared with infants with RDS or with other causes of respiratory distress [7, 8].

Moreover, TFC combined with lung ultrasound predicted the need for mechanical ventilation after 24 h and bronchopulmonary dysplasia (BPD) development in preterm infants with RDS [9].

To the best of our knowledge, TFC has not yet been compared in preterm infants ≤ 34 gestational weeks with and without RDS. The aim of the study was to test the hypothesis that TFC would be higher in infants with RDS at birth and in the first 48 h of life than in those without RDS; moreover, we tested whether TFC measured at birth was associated with RDS diagnosis and need for surfactant.

Materials and methods

This bicentric cross-sectional exploratory observational study was carried out at the University Hospital of Udine and the Institute for Maternal and Child Health, Trieste, Italy, both level three NICUs with an average of 250–300 preterm newborns admitted per year.

The institutional scientific board and Regional Ethics Committee approved the study (protocol number n. 374, 17.04.2020). We followed the STROBE reporting guideline for observational studies [10] (Online resource 1).

Subjects, clinical, and respiratory data

Inborn infants born at ≤ 34 weeks of gestational age (GA) whose parents provided written consent were included. Exclusion criteria were congenital malformations, no parental consent, and being outborn.

GA was based on the first-trimester sonogram. RDS was defined according to 2019 European Guidelines as $FiO_2 > 30\%$ with CPAP of at least 6 cmH20 and compatible imaging after exclusion of other causes of respiratory distress, indicating the need for surfactant [3]. Target $SatO_2$ was 90–95%. TTN was diagnosed on the basis of Montreux criteria [11].

The two participating centers shared the same management protocol for neonatal respiratory support (i.e., first-intention non-invasive ventilation (CPAP of at least 6 cmH20 or intermittent non-invasive ventilation), early surfactant according to European guidelines, preferably by less invasive administration technique, intubation criteria, i.e., repeated pH < 7.20 with PaCO2 exceeding 60 mmHg, FiO2 higher than 50%, recurrent apneas).

Pregnancy data and data of infants' postnatal course were collected from clinical charts and included: pregnancy complications, mode of delivery, 5-min Apgar score, prenatal betamethasone, surfactant doses, days of invasive and non-invasive respiratory support, and diagnosis of BPD as needed for supplemental oxygen or respiratory support at 36 weeks GA. Total fluid intake (TFI) (ml/Kg/day) and birth weight loss as % of birth weight in the first 24 (day 1) and 24–48 (day 2) h of life were calculated. Oxygen saturation index (OSI) was calculated as (mean airway pressure (MAP) (cmH20) × FiO_2 × 100) / $SatO_2$.

Thoracic electrical bioimpedance measurement

Monitoring by TB (ICON®Osypka Medical Gmbh, Germany) was started soon after NICU admission and maintained continuously for at least the first 48 h of life. TB values with 100% signal quality index were recorded at 5 timepoints: (1) "at birth" (defined as within the first 2 h of life, before surfactant therapy), (2) 4 h, (3) 12 h, (4) 24 h, and (5) 48 h of life. Moreover, TB was measured 1 h after intratracheal surfactant. A mean of 3 consecutive TB values was calculated at each time point. Concomitantly at each time point, respiratory data were prospectively recorded: modality of ventilatory support, FiO_2, $SatO_2$, and MAP.

A detailed description of ICON operating principles is provided elsewhere [1]. Body weight and length were entered into the monitor for normalization.

Statistical analysis

Variables were reported as mean (standard deviation, SD) if normally, or median (interquartile range) if non-normally distributed. Continuous variables were compared by parametric or non-parametric tests, if normally or non-normally distributed, respectively (independent sample *T*-test or Wilcoxon in case of variables from different groups and paired samples *T*-test or Mann–Whitney test in case of repeated measurements in the same group).

Considering a TFC SD of 11 1/KOhm/Kg [5] and an a priori hypothesis of a 15 1/Kohm/Kg difference in TFC between infants with and without RDS at the timepoint 1 [5], the calculated sample size was 12 infants per group, with a power of 90% and an alpha error of 0.05 (Snedecor and Cochran Eq. 1989) [12].

To address the potential confounding effect of birth weight, both in relation to TB [13] and RDS [2], TFC was normalized by body weight. Linear regression analysis was used to assess the association between TFC at timepoints 4 and 5 and days 1 and 2 TFI, respectively, as potential confounders. A multiple logistic regression analysis model was employed to test the association between TFC and RDS independently from TFI in case of a significant association at univariate analysis.

To test the accuracy of TFC at timepoint 1 in predicting the diagnosis of RDS and the need for surfactant, diagnosis receiver operating characteristic analysis (ROC) was calculated. Two-tailed statistical significance was assumed with an alfa value of 0.05. Statistical analyses were performed using SAS Enterprise Guide Version 7.15 and MedCalc® Statistical Software version 23.0.2.

Results

Thirty-two infants were enrolled from June 2020 to May 2021, of whom 12 (38%) developed RDS and received exogenous surfactant, 15 (47%) were diagnosed with TTN, and 5 (15%) did not need any respiratory support/supplemental oxygen. Infants with RDS were born at younger GA (29.0 (SD 2.6) vs 32.4 (SD 1.8) weeks, $p < 0.01$), with lower birth weight (1310 (SD 440) g vs 1780 (SD 340) g, $p < 0.01$) than infants without RDS. Clinical characteristics are reported in Table 1.

TFI (day 1: 80 (70–90) vs 67 (63–78) ml/Kg/day, $p = 0.06$; day 2: 98 (82–114) vs 96 (88–105) ml/Kg/day) and weight loss (day 1: 1.44 (− 0.29–2.5)% vs 2.21 (0.76–4.97)%, $p = 0.4$; day 2: 8.99 (5.27–12.71)% vs 6.80 (5.16–8.45)%, $p = 0.3$) did not significantly differ between infants who developed RDS and who did not.

TFC and OSI were higher in infants with RDS than in infants without RDS at all timepoints (Fig. 1).

TFC of infants with RDS was similar among different timepoints; conversely, OSI decreased from timepoints 1 to 4 (2.2 (1.9–2.6) vs 1.7 (1.4–1.8), $p < 0.05$). In infants without RDS, both TFC and OSI decreased from timepoints 1 to 5 (TFC: 16.8 (14.7–20.2) vs 14.8 (11.5–16.3) 1/KOhm/Kg, $p < 0.05$; OSI: 1.2 (0.3–1.4) vs 1.1 (0–1.3), $p < 0.05$).

In infants with RDS, TFC before surfactant was similar to TFC measured 1 h after exogenous surfactant (28.3 (23.3–33.3) vs 26.7 (22.9–30.6) 1/KOhm/Kg, $p = 0.8$).

Table 1 Clinical characteristics of infants with and without respiratory distress syndrome (RDS). Variables are reported as mean (SD) or median (interquartile range) or number of infants (%)

	RDS (N12)	No RDS (N20)	*p*
Gestational age (weeks)	29.0 (2.6)	32.4 (1.8)	< 0.01
Birth weight (g)	1310 (440)	1780 (340)	< 0.01
Females (*n*;%)	5 (42%)	8 (40%)	0.9
5 min Apgar score	9 (8–10)	8 (7–8)	0.04
Prenatal bethamethasone (2 doses) (*n*;%)	8 (67%)	17 (85%)	0.2
Maternal preeclampsia (*n*;%)	2 (17%)	3 (15%)	0.8
Maternal diabetes (*n*;%)	1 (8%)	2 (10%)	0.8
C-section (*n*;%)	7 (58%)	11 (55%)	0.8
Intubation and mechanical ventilation (*n*;%)	7 (58%)	1 (5%)	0.01
Intubation and mechanical ventilation (days)	2 (1–8)	0	n.a
Non-invasive ventilation (*n*;%)	12 (100%)	15 (75%)	0.03
Non-invasive ventilation (days)	41 (11–50)	5 (2–8)	< 0.01
Bronchopulmonary dysplasia (*n*;%)	4 (33%)	0	n.a
Need for surfactant	12 (100%)	0	n.a
Mortality	0	0	n.a

n.a. not applicable

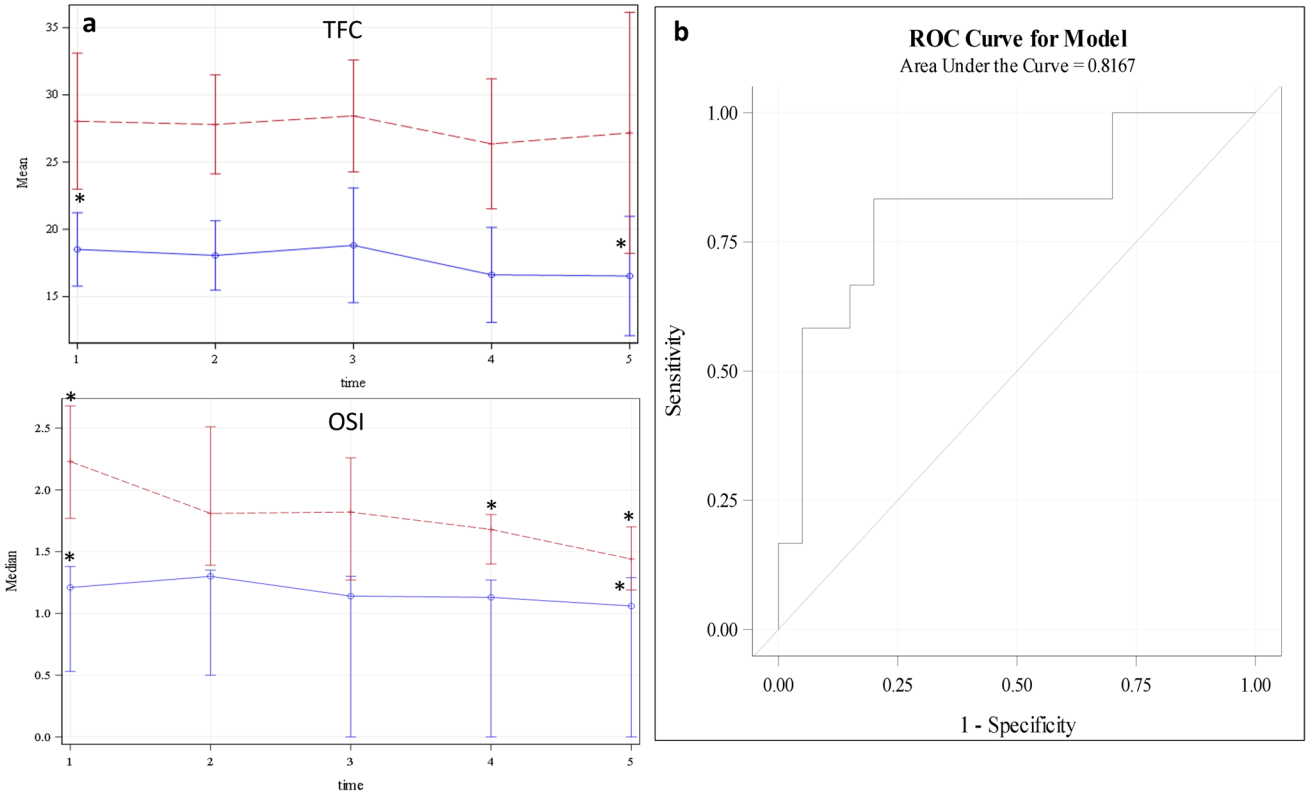

Fig. 1 **a** Comparison of thoracic fluid content (TFC) (1/KOhm/Kg) and oxygen saturation index (OSI) between infants with (red line) and without (blue line) respiratory distress syndrome (RDS) at 5 timepoints: (1) birth (within the first 2 h of life, before surfactant treatment), (2) 4 h, (3) 12 h, (4) 24 h, and (5) 48 h of life. Results are presented as means (95% confidence interval) for TFC and median (interquartile range) for OSI. $p < 0.05$ for all comparisons between infants with and without RDS. $*p < 0.05$ between timepoint 1 and subsequent timepoints; **b** ROC AUC of TFC measured at birth for RDS diagnosis and need for surfactant: 0.817 (95% CI 0.64–0.93; OR 1.2, 95% CI 1.1–1.4, $p < 0.001$)

Timepoint 4 TFC was significantly associated with RDS independently from day 1 TFI (adjusted OR 1.17 (1.01–1.26)). Timepoint 5 TFC was not associated with day 2 TFI.

TFC at birth was measured at 115 (93–140) and 116 (85–128) min of life in infants with and without RDS, respectively. The ROC AUC of TFC measured at birth for the need for surfactant was 0.817 (95% CI 0.64–0.93; OR 1.2, 95% CI 1.1–1.4, $p < 0.001$) (Fig. 1); a TFC cut-off of 20.4 1/KOhm/Kg yielded a sensitivity of 83% and specificity of 80% for the need for surfactant. No skin lesions due to sensors during ICON placement were detected.

Discussion

In our exploratory study, TFC in premature infants with RDS was higher than in infants without RDS in the first 48 h of life. Moreover, TFC measured within the first 2 h of life had a good association with the need for surfactant.

Early diagnosis of RDS and differentiation from other respiratory diseases is important to provide timely exogenous surfactant [2]; it is based on clinical, ventilatory, and supplementary oxygen criteria [3], and it is supported by imaging techniques that employ ionizing radiations (X-ray) or require adequate training (lung ultrasound). Whereas TB is an uniquely operator independent, as TFC values are displayed on the screen for all operators to read, continuous and non-invasive monitoring device. TFC is measured as baseline resistance (bioimpedance) to the passage of a small electrical current through all thoracic tissues; changes in TB reflect primarily modification of thoracic fluid [14].

In a previous small study by Yoon et al. TFC was not different between infants with RDS and those with TTN on the first day of life; however, only infants 34–40 weeks GA were included [7]. In the study by Bassiouny et al., TFC measured in the first 6 h of life in infants 37–42 gestational weeks with TTN was higher than in infants with other causes of respiratory distress, defined according to clinical presentation and need for respiratory support; a

drop of TFC > 12% and TFC ≤ 24 1/KOhm/Kg at 24 h were associated with TTN diagnosis versus non-TTN. However, in this paper, definitions of respiratory distress and study population gestational age range were different from our study, thus hindering direct comparisons [8].

In our study, TFC was unchanged in the first 48 h of life in infants with RDS. This is consistent with data reported by Martini et al. that showed a decrease in TFC in preterm infants with RDS after 48 h [9].

TFC values in our sample were lower than those reported by Martini, with none ≥ 40. This may reflect differences in the baseline severity of RDS between our populations [9].

Interestingly, TFC did not change after surfactant, possibly indicating that mechanisms other than change in lung fluid are implicated.

This study has several limitations. The main limitation is the small sample size; however, this is the first exploratory report of a comparison of TFC in the first 48 h of life in infants ≤ 34 weeks GA with and without RDS. Generalizability of results is limited by the paucity of extremely preterm infants; subgroup analysis, for instance, according to the level of respiratory support required, was hindered by the small sample size. Lung ultrasound data were not included.

We cannot rule out that the association between TFC and RDS is due to residual confounding or that normalization of TFC by body weight might have determined, at least partially, a double correction, given the inverse association between RDS and birth weight; calculated fluid intake and birth weight loss did not differ between infants with and without RDS; moreover, timepoint 4 TFC was associated with RDS independently from day 1 TFI.

Conclusions

TFC values were higher in preterm infants with RDS than in those without RDS in the first 48 h of life. TFC measured at birth correlated with RDS diagnosis and need for surfactant. Further larger studies are warranted to confirm these results.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00431-025-06049-0.

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Authors' contributions All authors contributed to the study conception and design. Material preparation and data collection were performed by G.P. and M.P. Statistical analyses were performed by G.P., M.D., Y.B., L.C. The first draft of the manuscript was written by G.P. and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. The institutional scientific boards of Udine University Hospital ("Nucleo di Ricerca") and of IRCCS "Burlo Garofolo" (Institutional Review Board) in Trieste and the Regional Ethics Committee (Comitato Etico Unico Regionale Friuli Venezia Giulia, CEUR FVG) approved the study (protocol number n. 374, 17.04.2020).

Consent to participate Written informed consent was obtained from all the parents of infants included in the study.

Consent for publication Consent for publication was obtained from all the parents of infants included in the study.

Competing interests The authors declare no competing interests.

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