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Inadequate Assessment of Patient–Ventilator Interaction Due to Suboptimal Diaphragm Electrical Activity Signal Filtering

To the Editor:

Monitoring diaphragm activity in mechanically ventilated patients is used to limit the adverse consequences of mechanical ventilation on the diaphragm (1). Ventilator overassist may result in disuse atrophy and ventilator underassist in load-induced injury (2). In addition, monitoring diaphragm activity allows for detection of patient–ventilator asynchronies (1). Esophageal pressure (Pes) measurement is the state-of-the-art technique to assess inspiratory muscle effort and patient–ventilator interaction but requires specific expertise and signals may be difficult to interpret (3), especially when expiratory muscles are activated (4). Monitoring the electrical activity of the diaphragm (EAdi) with a dedicated nasogastric catheter (EAdi catheter; Maquet) (5) is a valuable alternative for bedside assessment of patient–ventilator interaction (1). The EAdi catheter contains nine ring-shaped electrodes positioned at the level of the diaphragm and was originally designed to control the ventilator in neurally adjusted ventilatory assist mode (5). Ventilator algorithms continuously select the electrode pair closest to the diaphragm and correct for signal disturbances, such as interference from cardiac electrical activity and motion artifacts due to cardiac contractions and esophageal peristalsis. However, the reliability of EAdi-derived parameters to monitor the diaphragm (e.g., neuromechanical efficiency index and patient–ventilator breath contribution index) has been challenged recently due to possible artifacts in the EAdi signal as processed by the ventilator software (6, 7). This is of potential clinical and scientific importance because inadequate EAdi filtering may underestimate or overestimate the severity of patient–ventilator asynchrony and result in inadequate modulation of ventilator settings.

Notably, the BetterCare software was validated by using the EAdi signal as a reference standard to classify ineffective efforts during expiration (8). Ineffective efforts were defined as EAdi peaks of >1 μV above basal EAdi during expiration, not followed by a ventilator breath. More recently, Rolland-Debord and colleagues used this same threshold of >1 μV for detection of ineffective efforts based on EAdi solely (9). However, we challenge the origin of such small EAdi peaks and reason that EAdi filtering may underestimate or overestimate the severity of ineffective efforts. The aim of the current study was to establish the origin of expiratory EAdi peaks in the EAdi signal as displayed by the ventilator software. We performed an in-depth signal
analysis and explain how inadequate EAdi filtering may affect interpretation of patient–ventilator interaction.

Methods
Seventeen patients were included in this study. First, to assess the origin of expiratory EAdi peaks of >1 μV, we performed measurements in two patients ventilated in pressure support mode who had an EAdi catheter and catheter for Pes and/or transdiaphragmatic pressure (Pdi) measurements in situ for clinical purposes. Ventilator flow, airway pressure, and EAdi waveforms were obtained (sample frequency, 100 Hz) from the Servo-U ventilator using Servo-tracker software (Servo-tracker release 4.2; Maquet). Simultaneously, airway pressure, Pes and/or Pdi, ECG, and raw diaphragm electromyography (EMGdi) were acquired at 2 kHz using a dedicated measurement setup (Biopac MP160; BIOPAC Inc.). A Y-splitter cable (Telerex Nederland B.V.) allowed simultaneous acquisition of EMGdi and EAdi signals. Data were offline resampled to 2 kHz, synchronized based on airway pressure tracings that were acquired simultaneously using both measurement devices (i.e., an end-expiratory hold was performed at the start of a recording; the corresponding drop in airway pressure was used to synchronize the data) and processed using a software routine for MATLAB 2018b (Mathworks).

Additionally, we analyzed waveform data (EAdi, Pes, ventilator flow, and airway pressure) from 15 patients ventilated with continuous positive airway pressure (≥10 min per patient; subset from Reference 10) to assess the incidence of expiratory EAdi peaks of >1 μV. Expiration was defined based on flow zero-crossings. With Pes waveforms, we verified if expiratory EAdi peaks were true ineffective efforts.

Results
Prospectively acquired waveforms from two patients are shown in Figure 2. EAdi peaks during expiration were not the result of patient effort (no decrease in Pes or increase in Pdi) but, instead, occurred simultaneously with cardiac activity. Also, cardiac activity present at the start of an inspiratory effort resulted in a delay between EAdi onset and the start of EMGdi increase (see Figure 2A).

In total, 4,063 breaths from 15 patients (mean 271 ± 89 breaths per patient) were analyzed to describe the incidence of expiratory EAdi peaks. In total, 240 expiratory EAdi peaks were present in 12 patients (median number of expiratory EAdi peaks per patient per 10-min interval, 19 [minimum–maximum (min–max), 2–52]; median percentage of expiratory EAdi peaks with regard to total breaths per patient, 6.8% [min–max, 0.6–23.6%]). Only 21/240 (8.8%) peaks were true ineffective efforts as confirmed with Pes.

Figure 1. Left: Ventilator waveforms from a patient ventilated in pressure support (PS) mode with a PEEP of 6 cm H2O and PS of 22 cm H2O. Respiratory rate (RR) was 20/min. Dashed vertical lines indicate the start and end of mechanical inspiration (i.e., flow zero-crossings). A catheter was placed to monitor electrical activity of the diaphragm (EAdi). Adequate catheter position was verified with chest X-ray and the manufacturer’s guidelines provided within the ventilator software. Arrows indicate small EAdi peaks during mechanical expiration. Right: After switching ventilator mode to NAVA, all EAdi peaks resulted in proportional ventilator assist, and ventilator-RR increased to 36/min. Interestingly, no drop in Paw, indicating no patient effort, is observed for those breaths related to the smaller EAdi peaks (dashed circles), leading to the suspicion of cardiac activity–related artifacts and “EAdi auto-triggering.” NAVA = neurally adjusted ventilator assist; Paw = airway pressure; PEEP = positive end-expiratory pressure.
Ineffective efforts were present in only five patients. Cardiac activity–related EAdi peaks varied in amplitude (min–max, 1–20 \( \mu \text{V} \) but mostly \(<4 \mu \text{V}\)) and were always lower than those EAdi peaks corresponding to true diaphragmatic contractions.

**Discussion**

In this study we clearly demonstrate that patient–ventilator interaction can be misinterpreted because of suboptimal EAdi filtering by the ventilator software. Possible explanations are as follows:

1. **Electrical artifact:** Ineffective filtering and replacement of QRS complexes can appear as EAdi peaks or can lead to a delayed onset of EAdi increase. The EMGdi frequency is from 20 to 250 Hz, whereas the ECG frequency is from 0 to 100 Hz (but mostly \(<25\) Hz) (11). Owing to this frequency overlapping, it is difficult to fully eliminate cardiac activity from diaphragm activity, especially during real-time processing. Furthermore, removal of cardiac electrical activity is technically challenging in patients with arrhythmias, tachycardia, and/or low diaphragmatic activity (thus, low signal-to-noise ratio).

2. **Mechanical artifact:** Cardiac movement (contraction and filling of the heart) results in intrathoracic pressure changes and slight displacement of the EAdi catheter relative to the diaphragm. Insufficient filtering of these movement artifacts may result in EAdi peaks.

Recognizing filtering-related asynchrony is important for proper evaluation of patient–ventilator interaction. First, inappropriate filtering affects the reliability of EAdi-derived monitoring indices, as we published earlier (6, 7). Second, inadequate EAdi signal filtering at the start of inspiratory activity may cause a nonphysiologic delay between true neural inspiration and the start of EAdi-derived inspiration. Third, cardiac activity–related EAdi peaks during expiration result in an overestimation of the true amount of ineffective efforts when very sensitive criteria are used (e.g., increase in EAdi >1 \( \mu \text{V} \)). This may also explain the relatively low sensitivity (65.2%) of the Better Care algorithm when validating ineffective efforts with EAdi signal data as a reference standard (8). Finally, cardiac activity–related EAdi peaks result in proportional ventilator assist during neurally adjusted ventilatory assist mode (see Figure 1, right). This “EAdi auto-triggering” leads to high ventilator respiratory rates, which may cause patient agitation and might needlessly alarm nurses and staff.

**Conclusions.** Cardiac activity–related artifacts are often present in the EAdi signal filtered by ventilator software. This
might lead to incorrect interpretation of patient–ventilator interaction and highlights the need for proper technical and physiological understanding of monitoring signals and software used for research and clinical decision-making. Future analysis techniques may offer means to optimize bedside interpretation of patient–ventilator interaction.

Author disclosures are available with the text of this letter at www.atsjournals.org.

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References


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Traffic-related Air Pollution, Dust Mite Allergen, and Childhood Asthma in Puerto Ricans

To the Editor:

Traffic-related air pollution (TRAP) and indoor allergens may cause or worsen childhood asthma (1–4). Because findings from murine models suggest detrimental synergistic effects of concurrent exposure to TRAP and allergens on immune responses and asthma susceptibility (5), we examined whether residential distance to a major roadway (a marker of TRAP) and dust mite or cockroach allergen interact on asthma in a case–control study of Puerto Rican children. Some of these results have been reported in the form of an abstract (6).

Subject recruitment and study procedures have been previously described (7). From March 2009 through June 2010, participants were recruited from randomly selected households in the metropolitan area of San Juan and Caguas (Puerto Rico) using a multistage probabilistic sampling design. On the basis of this sampling design, 7,073 households were selected and 6,401 (91%) were contacted. Of these 6,401 households, 1,111 had one or more children who met inclusion criteria (age 6–14 yr, four Puerto Rican grandparents, and residence in the same household for ≥1 yr). Of these 1,111 households, 438 (39.4%) had one or more children with asthma (a “case”). From these 438 households, one child with asthma was selected (at random, if there was more than one such child). Similarly, only one child without asthma (a control subject) was randomly selected from the remaining 673 households. To reach a target sample size of 700 children, we attempted to enroll 783 of the 1,111 eligible children. Parents of 105 (13.4%) of these 783 households refused to participate or could not be reached, leaving 678 study participants (351 cases and 327 control subjects). There were no significant differences in age, sex, or area of residence between children who did (n = 678) and did not (n = 105) participate. Of the 678 participants, 563 (83%) had data on allergen levels in house dust and were thus included in this analysis.

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