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Estimated ECG Subtraction method for removing ECG artifacts in esophageal recordings of diaphragm EMG

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ABSTRACT

The accuracy of diaphragm electromyogram (EMGdi) derived parameters, as used in critically ill intensive care unit (ICU) patients, can be compromised due to electrocardiographic (ECG) interference in the EMGdi signal. Removal of ECG contamination from the esophageal recordings of the EMGdi is challenging due to spectral overlapping of EMG and ECG signals and because of variability in ECG shape and amplitude. Therefore, we designed an Estimated ECG Subtraction (EES) method, based on three steps: (1) identification of the timing of the ECG artifact without an ECG reference channel, (2) estimation of the normalized ECG, considering the EMGdi as noise, and (3) subtraction of the denormalized ECG estimate from the EMGdi recordings. We evaluated the EES method against the use of a single wavelet-based adaptive filter. Using EMGdi signals of ten ICU patients and simulated contaminated EMG, we demonstrated that the EES method yields uncontaminated EMGdi, and showed that it is more effective than a wavelet-based adaptive filter only. Implementation of this technique may offer means to improve diaphragm activity monitoring and control in clinical practice.

1. Introduction

The diaphragm is the most important respiratory muscle. Monitoring diaphragm activity in mechanically ventilated intensive care unit (ICU) patients is performed to facilitate diaphragm-protective ventilation, to assess patient-ventilator interaction and work of breathing, as well as to identify neuromuscular dysfunctions [1–4]. Bedside monitoring of diaphragm electrical activity (EAdi) is available on a specific ventilator (Getinge, Sweden) via a dedicated nasogastric (feeding) tube embedded with multiple ring-shaped electrodes positioned at the level of the diaphragm [5,6]. EAdi reflects the spatial and temporal recruitment of the crural diaphragm motor units, and is the closest available signal to the neural respiratory center output [5,7]. The EAdi catheter was originally designed to control the timing and level of ventilator pressurization in neurally adjusted ventilatory assist (NAVA) mode [5], but can also be used to monitor diaphragm activity in other ventilator modes or with unassisted breathing [1]. Signal processing algorithms within the ventilator continuously select the electrode pair closest to the diaphragm and filter out interferences, such as cardiac electrical activity (ECG) and motion artifacts due to cardiac contractions and esophageal peristalsis. However, we found that the reliability of EAdi-derived parameters to monitor diaphragm activity is compromised by these ventilator signal processing algorithms [8,9]. Furthermore, we demonstrated that ineffective filtering and inadequate removal of QRS complexes that interfere with the raw diaphragm electromyogram (EMGdi) limits interpretation of patient-ventilator interaction and detection of neural inspiration onset [10]. Improved filtering methods are needed for optimal use of the EMGdi – and its processed EAdi signal – in clinical decision-making and research.

Removal of ECG contamination from any type of EMG is a major challenge because of spectral overlapping of the ECG (0–100 Hz) and the EMG (20–250 Hz, but mostly <150 Hz) [11], causing an increase in power content of the EMG and distortion of its frequency information. Different methods for removal of ECG interference from the EMGdi have

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been described, using gating [12], subtraction techniques [13,14], wavelets [15–17], high-pass filtering [11], adaptive filtering [18,19], or independent component analysis [20–22]. However, most of these techniques could not fully eliminate cardiac activity noise without important information loss, or clinical application is limited due to computational complexity, user dependency, or the need for a multi-channel input or dedicated reference ECG recording. The latter is especially challenging with regard to esophageal recordings of the EMGdi, as the QRS complex may vary in shape and amplitude depending on the location of the electrode pairs relative to the heart. In 2009, Zhan et al. described a wavelet-based adaptive filtering technique for removal of ECG contamination from esophageal EMGdi recordings without requiring extra channels for ECG reference [15]. This method performs well in general; however, it is less robust for removal of ECG artifacts that overlap with diaphragm contraction, and selection of the mother wavelet is challenging. Also without the need for a reference ECG channel, Costa Junior et al. recently demonstrated that a template subtraction method was effective in attenuating the ECG present in surface EMG of the right erector spinae muscle [23]. In their work, a template was directly constructed from the contaminated EMG. We figured that this method could also be applicable in EMGdi processing. However, in esophageal EMGdi signals the ECG contamination can be more pronounced and variable due to the close proximity of the EAdi catheter to the heart and motion artifacts.

The aim of the current study is to design and evaluate a modified template subtraction method for offline attenuation of ECG interference in the EMGdi signal obtained with a nasogastric catheter in ICU patients. A second aim is to evaluate how this method compares to a wavelet-based adaptive filter, using clinical and simulated EMG data.

2. Materials and methods

2.1. Subjects and signal acquisition

Data were part of a previous study in which diaphragm activity was measured when patients were disconnected from the ventilator (SERVO-i, Getinge, Sweden) for performing a spontaneous breathing trial with T-tube and supplemental oxygen [24]. Recordings of raw EMGdi signals from ten ICU patients with varying amplitude and timing of diaphragm activity and ECG contamination were selected aiming to represent the variety range that was observed in the study population. Because the duration of the spontaneous breathing trial varied among subjects, in that study [24] stable recordings during ventilator disconnection were divided into six epochs of at least 1 minute taken at equal time intervals in between. We randomly selected two of these epochs per patient to evaluate the performance of the filtering method. The average duration of these recordings per patient was 7.2 minutes (min–max: 3–8 minutes). EMGdi signals were acquired with a nasogastric catheter which was embedded with two balloons and a multiple-array electrode consisting of nine stainless steel rings (width 2 mm, diameter 2 mm) placed 10 mm apart, creating an array of eight sequential differential electrode pairs (NeuroVent Research Inc., Canada). Signals were amplified and digitized (Porti 7-16, 22 bits, 71.5 nV/least significant bit, noise level <1 μV; TMSi B.V., The Netherlands) at a sampling frequency of 2000 Hz for each channel.

2.2. Signal pre-processing

All (offline) signal processing and analysis for this study was custom programmed in Matlab R2018b (Mathworks, Natick, USA). First, EMGdi recordings from all separate electrode pairs were bandpass filtered through a 2nd order Butterworth block with a frequency band of 30–400 Hz, to remove low-frequency and high-frequency noise. Interference from the 50 Hz power line was removed with a Notch filter. Subsequently, a cross-correlation and double-subtraction technique was applied to determine the center of the electrical active region of the contracting diaphragm (EARdi), as described in detail by Sinderby et al. [25]. The signal segments obtained from the electrode channel above and below this EARdi were subsequently subtracted from each other. This technique reduces influence of movement of the center of this EARdi relative to the electrode array and increases signal-to-noise ratio. The double-subtracted contaminated EMGdi signal is further referred to as the EMGdi-DS.

2.3. Wavelet-based adaptive filter

To remove ECG interference from the EMGdi-DS, a wavelet-based adaptive filter as designed by Zhan et al. [15] was applied. By using the discrete wavelet transform, the EMGdi-DS was decomposed into details and approximation parts. We performed a wavelet decomposition to level 5 using a 4th order Daubechies (*db4*) wavelet, which qualitatively best matched the shape and form of the ECG artifacts, consistent with earlier work [15]. Then, the signal was filtered in the wavelet space by using an adaptive threshold (sigmoid function). This improves performance as compared to a fixed threshold as the EMGdi to ECG amplitude varies over time. Finally, the wavelet-filtered signal (EMGdi-WA) was reconstructed using the inverse discrete wavelet transform.

2.4. Estimated ECG Subtraction method

Here, we describe an Estimated ECG Subtraction (EES) method, adapted from Costa Junior et al. [23]. The concept is based on three main actions: 1) identification of the timing of the ECG artifact without an ECG reference channel, 2) estimation of the normalized ECG, considering the EMGdi as noise, and 3) subtraction of the denormalized ECG estimate from the EMGdi recordings.

This was done according to the following algorithm, of which the steps are shown in Fig. 1.

A1. Algorithm of the Estimated ECG Subtraction method

INPUT: EMGdi-DS signal contaminated with ECG interference

OUTPUT: Denoised EMGdi-DS signal (EMGdi-EES signal)

Step 1: Apply a 4th order Butterworth 4–50 Hz bandpass filter (ECG frequency band) to promote the ECG amplitude relative to the EMGdi.

Step 2: Perform signal rectification.

Step 3: Compute the signal required for detection of QRS segments: apply a moving average filter (window width, 16.7 ms) and normalize the signal to the amplitude of the EMGdi-DS (EMGdi-DS-A).

Step 4: Compute a time-dependent threshold as the mid-range value of the EMGdi-DS-A signal over a fixed interval of 0.5 s, interpolated and filtered with a moving average filter (window width, 12.5 ms).

Step 5: Detect start and end time points of potential QRS segments as the crossing of the EMGdi-DS-A with the time-dependent threshold of step 4.

Step 6: Delete incorrectly detected QRS segments based on outliers in the interval between potential QRS segments (inter-QRS interval). Next, restore wrongfully deleted segments utilizing the quasi-periodic nature of the ECG, starting at the highest peak of the first potential QRS segment ($QRS_{i=1}$):

for i = 1

expected window of $QRS_{i+1} = QRS_i +$ [median inter-QRS length $\pm$ (0.66 $\times$ median inter-QRS length)].

if no QRS segment exists in expected window

insert QRS_{i+1} segment at location of highest peak above time-dependent threshold

$i = i + 1$

else $i = i + 1$

end

Step 7: For all identified locations of QRS segments, detect in the EMGdi-DS signal the R wave as the highest positive peak, and the Q and S waves as the nadir (negative peaks) before and after the R wave, respectively.

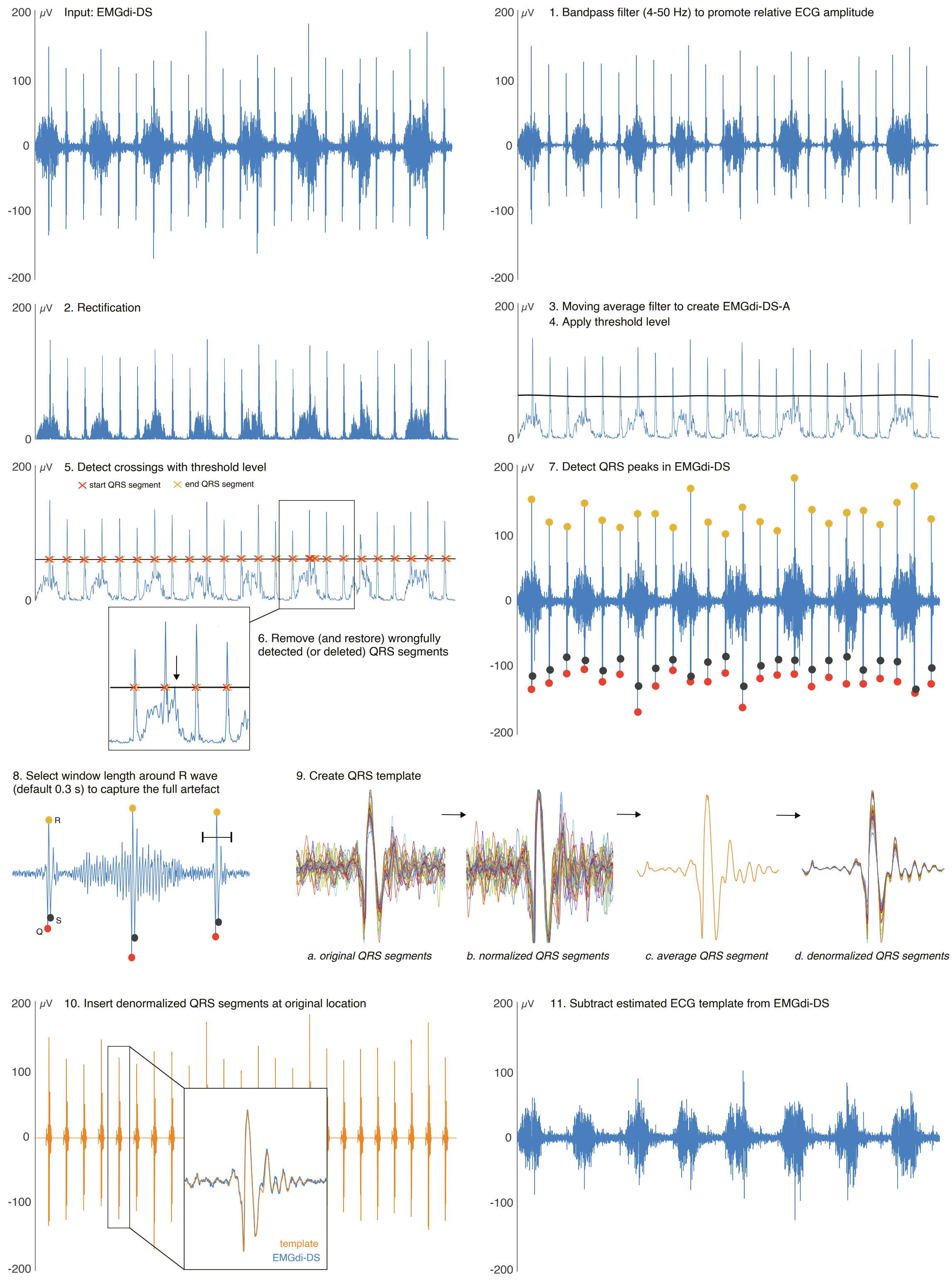

Fig. 1. Illustration of the Estimated ECG Subtraction algorithm. See text for further details on each step.

Step 8: Select a 0.3 s window length around each R wave to capture the complete QRS artifact. Adapt window length if deemed necessary (e.g., in patients with prolonged PQ time and/or large P waves or large T waves such as illustrated in Fig. 2)

Step 9: 9a: capture each selected QRS artifact; **9b**: normalize the artifact to the largest peak Q, R and S values in the original EMGdi-DS: perform local normalization to two negative peaks (Q and S waves) by dividing the QRS segment into QR and RS segments. **9c**: compute an average QRS template to retain the QRS pattern while reducing the stochastic elements in that segment. **9d**: for each selected QRS artifact (**9a**), denormalize the QRS template to the amplitude of the original QRS artifact

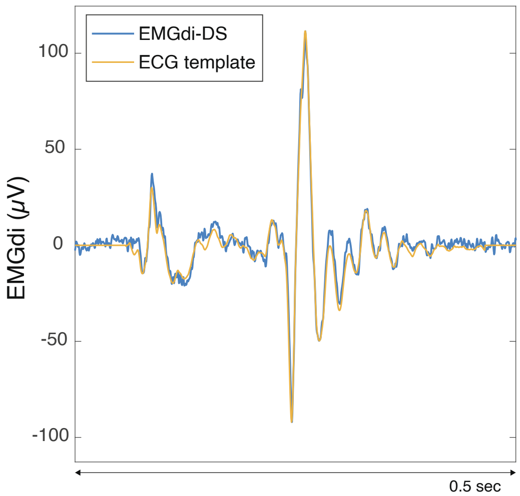

Fig. 2. Example of an ECG template for which the duration of the template was manually prolonged in order to capture the complete artifact.

Step 10: Construct a new time series starting with zero-baseline signal: at each instance of an R peak in the EMGdi-DS, insert the denormalized QRS segment.

Step 11: Subtract the new time series of the estimated ECG recording from the EMGdi-DS.

As these constructed ECGs will never be a perfect copy of the original ECG (e.g., because of variability in QR and RS duration), some residue of ECG noise could still be present after step 11. Residue noise was further attenuated by applying the wavelet-based adaptive filter as described in *Section 2.3*.

2.5. Evaluation of performance

The performance of the filtering technique was evaluated visually in the time domain and by quantitative analysis in the frequency domain. Spectral analysis of the EMGdi-DS, the EMGdi as processed by a wavelet-based adaptive filter only (EMGdi-WA) and by the Estimated ECG Subtraction method (EMGdi-EES) was performed using Welch's averaged periodogram method with a frequency resolution of 0.5 Hz. As we cannot obtain the true clean EMGdi of the clinical data, it is not possible to assess signal-to-noise ratio or relative error of the power spectrum. Differences in power spectral densities between clinical signals were quantitatively assessed by computing the total power and the median frequency for the full recordings. As we identified the location of the QRS artifacts, we also calculated the median frequency for those EMGdi-DS signal segments that were not contaminated with cardiac artifacts; results were compared with the median frequency obtained from the same ECG-free segments in the EMGdi-WA and EMGdi-EES signals.

Differences in total power and median frequency between signals were analyzed by repeated measures ANOVA with Greenhouse-Geisser correction at the 95% significance level; pairwise comparison was performed after Bonferroni correction. Assumption of normality was assessed with the Shapiro-Wilk normality test and a log-transformation of the data was applied if necessary. Statistical analysis was performed using SPSS (version 26, IBM Corp., USA). Data are presented as median with interquartile range [q_1-q_3] unless otherwise stated.

In addition, performance of the Estimated ECG Subtraction method was evaluated using simulated EMG data. To this end, one clean EMG signal (AcqKnowledge 5.0 sample data, BIOPAC Systems Inc., USA) was artificially contaminated by means of adding an ECG template that was constructed with the Estimated ECG Subtraction method (see *Section 2.4. Estimated ECG Subtraction method*, and Fig. 1, *step 10*). We used ECG templates derived from our clinical dataset instead of artificial or reference ECG signals obtained with surface electrodes, since the algorithm was developed for denoising of QRS artifacts obtained with a nasogastric catheter (i.e., different artifact shape and amplitude). As such, we generated ECG templates from two random patients; these templates were subsequently varied in amplitude and timing relative to the clean EMG signal, resulting in a set of four simulated contaminated EMG signals of about 40 s each. The performance of the filtering technique was evaluated 1) visually in the time domain, 2) by comparing the median frequency and power spectral densities (total power, ECG band power (0–100 Hz), and EMG band power (20–250 Hz)) in the frequency domain, and 3) by quantitatively assessing the difference between the simulated clean EMG and the processed EMG signal by calculating a relative error (in percentage) over the 0–250 Hz band, according to Chen et al. [26]:

$$\delta(\%) = \frac{\sum_0^{250}\left[P(f) - P^{'}(f)\right]^2}{\sum_0^{250} P^2(f)} \times 100\%$$

with $P(f)$ the spectral density of the original clean EMG signal, and $P'(f)$ the spectral density of the processed EMG signal. In addition, we evaluated how the Estimated ECG Subtraction method as applied to simulated data (EES-processed EMG) compares to a wavelet-based adaptive filter (WA-processed EMG).

3. Results

3.1. Clinical data

Fig. 3 presents the results from three patients with differences in ECG to EMGdi intensities and timing and demonstrates that the Estimated ECG Subtraction method was more successful in attenuating ECG contamination as compared to a wavelet-based adaptive filter only (Fig. 3**A-C**). In addition, the EMGdi-WA recordings illustrate that cardiac artifacts that are still present just before – or overlapping with – the start or end of diaphragm contraction may limit accuracy of neural inspiratory time detection. The periodogram of these examples (Fig. 3**D-F**) clearly demonstrates spectral overlapping of the ECG and EMGdi in the EMGdi-DS, and a reduction in power for the lower frequencies with corresponding increase in median frequency for the EMGdi-WA and EMGdi-EES, with effects more pronounced for the EMGdi-EES.

Median frequencies and total power for the full recordings of the EMGdi-DS, EMGdi-WA and EMGdi-EES signals obtained from all patients are presented in Table 1. Post-hoc tests revealed a significant increase in median frequency from 40.8 [35.7–51.4] to 66.3 [61.9–69.2] to 68.8 [67.8–73.3] Hz, and a reduction in total power from 390 [264–530] to 196 [157–236] to 167 [134–237] μV^2 when comparing the full recordings of the contaminated EMGdi-DS to EMGdi-WA to EMGdi-EES signals, respectively ($P < 0.001$ for both parameters). For those signal segments free of QRS artifacts, median frequency of the EMGdi-EES and EMGdi-WA was similar (69.7 [68.8–75.9] vs. 68.2 [64.2–75.9] Hz, respectively ($P = 0.11$)), but significantly different from the median frequency of the EMGdi-DS (65.6 [60.6–71.2] Hz ($P = 0.001$ for differences with the EMGdi-WA and the EMGdi-EES)), however absolute differences were small.

3.2. Experimental data

Fig. 4 demonstrates the performance of the Estimated ECG Subtraction method for two simulated contaminated EMG signals and as compared to the wavelet-based filtering technique (WA-processed signal). The median frequency, power spectral density (total, ECG band, and EMG band) and relative error for the four different simulations are presented in Table 2. On average, the relative error between the clean and EES-processed EMG was 0.97% (min–max: 0.50–1.22%). Although this was slightly higher than the relative error for the WA-processed signal (average: 0.35% (min–max: 0.16–0.52%)), both relative errors were low and the resulting median frequency of the EES-processed

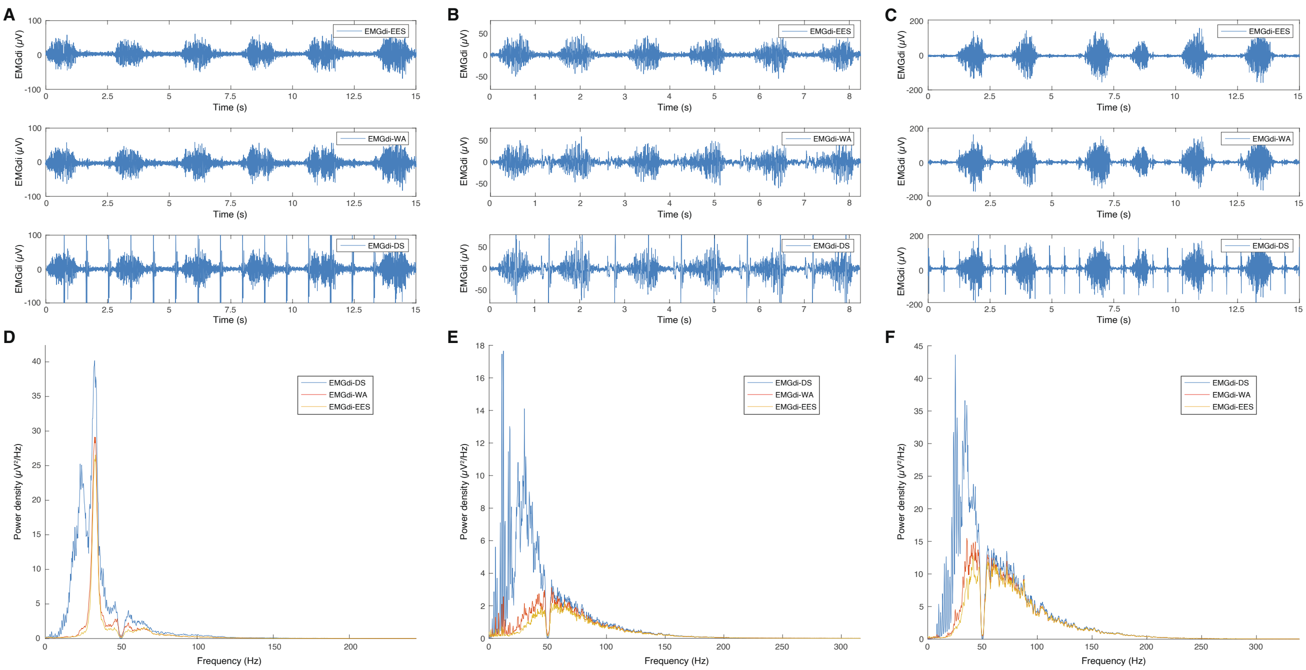

Fig. 3. Evaluation of the performance of the Estimated ECG Subtraction (EES) method for diaphragm electromyography (EMGdi) recordings from three representative patients with various EMGdi to ECG amplitudes and timing. **A-C:** EMGdi recordings of the original double subtracted EMGdi signal (EMGdi-DS, bottom tracing), the EMGdi as filtered by the wavelet filter (EMGdi-WA, middle tracing) and as processed using the EES method (EMGdi-EES, top tracing). **D-F***:* corresponding Welch's periodogram for the EMGdi-DS, EMGdi-WA and EMGdi-EES. Note that the drop at 50 Hz is the result of removal of the power line frequency. **Example 1 (A and D)**: data from the same patient as demonstrated in Fig. 1 and identified as patient 1 in Table 1. The EMGdi-EES demonstrates a clean EMGdi signal whereas ECG artifacts were not completely removed in the EMGdi-WA signal. The periodogram shows successful removal of the ECG frequency band. **Example 2 (B and E):** recordings of a patient with relatively low diaphragm activity and large ECG amplitudes (patient 3 from Table 1). The EMGdi-DS signal is zoomed for clarification as ECG amplitudes were as large as 100 μV. Due to the high respiratory rate of this patient (40 breaths/min), there is a consistent overlap of the ECG artifact with the start and end of diaphragm activity. Again, ECG artifacts were not fully removed in the EMGdi-WA signal, which limits accurate detection of neural inspiratory time. The ECG artifact was not fully captured in the wavelet (note the large P wave in the EMGdi-DS), while this was included in the estimated ECG template (same patient as presented in Fig. 2). As a result, the periodogram of the EMGdi-WA shows that low frequency harmonics (<20 Hz) related to ECG are still present. **Example 3 (C and F):** patient with high diaphragm activity and EMGdi amplitudes as large as ECG amplitudes (patient 9 from Table 1). This substantiates the need for promoting the relative ECG amplitudes as described in step 1 of the EES processing algorithm. A clear improvement of the EES method is observed as compared to the wavelet technique.

Table 1
Median frequency and total power derived from the Welch's periodogram for the EMGdi recordings as processed by the different filtering techniques. Data are presented per patient as well as the population median [q_1-q_3]. Median frequency and total power differed statistically significantly between the EMGdi-DS, EMGdi-WA and EMGdi-EES; all pairwise comparisons were significant ($P < 0.001$).

	Median frequency (Hz)				Total power (μV^2)			
Patient	EMGdi-DS	EMGdi-WA	EMGdi-EES	P-value	EMGdi-DS	EMGdi-WA	EMGdi-EES	P-value
1	29.8	34.6	35.1		535	180	146	
2	28.9	68.1	73.5		514	149	130	
3	41.2	63.5	67.8		356	186	160	
4	36.3	61.4	67.9		1029	513	427	
5	48.7	69.3	75.2		424	206	175	
6	35.5	64.6	68.6		142	76	70	
7	67.7	74.9	74.9		256	210	212	
8	40.4	56.3	60.5		72	41	38	
9	52.3	69.5	72.9		1297	838	766	
10	64.0	68.7	69.0		287	245	245	
Median [q_1-q_3]	40.8 [35.7–51.4]	66.3 [61.9–69.2]	68.8 [67.8–73.3]	<0.001	390 [264–530]	196 [157–236]	167 [134–237]	<0.001

Abbreviations: **EMGdi**, diaphragm electromyogram; **EMGdi-DS**, double-subtracted EMGdi; **EMGdi-WA**, EMGdi as processed with the wavelet-based adaptive filter; **EMGdi-EES**, EMGdi as filtered with the Estimated ECG Subtraction method.

signal was closer to the true median frequency (mean difference with the true median frequency: 1 Hz vs. 5.1 Hz for the EES-processed EMG vs. WA-processed EMG, respectively; P = 0.034 for differences between both methods). In addition, Fig. 4a demonstrates that remaining ECG frequencies were present in the WA-processed signal.

4. Discussion

In the current study we present a new method (template subtraction plus wavelet-based adaptive filtering technique) for removal of ECG artifacts from EMGdi recordings obtained with a nasogastric catheter in ICU patients. In recordings with different amplitudes and timing of EMGdi and ECG contamination, we demonstrate that the Estimated ECG

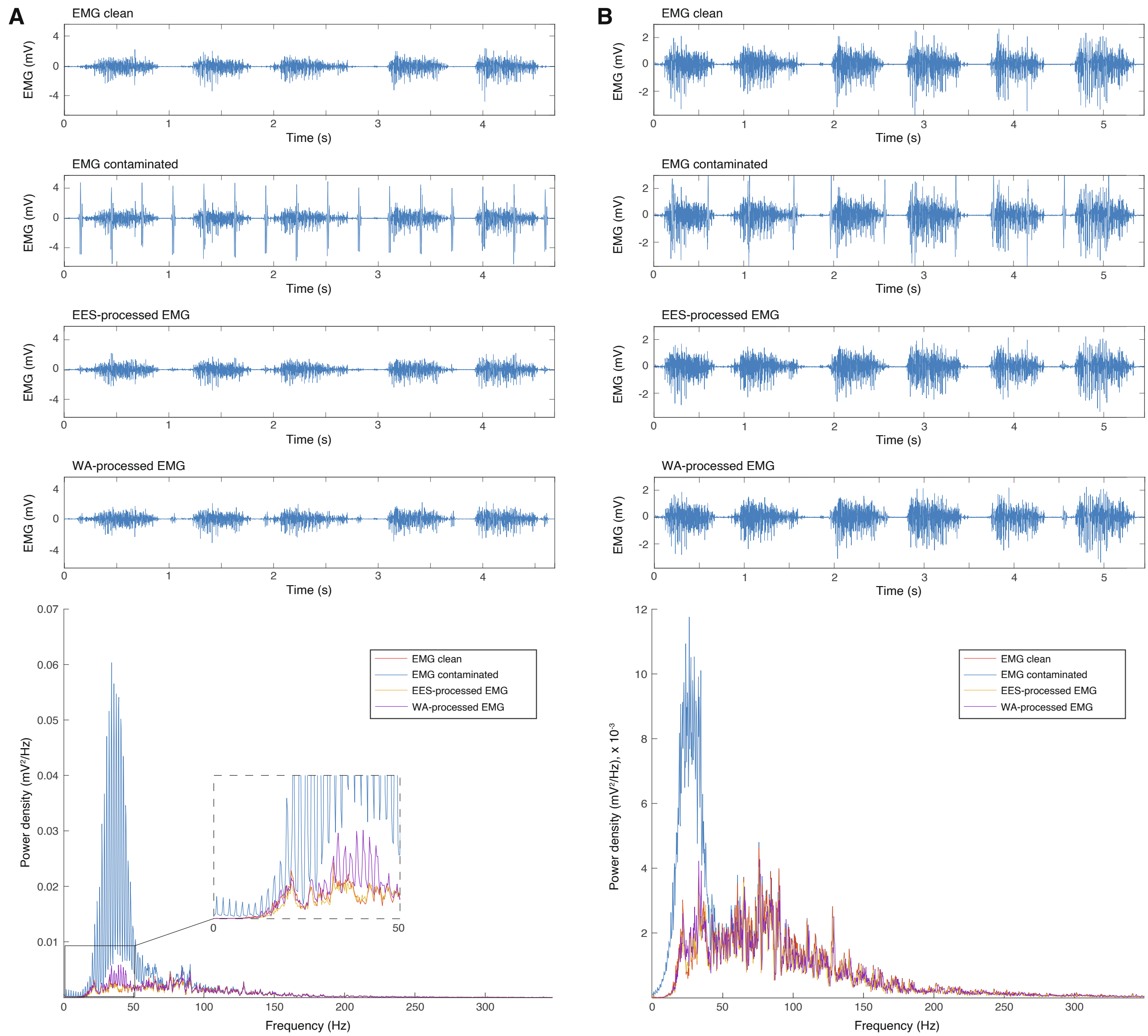

Fig. 4. Evaluation of the performance of the Estimated ECG Subtraction (EES) method for two simulated electromyography (EMG) recordings using a clean EMG signal that was contaminated with an ECG template as derived from clinical data (two different patients), and compared to the wavelet-based adaptive filter (WA) technique. Note the differences in power for the contaminated signals to demonstrate variations induced in ECG artifact amplitudes and timing. 4A: simulation 2 of Table 2; 4B: simulation 3 of Table 2.

Subtraction method is feasible and efficient in processing a clean EMGdi signal without the need for a dedicated reference ECG channel. Implementation of this technique could facilitate improved processing of the EMGdi and its derived parameters for diaphragm activity monitoring and control.

4.1. Development of the Estimated ECG Subtraction method

Template subtraction techniques for filtering ECG contamination from EMGdi recordings acquired with surface electrodes have been described previously, using different methods for template creation and QRS segment detection [11–13,27]. In general, a template can be obtained from additional recordings of the contamination (i.e., from a separate reference ECG recording), from a pre-existing template, or by estimating the template from an EMG recording when the muscle is in a relaxed state. Such methods cannot be applied to esophageal recordings of the EMGdi, because the shape of the artifact depends on the position of the catheter electrodes near the heart and varies among – and sometimes also within – patients; therefore, it will not match any artifact template when derived from a noninvasive simultaneous ECG recording or from a pre-existing ECG template. Moreover, obtaining a template from a recording with the muscle in a relaxed state (i.e., during expiration with very low amplitude of EMGdi as compared to ECG) could be challenging in ICU patients with high and variable respiratory rate, expiratory diaphragmatic activity, or EMG interference from extra-diaphragmatic muscles. Such method could require recordings during apnea events or when diaphragm activity is temporarily artificially suppressed (i.e., recordings under deep sedation or neuromuscular blockade), however such interventions may also change the shape and timing of the artifact and do not outweigh the benefits of obtaining a cleaner signal with our Estimated ECG Subtraction method as compared to other available filtering techniques.

Costa Junior et al. were the first that estimated an ECG template directly from the complete recording of the contaminated EMG of the

Table 2
Performance of the Estimate ECG Subtraction (EES) method for processing of simulated EMG that was contaminated with ECG artifacts, and compared to the wavelet-based adaptive filter (WA) method. Simulations 1 and 2, and simulations 3 and 4 were contaminated with the same ECG templates. Note the differences in power for the contaminated signals – especially in the ECG frequency band (0–100 Hz) – to confirm variations induced in ECG artifact amplitudes and timing.

		Power (μV^2)			Median frequency (Hz)	Relative error Clean vs. Processed EMG (0–250 Hz) (%)
	EMG	Total	0–100 Hz	20–250 Hz		
Simulation 1	*Contaminated*	1853	1751	1605	26.7	–
	Clean	262	164	242	82.8	–
	Processed, EES method	235	151	220	81.2	0.95
	Processed, WA method	269	183	249	75.6	0.16
Simulation 2	*Contaminated*	850	746	820	41.7	–
	Clean	264	165	244	82.8	–
	Processed, EES method	233	148	219	82.8	1.22
	Processed, WA method	279	190	262	76.7	0.52
Simulation 3	*Contaminated*	413	314	362	50.7	–
	Clean	261	163	241	82.8	–
	Processed, EES method	231	147	216	81.6	1.19
	Processed, WA method	242	157	226	80.2	0.44
Simulation 4	*Contaminated*	2636	2530	2118	27.2	–
	Clean	260	162	239	82.8	–
	Processed, EES method	240	153	227	81.5	0.50
	Processed, WA method	270	179	251	78.3	0.29

limb muscle [23]. The lack of need for an ECG reference channel is an important prerequisite for processing EMGdi signals using any template subtraction method. The core of this method is that, to estimate the ECG representation in the registration, first the EMG is considered as noise to estimate an ECG template from ensemble averaging over several heartbeats. With this template the ECG artifacts can be almost completely eliminated by subtraction of this template from the EMGdi registration. The method presented in the current study was partially based on their work [23], however important differences and improvements should be mentioned. First, as ECG artifacts may vary in amplitude due to slight catheter motion relative to the heart, we introduced a dynamic threshold for detection of QRS segments to account for low and varying ECG to EMGdi ratio. Second, we implemented an algorithm to delete and restore any wrongfully detected or removed QRS segments utilizing the quasi-periodic nature of the ECG. Third, an average QRS complex segment was constructed after local normalization to the Q, R and S amplitudes (i.e., normalization to one maximum value (R wave) and two local minima (Q and S waves)). Normalization to only the R wave has been described before [23,27,28], while our method takes into account the within-patient variability in relative Q, R and S amplitudes. Fourth, we created a template of longer duration (default 0.3 s instead of 0.16 s, which was manually prolonged if deemed necessary) to enable removal of the complete ECG segment as substantial P and T waves could be present due to the close proximity of the catheter near the heart. In addition, Costa Junior et al. did not evaluate the performance of their algorithm in clinical data, while we used EMGdi signals of ICU patients with varying intensity and timing of diaphragm activity and ECG contamination to design our method and to confirm its efficiency. Last, we additionally applied a wavelet-based adaptive filter to remove residual ECG noise, if present, since any estimated ECG template will never be the perfect copy of the original contamination.

4.2. Comparison with a wavelet-based adaptive filter and simulated EMG signal

We demonstrated that the Estimate ECG Substraction method was efficient in removing ECG artifacts from variable EMGdi recordings and yielded better performance as compared to a wavelet-based adaptive filtering technique only, as demonstrated visually, as well as indicated by the significant increase in median frequency from the Welch's periodogram for the full signal recordings. Although we could not compare both techniques with the true clean EMGdi for clinical data, this finding indicates that more lower frequencies (likely related to the ECG contamination) were present in the EMGdi-WA as compared to the EMGdi-EES. Using EMG simulations, we further confirmed efficacy of the new method, demonstrating low relative error between the denoised contaminated signal (EES-processed EMG) and the original clean EMG. Although the wavelet-based filter method showed low relative error with the true clean EMG as well, ECG frequencies were not fully removed in the WA-processed signal for all simulations; in line with results from clinical data. In addition, the median frequency of the EES-processed EMG was closer to the signal's true median frequency as compared to the WA-processed EMG.

Wavelet-based adaptive filters have been increasingly proposed for removal of ECG noise from EMG recordings of various muscles, including the diaphragm, and with and without the use of extra channels for ECG recording [15–17,20,29,30]. This method performs well particularly when the ECG to EMG amplitude is high. However, obtaining a clean EMGdi can be difficult when the ECG amplitude is similar to the EMGdi amplitude, when the artifact consistently overlaps with diaphragm contraction, or when the contamination cannot be fully captured in a wavelet. The current study also illustrates that residue ECG noise present in the EMGdi-WA – particularly when overlapping with the start or end of diaphragm contraction – may limit reliability of neural inspiratory time detection. In addition, robustness and efficiency of this method may be limited by the computational complexity of the technique, including defining the optimal threshold and wavelet type.

4.3. Clinical importance

Monitoring the respiratory drive and diaphragm activity in critically ill patients using EMGdi (or its further processed EAdi signal) facilitates the implementation of a diaphragm-protective ventilation strategy and assessment of neuromuscular dysfunctions [1–3]. Recording and interpreting adequate diaphragm activity signals requires specific expertise and may be challenging in ICU patients [4,10]. We have previously demonstrated that reliability of EAdi-derived parameters and detection of neural inspiratory onset could be limited by suboptimal filtering of the ECG contamination from the EMGdi signal as processed by the ventilator software [8–10]. This could result in ventilator settings poorly adapted to the patient's physiology. Adequate detection of neural inspiratory time promotes the identification and solving of patient-ventilator asynchronies, especially when expressed as the phase angle amongst the sequential onset or offset of the EMGdi and the start or end of ventilator pressurization (e.g., such as with premature cycling and reverse triggering) [31–33]. In addition, it is important for assessment of (changes in) the coordination and contribution of the diaphragm and extra-diaphragmatic muscles of the respiratory pump during increased loaded breathing [34,35], and for the quantification of expiratory diaphragmatic activity [24,36]. If translated into a (near) real-time algorithm for use at the bedside – ideally when implemented within the ventilator software – our proposed method could allow an important optimization for bedside monitoring of diaphragm activity. In addition, improved offline processing of the EMGdi signal will result in more accurate evaluation of the diaphragm for diagnostics and research purposes. Theoretically, the Estimated ECG Subtraction technique could allow application to EMG signals derived from any type of muscle, since the need for efficient removal of ECG contamination from EMG is not just limited to the diaphragm (e.g., motor control studies involving trunk muscles).

4.4. Limitations

Limitations of the Estimated ECG Subtraction method that should be mentioned are that our method would be less robust in the presence of changes in artifact shape within a recording (e.g., such as with arrhythmias like premature ventricular or atrial contractions); however, this is a common limitation for any EMG filtering method. In addition, the normalization operation accounts for variability in Q, R and S wave amplitudes, not for variability in QR and RS times. The latter may limit accuracy of the template generation; however, any remaining ECG contamination, if present, was subsequently removed with a wavelet filter. Second, for adequate ECG contamination detection and template creation the R wave amplitude should be larger than the EMGdi amplitude after promoting the ECG in the 4–50 Hz frequency band. This step is especially important for recordings where the EMGdi amplitude can be larger than the ECG artifact; it is needed for detection of potential QRS segments using the crossing of the EMGdi-DS-A with a dynamic threshold level, and to avoid subsequent removal of important EMGdi information after template subtraction. In all ten patients with various EMGdi to ECG intensities, artifacts could be detected sufficiently after promoting the ECG frequency band and wrongly detected QRS artifacts were adequately removed based on the estimation of the artifact location (step 6 of the algorithm). Third, we did not compare our method with other denoising techniques described in literature, such as independent component analysis, or adaptive and hybrid filters. However, most of these methods visually seem less efficient than our current comparator technique, have high computational costs, or are user dependent [19–22] Therefore, we reasoned that adding more comparator methods would go beyond the scope of this study. Instead, we employed EMG simulations to quantitatively confirm our findings. Last, the signals used for development and evaluation of the filtering technique were acquired with a nasogastric catheter embedded with both a multiple-array electrode and two pressure balloons, while the EAdi catheter (Getinge, Sweden) consists of electrodes only. Addition of these balloons may affect the presence of motion artifacts in our recordings.

4.5. Future work

Although it was not the focus of the current study, it would be interesting to investigate whether a template subtraction filtering method can be applied at the bedside in real-time. We are not aware of such applications in the current EMG literature, and this requires an accurate estimation of future QRS artifact events. It should be explored whether advanced time series analyses, e.g., employing probability forecasts, could be applied. In addition, a next study should evaluate the clinical impact of our filtering technique in a larger sample. For instance, it would be interesting to quantify whether assessment of patient-ventilator interaction or calculation of neural inspiratory time improves when directly comparing the EAdi signal as filtered by the ventilator software with the envelope signal of the EMGdi-EES. This should be studied prospectively as it requires a simultaneous recording of the raw EMGdi and of the ventilator-processed EAdi signal from one nasogastric catheter, which was not available in the current study.

5. Conclusion

In conclusion, we present and confirmed efficiency of a new method, i.e., Estimated ECG Subtraction method, for ECG contamination removal from the EMGdi that does not require a dedicated ECG reference channel and utilizes the quasi-periodic characteristics of the ECG for template creation. The Estimated ECG Subtraction method performs better to yield uncontaminated EMGdi as compared to a wavelet-based adaptive filter only. Implementation of this technique may offer means to improve diaphragm activity monitoring and control in clinical practice.

CRediT authorship contribution statement

Annemijn H. Jonkman: Conceptualization, Methodology, Formal analysis, Software, Data curation, Visualization, Writing - original draft. **Ricardo Juffermans:** Conceptualization, Methodology, Software, Visualization, Writing - review & editing. **Jonne Doorduin:** Writing - review & editing. **Leo M.A. Heunks:** Conceptualization, Writing - review & editing. **Jaap Harlaar:** Conceptualization, Methodology, Formal analysis, Supervision, Writing - review & editing.

Declaration of Competing Interest

The authors declare no conflicts of interest in relation to this work. Outside of the submitted work: Annemijn Jonkman reports consultancy fees from Liberate Medical; Leo Heunks has received grants from Orion Pharma and Liberate Medical and speakers fee from Getinge.

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