Transcutaneous electromyography of the diaphragm
Monitoring breathing and the effect of respiratory support in preterm infants
de Waal, C.G.

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Chapter 10

Future perspectives
In addition to the results presented in this thesis, several other clinical research questions might be answered by using transcutaneous dEMG. Furthermore, research is needed to improve the data acquisition and data analysis of transcutaneous dEMG signals before it could be implemented in clinical care to individualize respiratory treatment in preterm infants.

**Clinical research questions**

To start, it needs to be established if changes in neural breathing effort measured with transcutaneous dEMG reflect changes in actual work of breathing. A clinical study should be conducted to investigate the correlation between changes in work of breathing, measured with transesophageal pressure swings and volume changes, with changes in diaphragmatic activity measured with transcutaneous dEMG.

Transcutaneous dEMG might be used to describe the physiology of breathing in preterm infants, for example directly after birth when a transition takes place from fluid filled to air filled lungs. It would be of great interest to compare diaphragmatic activity and neural breathing effort during this pulmonary transition after birth between healthy term infants, term infants with breathing difficulties directly after birth and preterm infants, to get insight in the effect of illness and prematurity on this crucial transition.

The application of transcutaneous dEMG for guidance of respiratory treatment and, ultimately, prediction of weaning failure, both from invasive mechanical ventilation and non-invasive respiratory support, should be investigated in a large number of preterm infants based on a sample size calculation. Differences in diaphragmatic activity between infants successfully weaned and infants failing the weaning attempt need to be quantified. In addition, it would be of interest to investigate preterm infants in different clinical conditions, from just born up to weeks or months old and from an instable respiratory condition to a very stable respiratory condition, in a similar way as the research conducted before to compare the results between these groups.

The effects of patient-ventilator asynchrony, which is common in preterm infants on non-synchronized nasal intermittent positive pressure ventilation (nIPPV), on the clinical outcome and function of the diaphragm in these infants needs to be assessed and, more importantly, synchronization of nIPPV with spontaneous breathing is urgently needed. The algorithms used for breath detection need to be optimized and the filtering delays must be reduced as much as possible. The accuracy of improved breath detection algorithms needs to be tested in real-time transcutaneous dEMG measurements of spontaneously breathing preterm infants and might ultimately be incorporated in a ventilator for synchronization of ventilator inflations with spontaneous breathing efforts.
**Improvements in data acquisition and analysis**

Research needs to be done to improve data acquisition and analysis of transcutaneous dEMG signals to establish a readable signal on the bedside providing respiratory rates, apnea alarms and objective parameters which might be used to guide respiratory treatment in daily clinical care of preterm infants.

The data acquisition could be improved by the development of non-adhesive electrodes to obtain the transcutaneous dEMG signal which can be used in extremely preterm infants with a vulnerable skin. If non-adhesive electrodes come available, studies need to be conducted to determine if these electrodes are as accurate as the standard adhesive electrodes in measuring diaphragmatic activity. Furthermore, it might be of interest to investigate if more diaphragm-specific electrodes could be developed to reduce movement artefacts in the signal due to crosstalk of other muscles.

Furthermore, it needs to be investigated if diaphragmatic activity could accurately be measured with electrodes placed at different positions on the chest of the preterm infant. The electrical activity of the diaphragm measured and the signal stability at alternative electrode positions need to be compared with the standard electrode position to be able to use transcutaneous dEMG for continuous monitoring in daily clinical care.

The two most used filtering techniques to remove cardiac activity, i.e. gating and subtraction, need to be compared in transcutaneous dEMG data of preterm infants to establish which technique is most suitable in this specific population based on accurate cardiac activity removal with as less time delay as possible.

The algorithms used for analysis of transcutaneous dEMG data need to be optimized, making them transparent, adaptive and stable. It needs to be tested if assumptions made for cut-off values for breath detection algorithms based on data of adult intensive care patients are also applicable to data of preterm infants. If not, it needs to be investigated what the most accurate cut-off value is for the start of inspiration and expiration in spontaneously breathing preterm infants. To find these values, transcutaneous dEMG tracings need to be compared to flow measurements or direct measures of muscle contraction.

The last step in the use of transcutaneous dEMG data in daily clinical care is signal interpretation. For continuous monitoring of spontaneous breathing further development of the software is needed to provide accurate breath counts and apnea alarms, which can be incorporated in a bedside monitor. The application of transcutaneous dEMG for guidance of weaning and respiratory treatment needs standardization of the values of the measured parameters. To achieve these standardized values, big data analyses are required. Furthermore, prediction models might be needed to enable weaning based on transcutaneous dEMG parameters together with
clinical characteristics of the infants. Probably, a score could be calculated that reflects the clinical respiratory condition of an individual infant, which can be used for decision making to intensify or wean treatment.