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Transcutaneous Electromyography of the Diaphragm: A Cardio-Respiratory Monitor for Preterm Infants

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Summary. Introduction: Chest impedance (CI) is the current standard for cardio-respiratory monitoring in preterm infants but fails to provide direct and quantitative information on diaphragmatic activity. Transcutaneous electromyography (dEMG) is able to measure diaphragmatic activity, but its feasibility and repeatability to monitor respiratory rate (RR) and heart rate (HR) in preterm infants needs to be established. Methods: RR and HR were measured simultaneously by dEMG and CI for 1–hour on day 1, 3, and 7 of life in 31 preterm infants (gestational age 29.6 ± 1.8 weeks; birth weight 1380 ± 350 g) on non-invasive respiratory support. Six fixed 1-minute time intervals were selected from each 1-hour recording and both RR and HR were calculated using all intervals or only those with stable dEMG and CI recordings. Results: dEMG was well tolerated and signal quality was good. Both RR and HR measured by dEMG and CI were significantly correlated (RR: $r = 0.85$, HR: $r = 0.98$) and showed good agreement by the Bland–Altman plot (mean difference (limits of agreement): RR: −2.3 (−17.3 to 12.7) breaths/min and HR: −0.3 (−5.3 to 4.7) beats/min. When analyzing only stable recordings, the correlation ($r = 0.92$) and agreement (−1.8 (−12.3 to 8.7) breaths/min) for RR improved. Subgroup analyses for postnatal age, gestational age, and mode of support showed similar results suggesting good repeatability of dEMG. Conclusion: This study shows that monitoring RR and HR with transcutaneous dEMG is feasible and repeatable in preterm infants. **Pediatr Pulmonol. 2015;50:889–895.**

Key words: respiratory muscle; physiological monitoring; respiratory rate; heart rate; intensive care units; neonatal.

INTRODUCTION

Preterm infants with a gestational age less than 32 weeks are at high risk of respiratory failure with impaired control of breathing as one of the most common causes.[1,2] Under normal circumstances breathing is initiated by the breathing center in the brain stem and this impulse is directed via the phrenic nerve to the diaphragm, the most important breathing muscle.[3,4] Impaired control of breathing, often referred to as 'apnea of prematurity' (AOP), is caused by immaturity of the brain stem (central AOP), (upper) airway obstruction (obstructive AOP), or a combination of the two (mixed AOP).[2] It is clear that monitoring of the respiratory activity is essential in detecting and classifying AOP, since distinction of apnea type will determine the optimal mode of clinical intervention.[5]

In addition to impaired control of breathing, preterm infants often have a compromised lung function resulting in impaired gas exchange and an increased work of breathing.[6] For this reason, most preterm infants are supported non-invasively by either nasal continuous positive airway pressure (nCPAP) or flow provided via nasal cannula (nFlow). The goal is to optimize lung function and reduce the work of breathing.[7,8] Ideally, selection and weaning of the mode and level of non-invasive respiratory support should be based on bedside, continuous and quantitative information on (diaphragmatic) breathing activity, or the (diaphragmatic) work of breathing.[9]

To date, respiratory activity in preterm infants is mainly monitored by chest impedance (CI), which measures

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changes in electrical impedance caused by changes in lung aeration and chest wall movements via three transcutaneous ECG electrodes.[5] CI provides continuous monitoring of heart rate (HR) and respiratory rate (RR) and the latter is also used for detection of AOP. However, CI has important limitations as it does not provide direct and quantitative information on diaphragmatic activity and often provides inaccurate data due to non-breathing related chest wall movements and cardiac interference.[10,11] This limits its ability to detect and classify AOP and to select the optimal mode and level of non-invasive respiratory support.[5,12]

Measuring diaphragmatic activity directly via electromyography (dEMG) might overcome these shortcomings of CI. dEMG can be measured non-invasively using three transcutaneous chest electrodes.[13] Studies have shown that transcutaneous dEMG measurement is feasible in adults, children, and term infants.[14,15] Furthermore, studies in healthy term infants and infants with established bronchopulmonary dysplasia showed that dEMG provides information on both lung mechanics and work of breathing.[16] Explorative studies on transcutaneous dEMG in preterm infants have been reported over 30 years ago, but, to date, this technique has not been validated in this population.[17–19]

Therefore, the aim of this study was to determine the feasibility and repeatability of transcutaneous EMG of the diaphragm in preterm infants and to compare its most basic function as a cardio-respiratory monitor, that is providing online data on RR and HR, to CI. We considered this a first and essential step before future studies can address the additional value of dEMG in detection and classification of AOP and in determining the optimal mode and level of respiratory support in preterm infants.

MATERIALS AND METHODS

This prospective observational cohort study was performed in the Neonatal Intensive Care Unit (NICU) of the Emma Children's Hospital, Academic Medical Center, Amsterdam, The Netherlands. We enrolled clinically stable preterm infants with a GA between 26 and 32 weeks treated with nCPAP or nFlow (1 L/min). Patients with congenital anomalies were excluded from the study. The study protocol was approved by the Institutional Review Board and written informed consent was obtained from parents.

CI and dEMG Recording

All infants were studied in supine position and RR and HR were recorded simultaneously by CI and dEMG for 1 hour on days 1, 3, and 7 after birth. During recording no nursing procedures were performed.

The three CI electrodes were placed at the standard positions and connected to an Intellivue MP-90 monitor (Philips Healthcare, Eindhoven, The Netherlands). Using an isolated cable the MP-90 monitor was connected to a personal computer at the bedside and data on HR en RR were extracted and recorded at a sample rate of 500 Hz using a custom made software package (Polybench version 1.25.2, Applied Biosignals, Weener, Germany).

Transcutaneous dEMG measurements were performed using three electrodes (H59P Cloth Electrodes, Kendall) connected to a portable 16-channel digital physiological amplifier (Dipha-16, Inbiolab BV, Groningen, The Netherlands). Two electrodes were bilaterally placed at the costo-abdominal margin in the nipple line and one at the sternum.[14,15] Technical measurements aspects and details on validation, pre- and post-processing, sampling rate, filtering algorithm, and signal-to-noise ratio have been described by O'Brien et al.[14,20] Briefly, dEMG data were digitized without analogue filtering, conditioned by the Dipha-16 front-end and send to a personal computer via a wireless connection. The raw dEMG signal was digitally pre-processed and recorded in sync with the MP-90 data. The dEMG signal was band-pass filtered from 40 Hz to 160 Hz. The electrical activity of the heart was isolated from the signal according to the gating technique described by O'Brien et al.[20] and used for HR analyses. This technique involves removal of the QRS complex from the dEMG signal after which the remaining gate was filled with the running average. The resulting gated diaphragmatic muscle activity was averaged (Fig. 1) and used for RR analysis. On-line data acquisition, pre-processing, off-line post-processing and analysis were performed by the software package Polybench.

Data Collection and Analysis

We collected the following patient characteristics: gestational age, birth weight, and data on the mode and settings of respiratory support. The investigator reviewed the skin tolerance before and 30 min after removal of the dEMG electrodes and visually assessed the skin for redness, swelling, and lesions. The dEMG signal was checked for electrical interference.

From each 1-hour recording on day 1, 3, and 7, we selected 1-minute time intervals at six fixed time intervals (5, 15, 25, 35, 45, 55 min) and calculated the mean RR and mean HR of each interval, independent of the signal stability. This (fixed analysis) provided comparative data under normal clinical conditions and, more importantly, allowed us to compare signal stability between dEMG and CI. As signal instability will impact correlation and agreement, we repeated this analysis including only those 1-minute time intervals that showed stable CI and dEMG recordings. This (stable analysis) allowed us to have a true head to head comparison of both techniques. Finally,

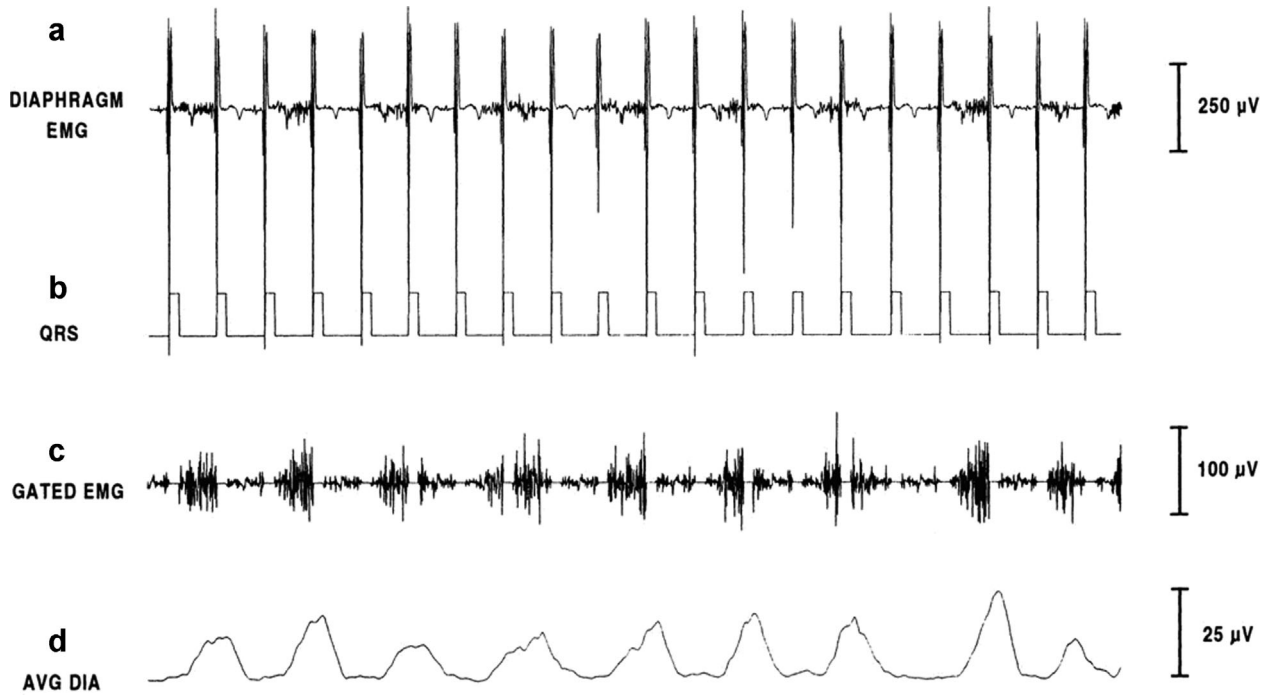

Fig. 1. Representative example of dEMG processing;[20] (a) the raw electrical activity of the diaphragm (low amplitude) and ECG components (high amplitude); (b) detection of QRS complex shown as normalized pulse; (c) gated dEMG signal; (d) averaged dEMG signal.

subgroup analyses were performed based on postnatal age (day 1, 3, and 7), GA (26–28, 28–30, 30–32 weeks) and mode of respiratory support (nCPAP or nFlow).

Data were expressed as mean ± standard deviation (SD), unless stated otherwise. Comparative analyses for RR and HR were performed by Pearson's correlation coefficient (r) and Bland–Altman plots to assess the mean difference (MD) and the limits of agreement (MD ± 1.96 SD) between the measurements on different postnatal age (repeatability).[21] For the Bland–Altman analyses we considered each 1-minute time interval as an independent observation, as HR and RR is a continuously changing parameter in preterm infants. To make sure this did not introduce a systematic error we performed an additional Bland–Altman analysis using only one time point from each patient. As this did not change the results, only the summarized analyses are reported. A P-value less than 0.05 was considered statistically significant. Statistical analyses and graphics were performed using SPSS version 19.0 (SPSS Inc. Chicago, IL) and Graphpad Prism 5.0 (GraphPad Software, San Diego, CA).

RESULTS

We included 31 preterm infants in the study with a mean GA of 29.6 ± 1.8 weeks and a birth weight of 1380 ± 350 g.

Due to the need for mechanical ventilation on day 1 (n = 4) and early transfer to regional hospitals between day 1–3 (n = 5) or day 3–7 (n = 6), 27 infants were measured on day 1, 26 infants on day 3, and 20 infants on day 7. Sixteen patients completed all three measurements.

All infants tolerated placement of the electrodes well and no skin lesions were detected after removal. In one recording (on day 1) the dEMG signal quality was poor due to electrical interference of 50 Hz and the measurement was therefore excluded from further analysis. dEMG signal quality was good for 72 of the 73 recordings (99%), leaving 432 1-minute time intervals for the final analysis.

RR measured by dEMG was significantly correlated to CI ($r = 0.85$, $P < 0.001$) and the Bland–Altman plot between both techniques showed a mean difference of −2.3 breaths/min with limits of agreement between −17.3 and 12.7 breaths/min (Fig. 2a, Table 1).

RR signal instability was present in 69 (16%) of the 432 1-minute time intervals and this was due to both dEMG and CI signals instability in 32 intervals (46%), during only CI instability in 21 intervals (31%; Fig. 3) and during only dEMG instability in 16 intervals (23%). Analysis of the remaining 363 stable time intervals showed an improved correlation for the RR between dEMG and CI ($r = 0.92$, $P < 0.001$) and an improved agreement with a mean difference of −1.8 breaths/min with limits of

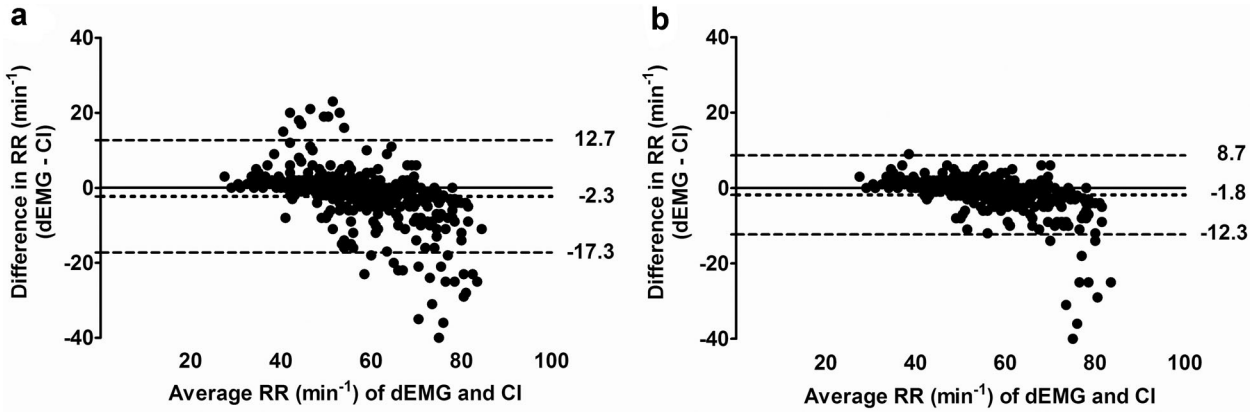

Fig. 2. Bland–Altman of RR between dEMG and CI. Bland–Altman plot comparing the RR (breaths/min) measured with dEMG and CI. The mean difference is indicated by the dotted line and the lower and upper limits of agreement by the striped line. (a) RR using fixed intervals; mean difference, −2.3 breaths/min; limits of agreement, −17.3 to 12.7 breaths/min. (b) RR using stable intervals; mean difference, −1.8 breaths/min; limits of agreement, −12.3 to 8.7 breaths/min.

agreement between −12.3 to 8.7 breaths/min (Fig. 2b, Table 1). All outliers were found in one patient (day 1, GA 30–32 weeks, nCPAP) in whom small amplitude breaths were not classified as separate breaths by the dEMG algorithm, resulting in a lower RR compared to CI (Fig. 4).

Analysis of the HR measured by dEMG and CI showed an excellent correlation ($r = 0.98$, $P < 0.001$) and agreement with a mean difference of −0.3 beats/min between dEMG and CI and limits of agreement between −5.3 and 4.7 beats/min (Table 1). In addition to quantitative data on HR, dEMG also provided more detailed information on the, P-wave, QRS complex, and T-wave (Fig. 5).

Subgroup analyses based on postnatal age, gestational age, and mode of respiratory support using all (432 fixed time) intervals showed similar correlations and agreements for RR and HR between dEMG and CI as compared to the overall group (Table 1).

DISCUSSION

Despite a few explorative studies in the 1980's,[17,18] the feasibility and repeatability of transcutaneous dEMG in preterm infants has so far not been studied. Our study shows, for the first time, that transcutaneous dEMG monitoring is feasible and repeatable in stable preterm infants on non-invasive respiratory support and provides continuous data on RR and HR comparable to the current standard, that is CI monitoring.

To date, transcutaneous dEMG has only been investigated and validated in adults, children, and term-born infants.[14,15] Preterm infants clearly differ in terms of chest size, diaphragmatic insertion, and skin condition, all of

TABLE 1—Correlation and Agreement Between dEMG and CI for RR and HR in Different Subgroups

	Fixed	Stable	Day 1	Day 3	Day 7	26–28w	28–30w	30–32w	nCPAP	nFlow
N	31	31	26	26	20	6	10	15	26	12
Intervals	432	363	156	156	120	96	174	162	330	102
RR										
r	0.85	0.92	0.79	0.85	0.93	0.87	0.92	0.79	0.83	0.92
MD	−2.3	−1.8	−3.8	−1.9	−0.8	−0.6	−1.7	−3.9	−2.4	−1.9
1.96 SD	14.9	10.4	17.4	15.1	9.8	12.3	11.2	18.8	16.5	9.0
HR										
r	0.98	0.98	0.98	0.98	0.95	0.99	1.00	0.94	0.98	0.98
MD	−0.3	−0.3	−0.5	−0.1	−0.4	−0.2	0.0	−0.8	−0.3	−0.5
1.96 SD	4.9	4.5	4.9	4.7	5.5	3.5	1.8	7.3	5.1	3.3

Postnatal age: day 1, 3, and 7. Gestational age strata 26–28 weeks, 28–30 weeks, and 30–32 weeks. Type of respiratory support nCPAP and nasal cannula (nFlow).
N = number of patients involved in the analysis. Intervals = amount of selected time intervals. *r* = Pearson's correlation coefficient, all statistical significant ($P < 0.01$). MD = Bland–Altman's mean difference and 1.96 SD.

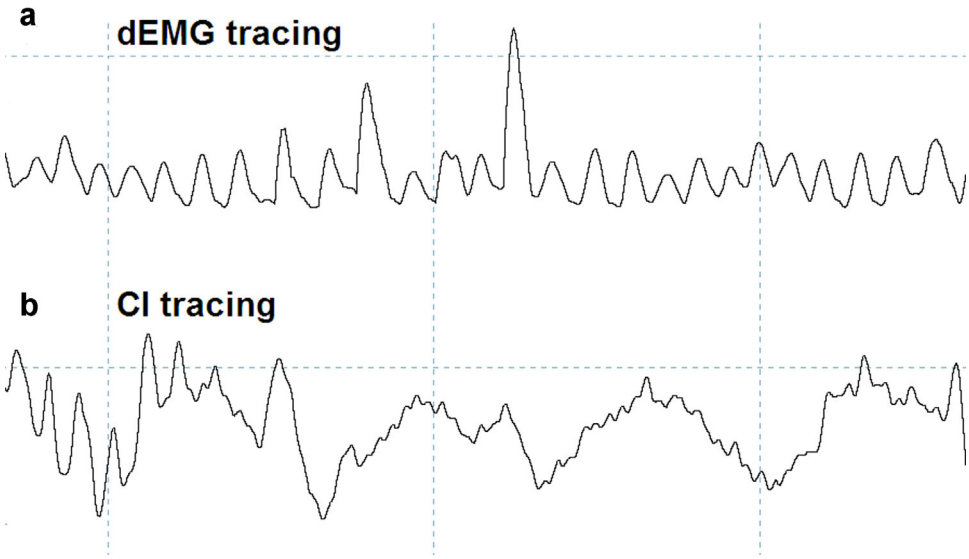

Fig. 3. Representative example of differences in signal stability between dEMG and CI, showing (a) a stable dEMG tracing in the top panel and (b) an instable CI tracing in the lower panel.

which may affect feasibility of dEMG measurements in this vulnerable population. Our feasibility study shows that despite these physiological differences, dEMG measurements are well tolerated and provide good signal quality in preterm infants. In only one recording the dEMG signal quality was poor due to a low frequency, most likely electrical, interference. However, we were unable to detect the origin of this interference. The good dEMG signal quality is reassuring, considering the fact that the NICU is filled with electrical equipment.

In addition to its feasibility we also assessed transcutaneous dEMG as a cardio-respiratory monitor in preterm infants. We compared dEMG to CI, as this is currently the most widely used method for cardio-respiratory monitoring in the NICU. In the initial analysis we selected 1-minute time intervals at six fixed time points and included all recordings in the analysis, independent of signal stability. Although this first analysis revealed a good correlation ($r = 0.85$) and agreement between CI and dEMG in terms of RR, the limits of agreement were relatively wide. Further analysis revealed the presence of CI and/or dEMG signal instability in 16% of the selected fixed intervals, which is consistent with daily clinical practice. In more than half of these intervals,

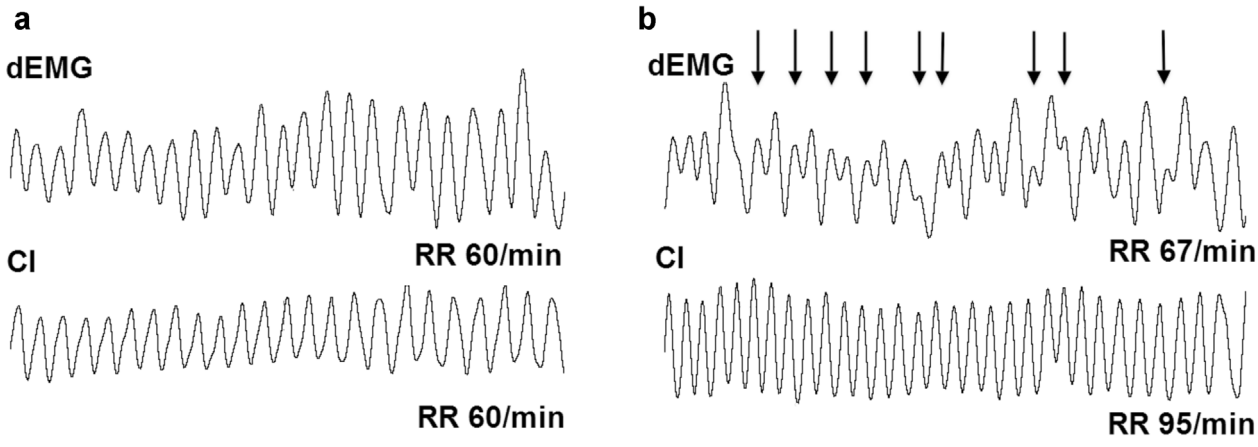

Fig. 4. Algorithm differences of dEMG. Panel (a) shows good agreement between the RR (60 breaths/min) measured by dEMG and CI. Panel (b) shows small fluctuations in the dEMG signal (black arrows) that are not classified by the detection algorithm as separate breaths, resulting in a RR of 67 breaths/min measured by dEMG and 95 breaths/min by CI. This finding was present in only one measurement.

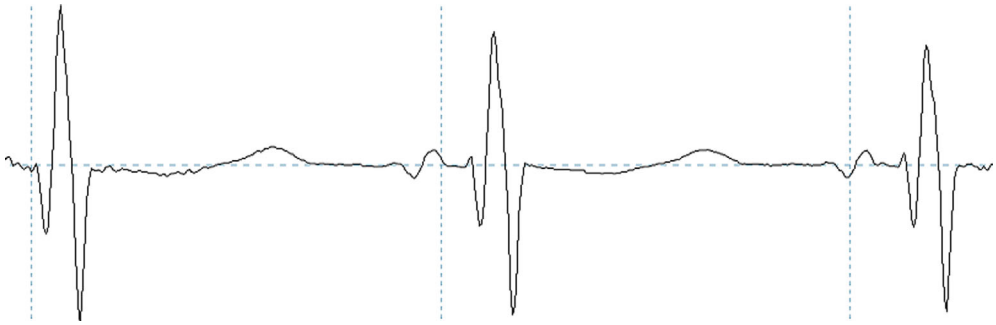

Fig. 5. Representative example of the filtered dEMG signal showing a P-wave, QRS complex, and T-wave.

only one of the signals (dEMG or CI) was instable, which is probably best explained by the fact that dEMG and CI use different techniques (electrical activity vs. impedance) to measure RR. It was reassuring to observe that the frequency of dEMG signal instability was slightly lower than CI signal instability. As the difference in signal stability between dEMG and CI will undoubtedly impact the RR agreement in the Bland–Altman plot, we performed a second analysis using only stable 1-minute time intervals, an approach often used when comparing respiratory signals.[14,16] As expected, RR correlation ($r = 0.92$) and agreement between dEMG and CI improved markedly with much narrower limits of agreement.

Interestingly, we also found a few outliers in the Bland–Altman plot, all originating from the same measurement of one particular patient. A closer look at the averaged signals of this measurement showed that the dEMG detection algorithm did not classify small diaphragmatic contractions as separate breaths resulting in a lower RR compared to CI (Fig. 4). Unfortunately, we are unable to determine which of the measurements (dEMG or CI) provided the correct RR. Possible explanations are overestimation of small superficial diaphragmatic contraction by the CI algorithm or underestimation of true small amplitude breaths by the dEMG algorithm. The fact that this observation only occurred in one measurement is reassuring and makes a structural flaw in the dEMG detection algorithm unlikely.

Our observation that RR and HR correlation and agreement between dEMG and CI was similar in the different subgroups based on postnatal age, gestational age, and mode of support, strongly indicates that dEMG monitoring in preterm infants also has good repeatability. The small differences in correlation and agreement observed between the different subgroups are mainly due to the outliers of one patient as discussed above. These results are in accordance with previous studies also showing good repeatability of dEMG in adults, children, and infants.[14,15]

dEMG also records electrical activity of the heart, which can be separated from diaphragmatic activity using a signal filtering algorithm. This way dEMG can also provide data on HR monitoring. Our study showed that there is an excellent correlation and agreement in terms of HR between dEMG and CI. In addition to quantitative data on HR, dEMG also allows for more qualitative analysis of the QRS complex, as shown in Fig. 5.

Although not primarily designed for cardio-respiratory monitoring, recent studies have shown that dEMG measurements are also feasible via an esophageal catheter incorporated in modern ventilators.[22,23] However, compared to this trans-esophageal route, transcutaneous dEMG is less invasive, easy applicable and less expensive as it requires only three basic skin electrodes, instead of a specially designed and manufactured catheter. Some authors have expressed concerns about signal contamination by adjacent muscles during transcutaneous dEMG monitoring, also referred to as crosstalk.[4] However, several studies have demonstrated that this crosstalk is not present when using the dEMG technique described in this study.[14,24]

This study has limitations that need to be addressed. First, our study did not include patients with a gestational age below 26 weeks. In our and many units this vulnerable population is not monitored by CI in order to avoid skin lesions caused by electrodes placement. Second, repeatability could not be studied in all patients as only a subgroup of 16 patients completed all three consecutive measurements on day 1, 3, and 7 of life. However, correlation and agreement of these 16 infants did not differ from the total group, suggesting that the missing values did not impact the findings on repeatability.

The results of this study may have important clinical implications. Although widely used for cardio-respiratory monitoring, CI has its limitations as it does not measure diaphragmatic activity directly and does not provide quantitative information on breathing activity. This limits its ability to detect and classify AOP and to optimize the mode and level of respiratory support based on

diaphragmatic activity. As dEMG provides direct information on breathing activity it might improve AOP detection and classification. We hypothesize that central AOP can be detected by absence of diaphragmatic activity and obstructive AOP when diaphragmatic activity is increased. Studies in preterm infants have also shown that electrical activity of the diaphragm measured by transcutaneous dEMG correlates well with diaphragmatic work of breathing.[9] In addition, it has been shown in adults and children that dEMG is able to detect changes in diaphragmatic activity in response to changes in disease state/condition.[16,25] Finally, studies in newborn infants have shown that breath-by-breath fluctuations in diaphragmatic activity are a reflection of the rapid adaptive capacity of the diaphragm to maintain optimal lung ventilation and to obtain a constant inspiratory flow.[15] Based on these studies, we hypothesize that dEMG monitoring can provide relevant information on diaphragm activity and that this information can be used to select the optimal mode and level of respiratory support. The results of this study should therefore be seen as a first step before determining the additional value of dEMG monitoring in preterm infants. The fact that we have shown that cardio-respiratory monitoring of RR and HR is feasible and comparable to CI warrants future studies to look at dEMG for AOP detection and classification and monitoring of breathing activity.

In conclusion, this study shows that transcutaneous electromyography of the diaphragm is feasible in preterm infants. Cardio-respiratory monitoring of RR and HR shows similar results compared to the CI technique. Future studies will have to investigate the additional value of dEMG in detection and classification of AOP and in selecting the optimal mode and level of respiratory support.

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