ORIGINAL ARTICLE: NEONATAL LUNG DISEASE

Transcutaneous monitoring of diaphragm activity as a measure of work of breathing in preterm infants

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Abstract

Objective: Monitoring work of breathing (WOB) is important to assess the pulmonary condition and adjust respiratory support in preterm infants. Conventional WOB measurement (esophageal pressure, tidal volume) is invasive and we hypothesized that monitoring diaphragm activity could be a noninvasive alternative to estimate WOB. The objective was to determine the correlation between conventional WOB measures and diaphragm activity, in preterm infants.

Methods: WOB and diaphragm activity, measured with transcutaneous electromyography (dEMG), were simultaneously recorded at different nasal continuous positive airway pressure (nCPAP) levels. During a 30-s recording at each nCPAP level, dEMG parameters, inspiratory WOB (WOB_i), and pressure time product (PTP_{in}) were calculated per breath. The correlation coefficient between WOB- and dEMG-measures was calculated using single breaths and after aggregating all breaths into deciles of incremental WOB_i.

Results: Fifteen preterm infants were included (median gestational age, 28 weeks). Single-breath analysis showed a poor median correlation of 0.27 (interquartile range [IQR], 0.03 to 0.33) and 0.08 (IQR, −0.03 to 0.28), respectively, for WOB_i and PTP_{in} with peak diaphragmatic activity ($dEMG_{peak}$). A modest median correlation coefficient of 0.65 (IQR, 0.13 to 0.79) and 0.43 (IQR, −0.33 to 0.69) was found for, respectively, WOB_i and PTP_{in} with $dEMG_{peak}$ in the aggregated analysis.

Conclusion: Diaphragm activity showed a modest correlation with WOB_i and PTP_{in} in an aggregated analysis. This finding warrants further studies in infants with more significant lung disease.

KEYWORDS
diaphragm activity, esophageal pressure, monitoring, preterm infant, work of breathing

1 | INTRODUCTION

Preterm infants are prone to an increased work of breathing (WOB) due to their immature respiratory system.[1–3] To unload this excessive WOB, preterm infants are often treated with either invasive or noninvasive respiratory support. Ideally, the optimal mode and level of respiratory support should be individually titrated in each patient, as both too little and too much support may have serious adverse effects.[4,5] Furthermore, titration of respiratory support should ideally be based on the actual WOB, instead of indirect measures (e.g., gas exchange) or nonspecific clinical signs like chest retractions and tachypnea.[6]

WOB is defined as the integral of the inspiratory pressure generated by the respiratory muscles, with respect to inspiratory volume. When determining the inspiratory pressure, the contribution of the chest wall is usually neglected and WOB is approximated by calculating the product of the change in intrapleural pressure and the resulting change in tidal volume.[7] Conventionally, esophageal pressure (P_{es}) is used as a measure for intrapleural pressure.[8,9] Measurement of this pressure requires specific catheters with mounted pressure transducers. Tidal volume can be measured with a flow sensor placed at the airway opening or by using calibrated respiratory inductance plethysmography (RIP) bands.[7,10]

Due to the invasive nature of measuring intrapleural pressure and the complexity of measuring tidal volumes during noninvasive respiratory support, traditional WOB measurements have not been implemented in daily respiratory care for preterm infants and are mainly used in a research setting.[8,11] Therefore, less invasive and less complex techniques to continuously monitor WOB are urgently needed in neonatal care.

The activity of the diaphragm is a potential target in the search for a new WOB monitoring technique, as it is this respiratory muscle that mainly generates WOB.[12] Diaphragmatic contraction lowers the intrapleural pressure which results in an influx of air (tidal volume) in the lungs during inspiration. Previous studies have shown an association between electrical activity generated by the diaphragm, measured with electromyography (EMG), and traditional WOB-measures in adults and infants.[8,13,14] However, these studies measured the activity of the diaphragm with an esophageal catheter with mounted electrodes. This method is still invasive and its availability is limited to one commercial ventilator. As an alternative, transcutaneous electromyography of the diaphragm (dEMG) is a noninvasive method to measure diaphragm activity using skin electrodes. To date, there is only one study in preterm infants that measured both WOB and diaphragmatic activity. However, the focus of this study was to assess the effect of rib cage distortion on diaphragmatic work, and the possible association between WOB and dEMG was not systematically analyzed.[15]

Therefore, the aim of this study was to measure WOB and diaphragm activity simultaneously in preterm infants to describe a potential relationship between these parameters.

2 | METHODS

A prospective observational study was conducted in the Emma Children's Hospital, Amsterdam University Medical Centres, the Netherlands, with the approval of the institutional review board.

2.1 | Study population

Preterm infants with a postmenstrual age between 26 and 37 weeks were included when treated with nasal continuous positive airway pressure (nCPAP) with a pressure level between 4 and 6 cmH$_2$O, an FiO$_2$ < 0.30, and when estimated to be clinically stable by the treating physician. Exclusion criteria were major congenital anomalies, frequent interventions by the nursing staff to treat apnea, or the inability of parents to speak and understand Dutch or English. Written informed consent was obtained from both parents.

2.2 | Data acquisition

The measurement setup is shown in Figure 1. Breathing volume was measured with two RIP bands placed around the chest and abdomen of the infant, and connected to a Bicore-II (Vyaire Medical). To calibrate the RIP signal, a facemask was placed over the nose and mouth, the infant's current nCPAP level was provided, and the inspiratory and expiratory flow was measured with a flow sensor (Varflex; Vyaire Medical) during a period of at least 30 breaths. Afterward, the standard nCPAP device was reconnected and the flow sensor was removed. Flow integration resulted in the spontaneous tidal volume signal, which was used to calibrate the RIP signal. P_{es} was measured with a feeding tube which was filled with water[16] and attached with the proximal end to a pressure transducer (TruWave; Edwards Lifesciences) connected to the patient monitor (MP90; Philips). P_{es} data was extracted from the patient monitor and sent to a bedside research computer. To determine and correct for the pressure data transmission delay, a calibration measurement was done before the sensor was connected to the patient. For this, an additional pressure sensor was connected to the Bicore-II. A pressure change was manually applied to both the Bicore-II and the P_{es} pressure sensor. The resulting spikes in both signals were used to determine the transmission delay of the P_{es} signal. Next, the P_{es} sensor was connected to the fluid-filled feeding tube of the patient. While evaluating the P_{es} pressure tracing in real-time, the feeding tube was slowly retracted from the stomach into the esophagus until a negative deflection was seen during inspiration and no cardiac artefacts were visible. The position of the feeding tube was checked with an occlusion test.[17]

To record diaphragm activity, three skin electrodes were placed on the chest of the infant and connected to the Dipha-16 signal amplifier (Demcon; Macawi Medical Systems): A reference electrode
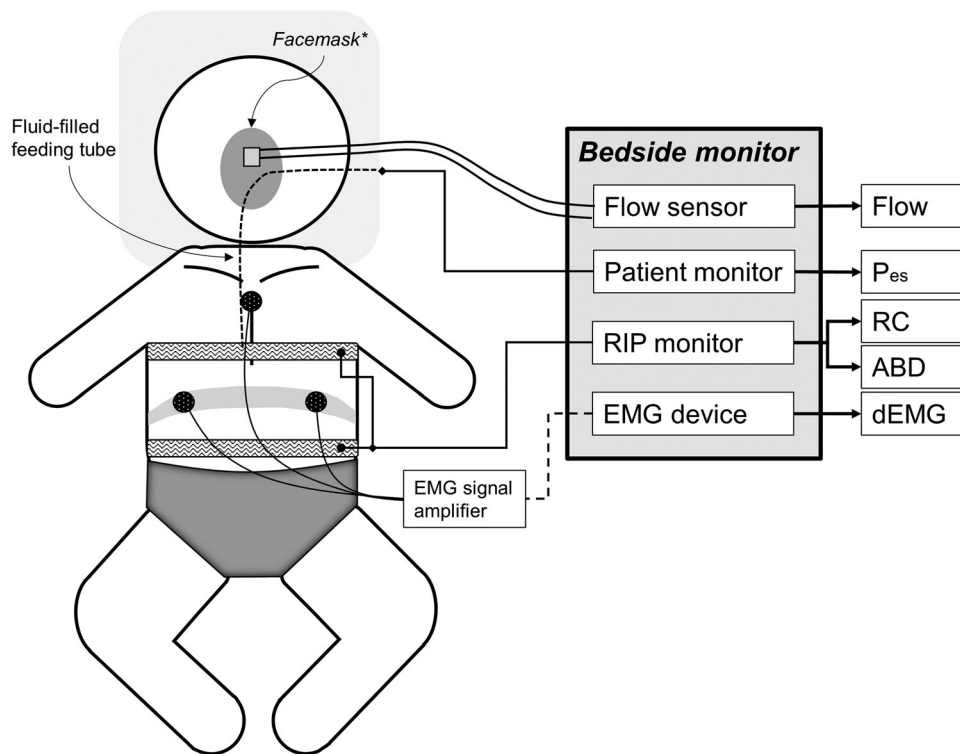
FIGURE 1 Measurement setup. Esophageal pressure (P_{es}) was measured with a pressure transducer connected to a retracted fluid-filled feeding tube. Respiratory inductance plethysmography (RIP) bands were placed around the rib cage (RC) and abdomen (ABD) to monitor breathing volume. Transcutaneous electromyography of the diaphragm (dEMG) was measured with three skin electrodes attached to an amplifier and wirelessly transferred to the bedside research monitor. *Facemask was only used for RIP calibration with a flow measurement, after which nasal continuous positive airway pressure was reconnected

was positioned on the sternum and two measuring electrodes left and right in the midclavicular line just below the costal margin.[18] The raw dEMG signals were wirelessly sent to the bedside computer. All measured signals were incorporated in a dedicated and custom-made software application (Polybench; Applied Biosignals).

2.3 | Study protocol

To induce variability in WOB, measurements were conducted at three different nCPAP levels (2, 4, and 6 cmH$_2$O) which were changed every 10 min. Regardless of the pre-study nCPAP level, the study was started at a baseline pressure of 6 cmH$_2$O. After 10 min, the pressure level was randomly lowered to 4 or 2 cmH$_2$O. After the first reduction in nCPAP, a "recovery" step was introduced by resetting nCPAP to the baseline level. Subsequently, the pressure was changed to 2 or 4 cmH$_2$O.

Changes in nCPAP level were discontinued and the infants were reset to their pre-study nCPAP level if one of the following changes occurred: more than two cardiorespiratory events during a study nCPAP step, an increase in oxygen need and/or when a clinical increase of respiratory distress was observed (e.g., expiratory grunting or subcostal retraction). At the end of the study, RIP-bands, dEMG electrodes and the pressure sensor were removed and the feeding tube was repositioned in the stomach.

2.4 | Data analysis

Data analysis was done offline with a custom-made user interface in MATLAB (v2018a; Mathworks). First, RIP calibration from arbitrary units to volume (ml) was performed by fitting the RIP signals to the actual volume measured according to the following formula[10]:

$$\text{Volume (ml)} = M (K \times \text{RIP}_{RC} + \text{RIP}_{ABD}). \quad (1)$$

The constants M and K were derived by least-squares analysis, RIP$_{RC}$ and RIP$_{ABD}$ are the raw signals from the rib cage and abdominal RIP band, respectively.

Subsequently, one data segment was selected at each nCPAP level. To wash-out any potential influence of a previous pressure step, segments were selected closest to the switch to another pressure level. As this kind of measurement is prone to signal artefacts, the choice was made to strive for segments of at least 30 s of continuous, artefact-free (P_{es}, volume, and dEMG) data, to include a representative amount of breaths according to the standard.[19] Breath detection was performed to determine the start and end of inspiration in all three signals. Subsequently, breaths were matched to compare the same breaths in all three signals. For this, the start of inspiration in the volume (calibrated RIP) signal was used as the reference. If the start of inspiration of both the P_{es} and the dEMG trace occurred within 300 ms before or after this RIP reference point, the match was considered successful and the breath was used for further analysis.

TABLE 1 Patient characteristics

	n = 15
Gestational age (weeks)	28 (26.3–28.9)
Age at measurement (days)	16 (11–33)
Birth weight (g)	955 ± 259
Weight at measurement (g)	1247 ± 282
Male gender, n (%)	8 (53)
Antenatal corticosteroids	
Full course, n (%)	8 (53)
Partial course, n (%)	4 (27)
None, n (%)	3 (20)
Apgar at 1 min	5 ± 3
Apgar at 5 min	8 ± 2
Respiratory support	
nCPAP level	4 (4–5)
FiO$_2$	0.21 (0.21–0.22)

Note: Continuous values are expressed as mean ± *SD* or median (interquartile range), categorical variables as n (%).

Abbreviations: FiO$_2$, fraction of inspired oxygen; nCPAP, nasal continuous positive airway pressure.

If multiple breaths were found within the window, the one closest to the RIP reference was considered the appropriate match.

From the matched breaths, several parameters were calculated. Conventional WOB was assessed by calculating the inspiratory work of breathing (WOB$_i$) from the start of inspiration (t_o) till the end of inspiration (t_i). To adjust for interpatient variation in tidal volume (TV), WOB$_i$ was normalized for TV[7,20]:

$$WOB_i \, (cmH_2O) = \frac{\int_{t_0}^{t_i} P \times V dt}{TV}. \quad (2)$$

As WOB-surrogate, the inspiratory pressure time product (PTP$_{in}$) was determined as well. PTP$_{in}$ was defined as the area subtended by the P_{es} curve during inspiration,[8] multiplied with the respiratory rate (RR; derived from the volume signal):

$$PTP_{in} \, (cmH_2O \cdot s/min) = \int_{t_0}^{t_i} P_{es} dt \times RR. \quad (3)$$

From each breath in the dEMG signal tonic (end-expiratory) activity (dEMG$_{ton}$) and peak (end-inspiratory) activity (dEMG$_{peak}$) were determined. As a measure for the dEMG signal power, the area under the dEMG-curve (dEMG$_{AUC}$) was calculated during the entire respiratory cycle, as the diaphragm is known to show activity during expiration as well.[21] The dEMG$_{AUC}$ was corrected for the level of dEMG$_{ton}$ at the start of the respiratory cycle.

2.5 | Statistical analysis

Data are expressed as mean ± *SD* or median with interquartile ranges (IQRs), depending on their distribution. A convenience sample of 15 infants was included. All statistical analyses were performed using SPSS (version 26; IBM).

To test the hypothesis of a positive correlation between WOB and diaphragm activity, WOB$_i$ and PTP$_{in}$ were compared with the dEMG parameters. To cluster breaths and reduce the influence of intrabreath noise, single-breath data were aggregated in deciles of breaths with incrementing WOB$_i$. Breath aggregation and correlation analysis were done according to the method described in adults by Bellani et al.[13,22] The mean for each decile of WOB$_i$ and corresponding dEMG-parameter was calculated resulting in 10 values, representing the clusters of breaths from low to high WOB$_i$.

Both the decile and single-breath values were captured in a scatter plot and the Pearson R correlation coefficient was calculated for each infant. The same approach was used to compare incremental PTP$_{in}$ deciles with dEMG parameters. The median (IQR) correlation coefficients were reported as well as the individual values, to reflect the potential variation between infants.

To assess if the changes in nCPAP level induced significant changes in WOB, we also assessed the average WOB-measures and diaphragm activity in each infant at each nCPAP level. Differences between nCPAP levels were tested with a repeated measurements Friedman test with post hoc Dunn's test.

3 | RESULTS

Fifteen preterm infants were included in this study in whom WOB and dEMG measurements were performed simultaneously (Table 1). Fourteen infants tolerated the nCPAP changes well. Due to bradycardia, the nCPAP reduction to 2 cmH$_2$O step was aborted early in one infant, but the rest of the measurement could be performed according to the study protocol. RIP calibration showed accuracy with a mean R^2 value of .83 (range, .53 to .94) in the linear regression.

3.1 | Relation between WOB and diaphragm activity

Table 2 shows the correlation coefficients for each infant based on the single-breath and the aggregated analysis comparing WOB$_i$ and PTP$_{in}$ with dEMG$_{peak}$. Comparison with dEMG$_{ton}$ and dEMG$_{AUC}$ showed comparable correlation coefficients. WOB$_i$ and PTP$_{in}$ showed a poor correlation with dEMG$_{peak}$ using the single-breath analysis (median R, 0.27 [IQR, 0.03 to 0.33] and 0.08 [IQR, −0.03 to 0.28] for WOB$_i$ and PTP$_{in}$, respectively). The aggregated analysis showed a modest correlation with a median Pearson R correlation coefficient of 0.65 (IQR, 0.13 to 0.79) and 0.43 (IQR, −0.33 to 0.69) for, respectively, WOB$_i$ and PTP$_{in}$ to dEMG$_{peak}$. The individual patient correlations showed considerable variation between subjects (minimum R, −0.74 and maximum, 0.95 for WOB$_i$ vs. dEMG$_{peak}$). Figure 2 shows an example of the single-breath and aggregated correlation analysis for a subject with poor-to-good correlation between WOB$_i$ and dEMG$_{peak}$, depending on the analysis used.

TABLE 2 Correlation coefficients between WOB-parameters and diaphragm activity

| | WOB$_i$ versus dEMG$_{peak}$ | | PTP$_{in}$ versus dEMG$_{peak}$ | |
Subject	Single-breath	Aggregated	Single-breath	Aggregated
1	0.27*	0.73*	0.27*	0.68*
2	0.20*	0.50	0.23*	0.54
3	0.58*	0.89*	0.49*	0.76*
4	0.09	0.20	0.05	0.17
5	−0.15*	−0.58	−0.17*	−0.62
6	−0.02	0.07	−0.18*	−0.64*
7	0.36*	0.65*	−0.01	−0.44
8	0.15*	0.67*	0.08	0.53
9	0.46*	0.83*	0.28*	0.70*
10	0.27*	0.85*	0.04	0.27
11	−0.08	−0.22	0.13	0.43
12	0.32*	0.74*	0.45*	0.76*
13	0.28*	0.95*	0.28*	0.92*
14	0.33*	0.44	−0.05	−0.22
15	−0.30*	−0.74*	−0.43*	−0.84*
Median (IQR)	0.27 (0.03 to 0.33)	0.65 (0.13 to 0.79)	0.08 (−0.03 to 0.28)	0.43 (−0.33 to 0.69)

Note: Pearson correlation coefficients for each patient between WOB and diaphragm activity. Group values are presented as median (IQR).
Abbreviations: dEMGpeak, peak diaphragm activity; IQR, interquartile range; PTP$_{in}$, inspiratory pressure time product; WOB$_i$, inspiratory work of breathing.
*Significant correlation ($p < .05$).

The median correlation between TV and dEMG$_{amp}$ was 0.11 (IQR, 0.04 to 0.28) and 0.37 (IQR, 0.26 to 0.76) for the single-breath and aggregated analysis, respectively.

Interestingly, four infants showed a negative single-breath correlation between WOB$_i$ and dEMG$_{peak}$. As there is no physiological explanation for this finding, we also calculated the median correlation coefficient based on the subset of 11 infants with positive correlation values between WOB$_i$ and dEMG$_{peak}$. This exploratory analysis resulted in a slightly improved median correlation coefficient of 0.28 (IQR, 0.23 to 0.35) and 0.23 (IQR, 0.05 to 0.28) for WOB$_i$ and PTP$_{in}$ to dEMG$_{peak}$ in the single-breath analysis. Aggregated analysis' correlation coefficient showed values of 0.73 (IQR, 0.57 to 0.84) and 0.54 (IQR, 0.22 to 0.73) comparing WOB$_i$ and PTP$_{in}$ to dEMG$_{peak}$.

3.2 | nCPAP level dependent variation in WOB

Overall, the median inspiratory P_{es} deflection was −4.1 cmH$_2$O (IQR, −3.0 to −5.7), resulting in median TV of 3.3 ml/kg (IQR, 2.3 to 4.8). The median RR was 77 breaths/min (IQR, 64 to 81).

Figure 3 shows the results of WOB$_i$, PTP$_{in}$, and dEMG$_{peak}$ calculated at each nCPAP level. These three parameters did not show significant differences with changing nCPAP levels ($p > .05$). There were some statistically significant differences in dEMG$_{AUC}$ and dEMG$_{ton}$ between CPAP levels but the absolute differences were small (median dEMG$_{AUC}$, 0.86, 0.66, and 0.71 µV·s for CPAP 6, 4, and 2 cmH$_2$O, respectively; Friedman $p < .05$) and median dEMG$_{ton}$, 0.60, 0.51, and 0.55 µV for CPAP 6, 4, and 2 cmH$_2$O, respectively; Friedman $p < .05$).

4 | DISCUSSION

In this observational study, we studied the relation between WOB and diaphragm activity measured transcutaneously in preterm infants. The results show a modest correlation between these two entities when using an aggregated trend analysis, but not when analyzing single breaths. Overall, the correlation between infants showed large variability.

The relatively poor correlation between WOB and dEMG based on the single-breath analysis is similar to the results Bellani et al.[22] reported, although the study design and population were different. There are several technical and physiological factors that may contribute to this finding. First, the combination of signals acquired in this study is unique and deriving them is challenging. All the necessary steps have an inherent level of noise, which could have reduced the sensitivity of the individual techniques. In preterm infants, the signal to (overall) noise ratio may become especially unfavorable as the differences in WOB between breaths are relatively small and occur over a short period of time. At the same time, diaphragm activity was low in our study and as a result the impact of noise caused by interelectrode or muscle–electrode distance and skin–electrode contact will increase.[18,23]

Second, although some pediatric and adult studies have reported that the activity of the diaphragm (measured in the esophagus) is linearly related to factors like P_{es} and airway pressure,[11,13] a recent study in adults showed that the repeatability of determining the neuromuscular efficiency (µV/cmH$_2$O) of the diaphragm by repetitive occlusion tests was low.[24] In other words, the pressure changes following the diaphragm's contraction, are variable within and between subjects. However, comparisons with studies in adults or older children should be made with caution. Large differences in basic pulmonary and chest wall physiology[15] and measuring airway pressure instead of P_{es} may add to the observed variability. These differences might support the hypothesis that single-breath comparisons are not suitable in this setting. As a result, the lower correlation found in this study could be based on physiology.

Third, in this relatively stable group of preterm infants, the variation in WOB was probably too small to optimally assess the relation between WOB and diaphragm activity. Anticipating this possible limitation, we varied the nCPAP level with the intention to change functional residual capacity and lung mechanics, thereby creating (significant) variations in WOB. The lack of significant and
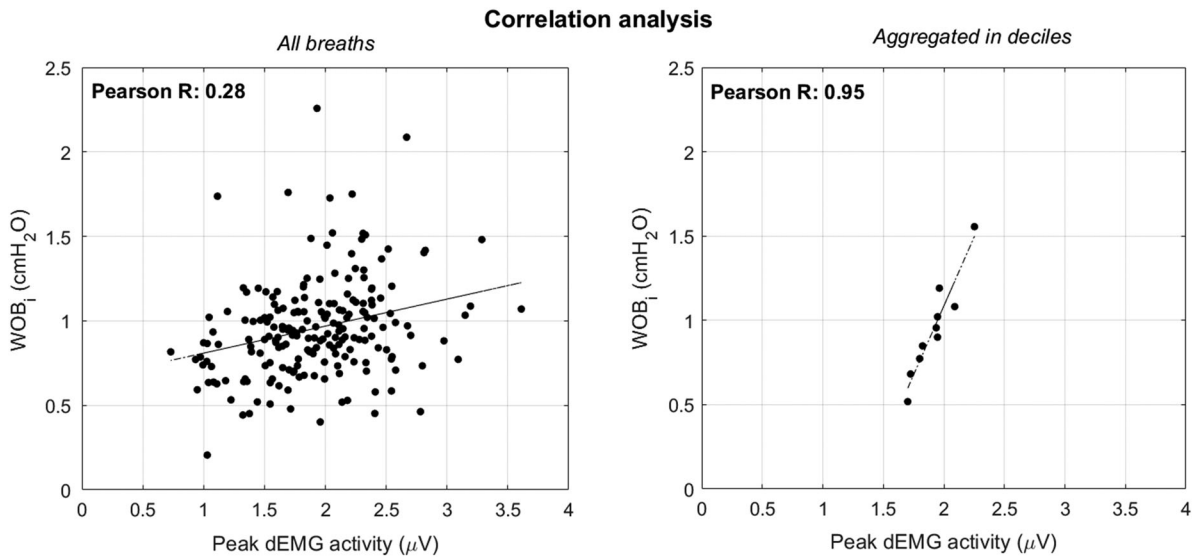
Correlation analysis

FIGURE 2 Correlation analysis of one infant between peak diaphragm activity ($dEMG_{peak}$) measured with electromyography and inspiratory work of breathing (WOB_i) for the single-breath (left) and the aggregated (decile) approach (right) with the respective Pearson R-coefficient in the top-left corner of the graph
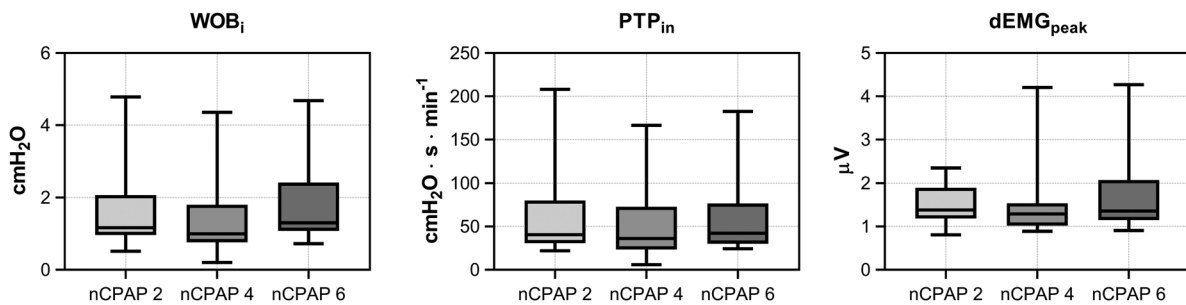

FIGURE 3 Box and whiskers plots showing the level of inspiratory work of breathing (WOB_i), pressure-time product (PTP_{in}), and peak diaphragm activity ($dEMG_{peak}$) during different nasal continuous positive airway pressure (nCPAP) levels (in cmH_2O). No significant differences were found between nCPAP levels for any variable

clinically relevant WOB differences between the nCPAP levels indicates that this attempt was not successful, even though data were selected at the end of each nCPAP level.

To address some of these technical and physiological factors, we performed an aggregated data analysis, clustering single-breath data into WOB_i deciles. Although the use of incremental deciles to cluster data is relatively new, clinical monitoring techniques often use some kind of averaging over time to present their outcome measure and reduce noise, for example, in pulse oximetry.[25,26] The aggregated analysis showed a clear improvement of the median correlation between WOB and dEMG, indicating that noise and lack of contrast were indeed factors of importance when explaining the poor correlation based on single breaths. This finding is in accordance with the study by Bellani et al.[22] who were the first to describe this noise-reduction approach.

Furthermore, we also recalculated the median correlation between WOB and dEMG after excluding four infants with a negative correlation between WOB_i and $dEMG_{peak}$. The most plausible

explanation for this negative correlation is an unrecognized measurement error in either the P_{es} or volume signal. These signals were more prone to small errors (e.g., due to changes in tip position and fluid leakage from the feeding tube) than dEMG, which was properly fixated. Excluding these infants improved the correlation and reduced its variation.

Some have suggested to use PTP_{in} as a measure of WOB, as it only requires P_{es} and not tidal volume, thereby reducing the complexity of the measurement and thus the level of noise.[11,27] However, in the present study, the correlation between PTP_{in} and $dEMG_{peak}$ was similar to WOB_i and $dEMG_{peak}$, indicating no additional benefit of using PTP_{in}, besides the practical considerations.

4.1 | Limitations

This study has several limitations that need to be addressed. First, we used a fluid-filled feeding tube instead of a

balloon-catheter to measure P_{es}. Although we found similar levels of WOB_i compared with studies using a balloon-catheter,[28] tip position changes and fluid leakage may have impacted the P_{es} measurements. Delivering a continuous low-speed fluid infusion may overcome this limitation in future studies.[8,15] Second, the time delay between the P_{es} signal measured by the patient monitor and the other signals had to be corrected. A minor residual delay cannot be ruled out but the impact of this delay was minor because the breaths could be accurately matched offline.

Finally, as indicated by the (unanticipated) low variation in WOB, the included infants had a relatively stable respiratory condition and the sample size of this physiological study was limited. A future study with a larger sample size, also including infants with more severe lung disease, needs to confirm if our results are generalizable to the NICU population.

4.2 | Clinical implication and future perspectives

Our findings seem to suggest that on a single-breath level the correlation between WOB and dEMG is poor. Using this approach in clinical practice cannot be recommended and does not seem very informative. However, in clinical practice, changes in respiratory support are not based on single breaths but more on a trend over time. Recent studies already showed that dEMG is able to monitor breathing in preterm infants and detect changes in diaphragm activity over time following changes in the mode or level of respiratory support.[6,29] The aggregated analysis in this study showed that combining individual breath data results in a modest-to-good correlation between dEMG and WOB. The current analysis is done offline but further development of this technique could result in a bedside tool, which provides a useful WOB assessment from time to time. Our findings warrant further study on dEMG as a noninvasive measure of WOB in preterm infants. These future studies should investigate a larger sample size with more dependency on respiratory support to investigate the relation between diaphragm activity and WOB across a wider range.

5 | CONCLUSION

This study shows a modest but variable correlation between conventional WOB and diaphragm activity, measured with transcutaneous electromyography, in preterm infants on nasal CPAP. Future studies need to confirm this finding in a larger group of infants with more significant lung disease.

CONFLICT OF INTERESTS
AvK received a grant from Vyaire Medical. The remaining authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS
Ruud W. van Leuteren: Conceptualization (equal); data curation (equal); formal analysis (lead); investigation (equal); methodology (equal); project administration (equal); software (equal); writing—original draft (lead); writing—review and editing (equal). **Cornelia G. de Waal**: Conceptualization (equal); data curation (equal); formal analysis (supporting); investigation (equal); methodology (equal); project administration (equal); software (equal); writing—review and editing (equal). **Gerard J. Hutten**: Conceptualization (equal); data curation (equal); formal analysis (supporting); investigation (equal); methodology (equal); project administration (equal); supervision (equal); writing—review and editing (equal). **Frans H. de Jongh**: Conceptualization (equal); data curation (equal); formal analysis (supporting); investigation (equal); methodology (equal); project administration (equal); supervision (equal); writing—review and editing (equal). **Anton H. van Kaam**: Conceptualization (equal); data curation (equal); formal analysis (supporting); investigation (equal); methodology (equal); project administration (equal); supervision (equal); writing—review and editing (equal).

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