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Simultaneous measurement of diaphragm activity, chest impedance, and ECG using three standard cardiorespiratory monitoring electrodes

Anouk W. J. Scholten MSc[1,2] | Ruud W. van Leuteren PhD[1,2] | Frans H. de Jongh PhD[1,3] | Anton H. van Kaam MD, PhD[1,2] | Gerard J. Hutten MD, PhD[1,2]

[1]Department of Neonatology, Amsterdam UMC location University of Amsterdam, Amsterdam, The Netherlands

[2]Amsterdam Reproduction & Development research institute, Amsterdam, The Netherlands

[3]Faculty of Science and Technology, University of Twente, Enschede, The Netherlands

Correspondence

Anouk W. J. Scholten, MSc, Department of Neonatology, Amsterdam UMC location University of Amsterdam, Meibergdreef 9, 1105AZ Amsterdam, The Netherlands.
Email: a.w.j.scholten@amsterdamumc.nl

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Abstract

Introduction: Current cardiorespiratory monitoring in neonates with electrocardiogram (ECG) and chest impedance (CI) has limitations. Adding transcutaneous electromyography of the diaphragm (dEMG) may improve respiratory monitoring, but requires additional hardware. We aimed to determine the feasibility of measuring dEMG and ECG/CI simultaneously using the standard ECG/CI hardware, with its three electrodes repositioned to dEMG electrode locations.

Methods: Thirty infants (median postmenstrual age 30.4 weeks) were included. First, we assessed the feasibility of extracting dEMG from the ECG-signal. If successful, the agreement between dEMG-based respiratory rate (RR), using three different ECG-leads, and a respiratory reference signal was assessed using the Bland-Altman analysis and the intraclass correlation coefficient (ICC). Furthermore, we studied the agreement between CI-based RR and the reference signal with the electrodes placed at the standard and dEMG position. Finally, we explored the quality of the ECG-signal at the different electrode positions.

Results: In 15 infants, feasibility of measuring dEMG with the monitoring electrodes was confirmed. In the next 15 infants, comparing dEMG-based RR to the reference signal resulted in a mean difference and limits of agreement for ECG-lead I, II and III of 4.2 [−8.2 to 16.6], 4.3 [−10.7 to 19.3] and 5.0 [−14.2 to 24.2] breaths/min, respectively. ICC analysis showed a moderate agreement for all ECG-leads. CI-based RR agreement was similar at the standard and dEMG electrode position. An exploratory analysis suggested similar quality of the ECG-signal at both electrode positions.

Conclusion: Measuring dEMG using the ECG/CI hardware with its electrodes on the diaphragm is feasible, leaving ECG/CI monitoring unaffected.

KEYWORDS

neonates, respiration, transcutaneous electromyography

1 | INTRODUCTION

Preterm infants often experience apnea of prematurity, resulting in intermittent hypoxemia and bradycardia due to their immature lungs and respiratory control.[1] Cardiorespiratory monitoring is therefore required to detect and subsequently treat these events to prevent associated morbidity and mortality.[2] Currently, this is performed by measuring heart rhythm and rate (HR), respiratory rate (RR), and breathing pattern with the electrocardiogram (ECG) and chest impedance (CI), respectively, using three adhesive electrodes. However, CI provides an indirect measure of spontaneous breathing, as this technique measures changes in thoracic impedance caused by alterations in lung aeration. Measuring the RR with CI can become inaccurate as the impedance is also influenced by nonbreathing related chest wall movements.[3] Furthermore, CI only provides information on the RR and not the breathing effort of the infants.

These possible disadvantages of using CI for RR monitoring may be overcome by measuring the electrical activity of the diaphragm, the main respiratory muscle, using an esophageal or transcutaneous electromyography (dEMG) interface. Transcutaneous dEMG has the advantages of being noninvasive, cheap and independent of the type of ventilator. Previous studies have shown that cardiorespiratory monitoring with dEMG is feasible in preterm infants, improves apnea detection, and allows assessment of the effect of respiratory medication (e.g., caffein) or changes in respiratory support on the infant's breathing effort.[4–8] Simultaneous measurement of ECG and dEMG might therefore be the most ideal combination for cardiorespiratory monitoring. However, this setup would require additional dEMG hardware and the placement of three extra adhesive electrodes on the vulnerable skin of preterm infants as the electrode positions differ between dEMG and ECG/CI.

If the dEMG-signal could be retrieved from the ECG/CI signal using the three standard ECG/CI electrodes and its hardware, this would be an important step toward clinical implementation of dEMG for cardiorespiratory monitoring. dEMG recording would become available in all units with standard ECG/CI monitoring equipment and this would allow collection of dEMG data in a large group of infants, which could result in normative dEMG data for different clinical conditions and treatment modalities. A previous study in adults already showed that dEMG can be retrieved from surface ECG but to date this has not been studied in preterm infants.[9]

Therefore, this study aims to assess the feasibility and accuracy of measuring the RR with dEMG and ECG/CI simultaneously, using the ECG/CI hardware with the three electrodes placed at the standard dEMG electrode position. We hypothesize that dual monitoring is feasible and that RR monitoring using dEMG is at least as accurate as CI.

2 | METHODS

This prospective, observational study was performed in the level III neonatal intensive care unit (NICU) of the Emma Children's Hospital, Amsterdam UMC, Amsterdam, the Netherlands between August 2020 and December 2021. The medical ethical committee provided a waiver with respect to the necessity of informed consent, as participants were not subjected to procedures nor were they required to follow rules of behavior. Nevertheless, written parental consent was obtained for anonymous data storage and use within the study.

This study consisted of two phases. In the first phase, we studied the general feasibility of retrieving dEMG from the ECG-signal and the ability to convert this signal to a respiration waveform using a developed algorithm. Only when the first phase confirmed feasibility, a second phase was started, in which the RR calculated with the dEMG algorithm was compared to a reference respiratory signal. This comparison was made per ECG-lead to observe if the ability to measure respiration with dEMG varied per lead. Moreover, the ability to maintain adequate measurement of CI and ECG at the dEMG measurement location was investigated.

2.1 | Study population

In both phases, infants born with a gestational age (GA) >26 weeks admitted to the NICU requiring standard ECG/CI-monitoring were included. However, in phase 2 of the study the infants needed to receive nasal continuous positive airway pressure (nCPAP) as well to enable an airway pressure measurement in the nCPAP circuit, which only served as a reference for the RR over time. Infants in whom it was not possible to place the electrodes at the height of the diaphragm (e.g., chest drain or stoma) were excluded.

2.2 | Study procedures

2.2.1 | Phase 1

During routine care the ECG/CI electrodes (Figure 1A) were repositioned to the dEMG positions; the light and dark gray electrode were placed bilaterally at the costo-abdominal margin in the nipple line, while the medium gray reference electrode was placed at the sternum (Figure 1B). An intentional signal artifact was created by reconnecting one electrode cable to mark the start of the measurement. This was repeated once more after approximately 3 h, to mark the end of the measurement and the electrodes were placed back to their original position.

2.2.2 | Phase 2

A pressure sensor was incorporated in the expiratory limb of the nCPAP device as close as possible to the patient and the fluctuations in pressure during spontaneous breathing were used to obtain a reference for RR. First, a baseline measurement was performed at standard ECG/CI electrode positions. Artifacts were introduced to mark the start and end of a 30-min measurement. Next, during nursing care the electrodes were repositioned to the dEMG positions.

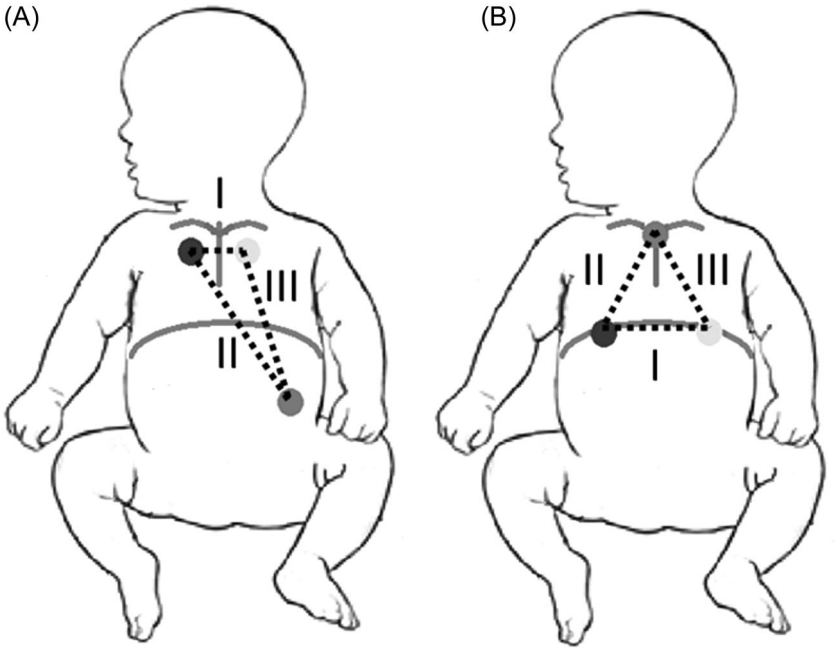

FIGURE 1 The standard electrode positions to measure the electrocardiogram (ECG) and chest impedance (CI) with the corresponding three ECG-leads (A). The ECG/CI electrodes placed at the positions of a transcutaneous electromyography measurement of the diaphragm (dEMG), with the corresponding ECG-leads (B).

Subsequently, data was collected for 30 min for each individual ECG-lead available in the patient monitor (Lead I, II, and III) as only the chosen ECG-lead on the patient monitor could be stored.

2.3 | Data acquisition

In contrast to previous studies no dEMG specific hardware was used to record electrical activity of the diaphragm in phase 1 and 2 of the study. Instead we used the standard ECG/CI set-up with unshielded electrodes to capture all electrical data, which was stored in a data warehouse (DWH; Data WareHouse Connect; Philips Healthcare) with a sampling frequency of 500 Hz.[10,11] Moreover, the dEMG recording based on the ECG data was unipolar instead of bipolar. During phase 2 of the study the pressure sensor was connected to a Bicore-II (Vyaire Medical), which communicated with a bedside computer that recorded the data with customized software (Polybench; Applied Biosignals). The ECG and CI waveforms from the patient monitor (Intellivue MP90; Philips Healthcare) were also imported in this bedside computer, but at a lower sampling frequency of 200 Hz.

2.4 | Data analysis

In the first phase, feasibility of obtaining the dEMG out of the ECG was determined by assessing if a respiratory waveform could be acquired. Based on previously described signal analysis steps we developed an algorithm to retrieve a dEMG based respiratory waveform out of the ECG-signal extracted from DWH.[12] First, the ECG, with incorporated dEMG, was high-pass filtered to remove offset, signal drift and T-waves. A copy of this filtered signal was rectified and low-pass filtered to ease QRS-detection, using a peak follower. The detected QRS-complexes and P-waves (at a fixed distance from the QRS-complex) were gated out and filled with a copy of preceding data. Then, the data was filtered with a 50 Hz notch filter, to remove power supply interference caused by electromagnetic fields produced by surrounding hardware that are picked up by the electrode wires and induce an unwanted current at this frequency.[12,13] The resulting signal was moving averaged to obtain a smoothened respiratory waveform.

During the second phase, the ECG, CI, and airway pressure were collected from the bedside computer. Separately, the dEMG was extracted from the ECG stored at a higher sampling frequency in DWH. All data was synchronized using the start and end artifacts captured in the ECG that was stored in both the bedside computer and the DWH. To correct for potential remaining minor differences in time between the two signals, additional synchronization was performed per 10 min using cross-correlation analysis. First, stable data was manually selected in all pressure signals independent of dEMG or CI signal stability, as this was our reference measurement. Therefore, during periods of low-quality pressure signals, no comparison was made between pressure, CI, and dEMG. Second, in the parts with stable pressure, stable CI data (at the standard position and at the dEMG position) and stable dEMG data (per ECG-lead) were manually selected using the waveform data and expressed as the percentages of the total recording with a stable pressure signal. Then, during stable pressure breaths the CI and dEMG signals were used to calculate the minute average RR-values. This analysis was repeated using only the recordings showing stability in all three signals (pressure, CI, and dEMG).

To exploratively study the interpretability of the ECG at the dEMG position compared to the standard position, a random 5 s ECG-signal was selected on the standard position and per ECG-lead on the dEMG position. These signals were incorporated into one plot

TABLE 1 Patient characteristics

	First study phase (*n* = 15)	Second study phase (*n* = 15)
Gestational age (weeks)	27.4 (26.3–28.0)	28.7 (25.6–30.6)
Birth weight (g)	902.9 ± 122.8	1106.0 ± 428.5
Post-menstrual age at the start of the measurement (weeks)	30.5 ± 1.4	30.1 (28.9–31.1)
Weight at the start of the measurement (g)	1146.3 ± 252.6	1176.6 ± 370.9
Male gender, *n* (%)	7 (46.7)	8 (53.3)
Caffeine, *n* (%)	7 (46.7)	15 (100)
Mode of respiratory support, *n* (%)		
nIPPV	1 (6.7)	N/A
nCPAP	9 (60.0)	10 (100)
HFNC	5 (33.3)	N/A
nCPAP pressure at the start of the measurement (cmH_2O)	N/A	6.3 ± 1.0

Note: All continuous values are expressed as mean ± standard deviation or median (interquartile range). Categorical values are expressed as *n* (%).
Abbreviations: HFNC, High-Flow Nasal Cannula; N/A, not applicable; nCPAP, nasal continuous positive airway pressure; nIPPV, nasal intermittent positive pressure ventilation.

per infant. These plots were exploratively and visually assessed on clinical usability by a clinical expert (J. H.). All data analysis was performed offline in Matlab (v2019b; MathWorks).

2.5 | Outcome measures

To study the feasibility and accuracy of measuring dEMG with standard ECG/CI electrodes, the following outcome measures were studied:

(1) The ability to obtain a respiratory waveform out of the ECG measured with ECG/CI electrodes, repositioned to the diaphragm (phase 1).
(2) Level of RR-agreement between dEMG and airway pressure per ECG-lead (phase 2).
(3) Level of RR-agreement between CI and airway pressure at the standard electrode positions and at the dEMG positions (phase 2). Of note, the CI is always measured with the same two electrodes.

The percentage of stable dEMG data (per ECG-lead) during periods with a stable pressure signal was calculated to determine which ECG-lead provided the highest amount of usable dEMG data. Moreover, the percentage of stable CI data during a stable pressure signal was calculated to determine if the CI quality was comparable at both electrode positions. Finally, the ability to measure a clinically useful ECG-signal (at each ECG-lead) at the dEMG position was studied.

2.6 | Statistical analysis

All continuous parametric data were presented as mean ± standard deviation and nonparametric data as median with interquartile range (IQR). The level of agreement for the various endpoints was expressed with the Bland–Altman analysis and the intraclass correlation coefficient (ICC). Statistical testing was performed to compare the RR-difference (RR measured with airway pressure minus RR measured with CI) between the standard position and the dEMG position using the independent samples *t*-test or Mann–Whitney *U* test, depending on the data's distribution. These tests were also used to compare the percentages of stable dEMG data measured in the three ECG-leads as well as the percentages of stable CI data measured at the standard position and the dEMG position. All statistical analyses were performed using SPSS (Version 28; IBM). As this is the first study in preterm infants exploring the feasibility and accuracy of measuring RR with ECG hardware, a formal sample size calculation could not be performed and a convenience sample of 30 infants was included.

3 | RESULTS

Fifteen infants were included in phase 1 with a median GA of 27.4 (IQR: 26.3–28.0) weeks (see Table 1). The ECG-lead that was used in clinical care before the start of the first study phase, was not changed and this resulted in lead I, II, and III being used in 1, 11, and 3 measurements, respectively. In all measurements, respiratory activity was observed after removing the cardiac activity. Moreover, using our developed algorithm, a dEMG based respiratory waveform could be derived from all patients. Figure 2 shows a representative ECG-tracing, with incorporated dEMG, during the different signal analysis steps that eventually result in a respiration waveform. Parts of the dEMG measurements showed baseline fluctuations, though breathing cycles could be easily distinguished.

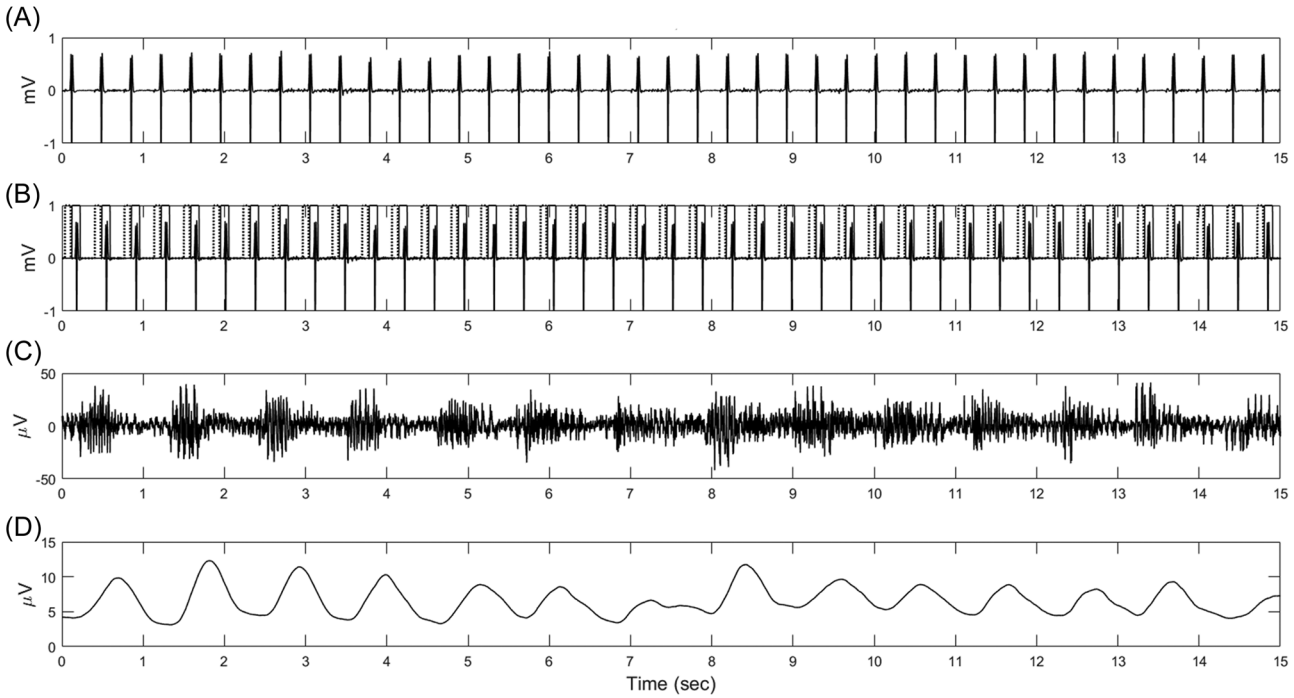

FIGURE 2 Steps to obtain a respiratory waveform out of a representative ECG-tracing with incorporated electrical activity of the diaphragm. (A) The ECG-signal (in this case lead 2) after high pass filtering to remove the offset and drift. (B) The shifted (due to delay caused by QRS-detection) ECG-signal with gates around the detected QRS-complexes (solid line) and P-waves (dotted line, at a fixed distance). (C) The result after gating, filling with a copy of previous data and 50 Hz notch filtering. (D) The respiratory waveform after rectification and moving average filtering. ECG, electrocardiogram.

In phase 2, 15 infants were included as well with a median GA of 28.7 (IQR: 25.6–30.6) weeks (Table 1). The median percentage of time with a stable pressure signal in all measurements was 52.6% (44.9%–64.6%). In these periods with stable pressure, the percentages of time with stable dEMG data in lead I, II and III were 76.1% (68.8%–80.4%), 75.4% (64.4%–87.3%) and 61.7% (44.1%–77.6%), respectively, with only the difference between lead II and III reaching statistical significance ($p = 0.036$). For CI, the percentages with data during stable pressure were similar at both positions (standard: 75.6% (54.1%–88.3%), dEMG positions: 63.9% (47.7–80.8%), $p = 0.22$).

During stable pressure, the Bland-Altman analysis and ICC showed a moderate agreement for the RR measured with dEMG at each ECG-lead compared to the pressure-based RR (Table 2). The RR-agreement between CI and pressure was low but comparable at the standard location and at the dEMG location (Table 2). This was also confirmed by the finding that the mean RR-difference (pressure minus CI) at the standard position and at the dEMG position were similar ($p = 0.20$).

The RR-agreement between airway pressure and CI or dEMG improved when all three signals were stable (Table 3). This is also shown in Figure 3, where breathing cycles could be easily distinguished in simultaneously measured stable tracings of the pressure, CI and dEMG (ECG-lead I).

Generally, a reasonably stable ECG-waveform was obtained in all three ECG-leads on the dEMG electrode position in all patients. Moreover, P-waves and QRS-complexes were observed. Representative tracings on the standard position and on the dEMG positions are shown in Figure 4.

4 | DISCUSSION

To our knowledge, this is the first study investigating and confirming the feasibility of measuring dEMG using the ECG/CI hardware with its electrodes placed at the height of the diaphragm. We show that most (75%) of the dEMG recording is stable and that dEMG-based RR in all three ECG-leads shows a moderate agreement with an airway pressure reference signal. This agreement is similar or better than CI-based RR measured at the standard ECG/CI and dEMG electrode position.

In the first study phase, we confirmed a previous observation in adults, that the dEMG can be measured in the ECG recording in neonates.[9] In contrast to the study of Helfenbein et al. we placed the electrodes at the height of the diaphragm in accordance with previous dEMG studies as we were solely interested in diaphragm activity, which may have improved dEMG-signal quality as crosstalk at this position is reduced.[4,14,15] On the other hand, the used ECG/CI electrodes were not actively shielded, like in previous dEMG studies in neonates.[4,6,16,17] In these studies, the dedicated dEMG cables were micro coaxial cables using active shielding to prevent capacitive coupling of the measurement wire with the environment.[18] This reduced power supply interference and cable movement artifacts.

TABLE 2 The agreement in RR between pressure and diaphragm activity as well as CI during periods with a stable pressure signal

	Bland–Altman mean difference (LoA) In breaths/min	ICC
Standard position		
RR_P versus RR_{CI}	6.6 [−12.5 to 25.7]	0.43
At dEMG position		
RR_P versus RR_{CI} of all three ECG-leads combined	7.3 [−11.8 to 26.4]	0.44
RR_P versus RR_{EMG} at ECG-lead I	4.2 [−8.2 to 16.6]	0.67
RR_P versus RR_{EMG} at ECG-lead II	4.3 [−10.7 to 19.3]	0.62
RR_P versus RR_{EMG} at ECG-lead III	5.0 [−14.2 to 24.2]	0.52

Abbreviatons: CI, chest impedance; dEMG, diaphragm activity measured with transcutaneous electromyography; ICC, intraclass correlation coefficient; LoA, limits of agreement; P, airway pressure; RR, respiratory rate.

TABLE 3 The agreement in RR between pressure and diaphragm activity as well as CI during periods with a stable pressure, CI, and dEMG signal

	Bland–Altman (mean difference [LoA] in breaths/min)	ICC
Standard position		
RR_P versus RR_{CI}	1.2 [−6.5 to 8.8]	0.89
At dEMG position		
RR_P versus RR_{CI} of all three ECG-leads combined	1.6 [−8.3 to 11.5]	0.83
RR_P versus RR_{EMG} at ECG-lead I	0.80 [−9.0 to 10.6]	0.85
RR_P versus RR_{EMG} at ECG-lead II	0.44 [−10.0 to 10.9]	0.83
RR_P versus RR_{EMG} at ECG-lead III	−0.19 [−9.51 to 9.13]	0.85

Abbreviatons: CI, chest impedance; dEMG, diaphragm activity measured with transcutaneous electromyography; ICC, intraclass correlation coefficient; LoA, limits of agreement; P, airway pressure; RR, respiratory rate.

Another difference with former studies was the used derivation to obtain a dEMG-signal. Usually, a bipolar derivation is used to cancel out common noise by subtraction of two unipolar derivations, while in this study only one ECG-lead could be measured at a time, resulting in a single unipolar derivation being obtained.[12,19] As a result, an additional filter to remove the power supply interference was required and baseline fluctuations were observed in the dEMG measurement. However, breathing cycles could still be easily distinguished in all three ECG-leads.

Once we determined the feasibility of extracting a dEMG-signal from the ECG, we also needed to compare the accuracy of measuring RR with dEMG in the different ECG-leads to a reference signal based on breathing induced pressure fluctuations at the airway opening. For this reason, we could only use measurements with stable pressure signals, which were present in approximately 50% of the total recording time. In our initial analysis we used both stable and unstable dEMG and CI measurements during these stable pressure periods, as this best reflects standard clinical care. It was interesting to observe that dEMG signal stability was best in ECG-leads I and II. The lower percentage of stable dEMG recording in ECG-lead III may be explained by a less optimal signal-to-noise ratio due to orientation of the lead derivation through the heart, resulting in more cardiac activity superimposed on the electrical activity of the diaphragm. The RR-agreement between pressure and dEMG was moderate in all three ECG-leads, although, similar to the percentage of stable recordings, the ICC was lowest in ECG-lead III. Interestingly, the agreement between RR based on CI and the pressure signal was low, indicating that RR based on dEMG is at least as accurate as RR based on standard CI. These findings are similar to the RR-agreement between conventional dEMG and CI, as previously reported.[4] Repeating the analyses using only stable recordings in all three signals resulted in a clear improvement in agreement (all high), indicating that signal stability is an important determinant for accuracy of RR monitoring. Improving stability by using for instance shielded electrodes may therefore also improve the accuracy of RR-monitoring using dEMG.

Although the focus of our study was on dEMG-based RR, we also assessed if changing the electrodes position to the diaphragm would still allow for measuring CI-based RR and explored if the quality of the ECG-signal was maintained. We were able to show that the

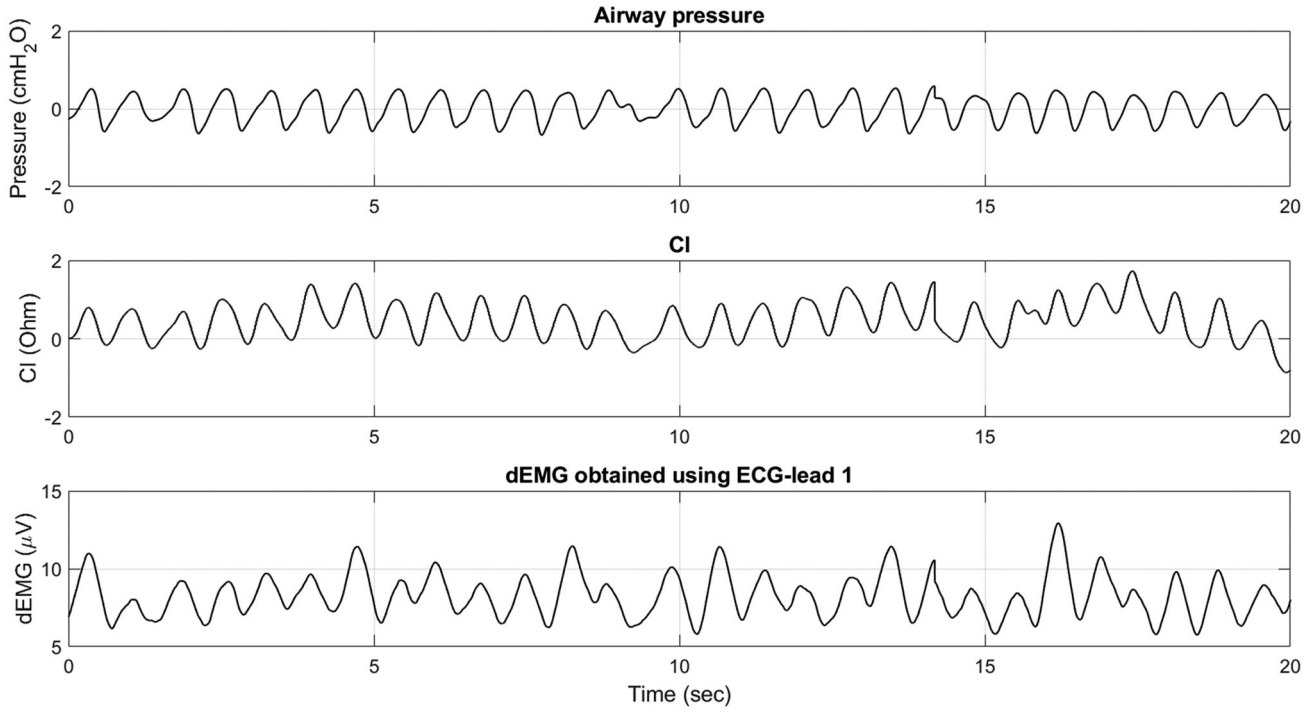

FIGURE 3 A representative tracing of simultaneously measured airway pressure, chest impedance (CI) and diaphragm activity. The latter was measured with transcutaneous electromyography (dEMG) incorporated in the electrocardiogram (ECG), in this case ECG-lead I. Airway pressure, CI and dEMG are comparable in terms of the recorded breathing cycles.

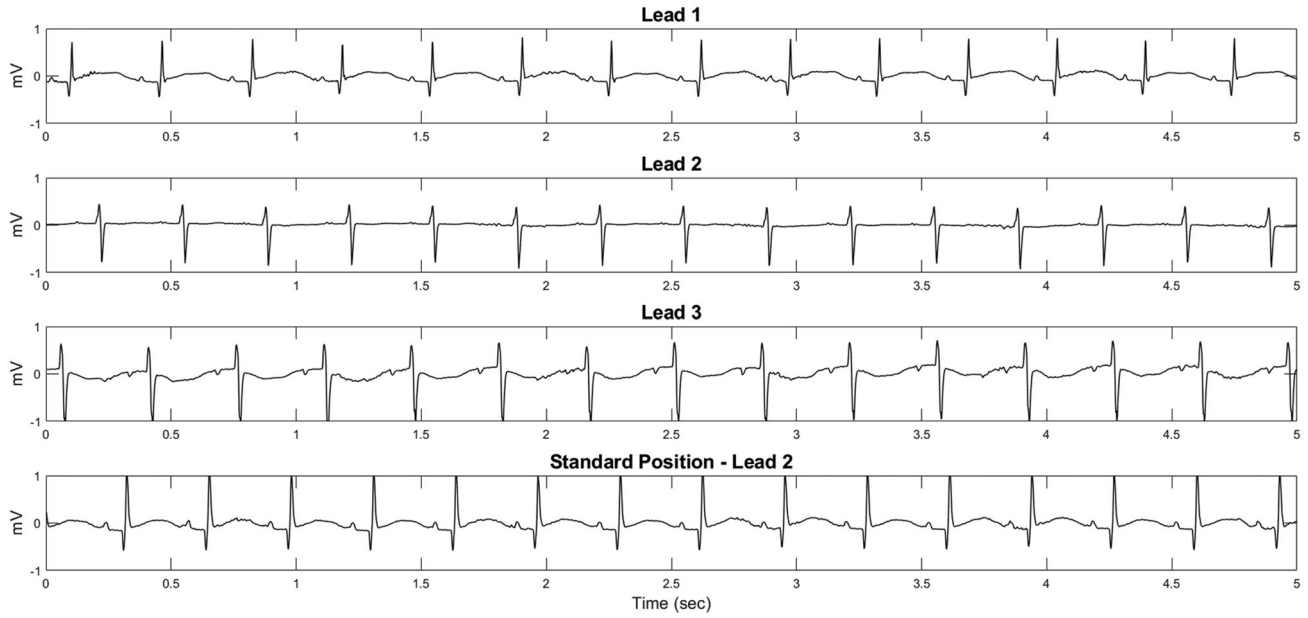

FIGURE 4 Random 5 second tracings of the ECG-signal measured per lead with the electrodes placed at the height of the diaphragm (top three subplots) and at the standard location (bottom, in this case lead II). Note: the four ECG-tracings are not measured simultaneously.

accuracy of RR monitoring using CI was not impacted by the positioning of the ECG electrodes. Although exploratory in nature, our analysis also suggests that the signal quality of the ECG-signal remained stable after electrode repositioning as indicated by clearly identifiable P-waves and QRS-complexes.

4.1 | Strengths

The first strength of this study was the use of an independent reference signal to assess the accuracy of RR monitoring using dEMG and CI. Second, the ability to measure dEMG was studied in all three

ECG-leads, thereby determining the most ideal setup. Finally, we assessed if ECG and CI-monitoring were still feasible when using the dEMG electrode positions, providing insight if simultaneous measurement of both techniques is an option in clinical practice.

4.2 | Limitations

There are several limitations in our study that are worth mentioning. First, we did not use airway flow, the gold standard, as the respiratory reference in this study.[3] Preliminary testing in our setup showed that measurement of expiratory pressure during noninvasive respiratory support had a higher signal resolution than flow. Second, only one ECG-lead could be measured at a time and thus solely one unipolar derivation was obtained resulting in more signal interference and baseline fluctuations in the measured dEMG. A possible future improvement would be acquiring and saving all three ECG-leads simultaneously, because then a bipolar derivation can be constructed to obtain a cleaner dEMG-signal. Moreover, it could also facilitate a head-to-head comparison of the performance of the individual leads, at the same time, which could not be done in this study. Third, the clinical usability of the ECG-signal at the dEMG position was solely studied exploratively. Future studies should systematically study robustness of the obtained ECG-signals at this location.

4.3 | Clinical implications

Our finding that dEMG can be measured with the ECG/CI hardware, while still reliably measuring the ECG/CI, opens the possibility for a broader use of dEMG. The fact that no special dEMG hardware is needed makes this technique accessible for all units using ECG monitoring. dEMG can first of all be used as a new potentially more optimal technique to measure RR, while maintaining ECG for HR monitoring. Another option to improve respiratory monitoring could be recording both dEMG and CI to improve the percentage of time during which respiratory monitoring is reliable by combining the results of both techniques. Based on the percentage of stable dEMG data and the agreement with a respiratory reference signal, it is recommended to use ECG leads I or II for dEMG recording. In addition to RR monitoring, dEMG also provides data on breathing effort which could prove useful in selecting the optimal mode and level of respiratory support in neonates. Lastly, the ability to measure dEMG in a large group of ECG monitored neonates will make it easier to establish normative data on dEMG activity under different clinical conditions and when treated with different respiratory interventions.

5 | CONCLUSION

This study shows that diaphragm activity can be measured using the ECG/CI hardware by placing its monitoring electrodes at the height of the diaphragm, leaving ECG/CI monitoring unaffected. The results pave the way for clinical implementation of dEMG in the entire NICU population. This would provide the opportunity to improve the cardiorespiratory monitoring and get insight in apparent work of breathing using dEMG.

AUTHOR CONTRIBUTIONS

Anouk W. J. Scholten: Conceptualization; investigation; writing—original draft; methodology; writing—review and editing; formal analysis; project administration. **Ruud W. van Leuteren**: Conceptualization; writing—review and editing; methodology. **Frans H. de Jongh**: Conceptualization; methodology; writing—review and editing. **Anton H. van Kaam**: Conceptualization; methodology; writing—review and editing. **Gerard J. Hutten**: Conceptualization; investigation; methodology; writing—review and editing.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The measurement data are available upon reasonable request.

ORCID

Anouk W. J. Scholten http://orcid.org/0000-0002-6175-1436
Ruud W. van Leuteren https://orcid.org/0000-0001-8468-2544
Frans H. de Jongh https://orcid.org/0000-0002-6052-7504
Anton H. van Kaam https://orcid.org/0000-0003-4030-7085
Gerard J. Hutten https://orcid.org/0000-0003-4368-6519

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