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ORIGINAL RESEARCH

Tracheal sounds accurately detect apnea in patients recovering from anesthesia

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Abstract
Apnea should be monitored continuously in the post anesthesia care unit (PACU) to avoid serious complications. It has been confirmed that tracheal sounds can be used to detect apnea during sedation in healthy subjects, but the performance of this acoustic method has not been evaluated in patients with frequent apnea events in the PACU. Tracheal sounds were acquired from the patients in the PACU using a microphone encased in a plastic bell. Concurrently, a processed nasal pressure signal was used as a reference standard to identify real respiratory events. The logarithm of the tracheal sound variance (log-var) was used to detect apnea, and the results were compared to the reference method. Sensitivity, specificity, positive likelihood ratios (PLR), and negative likelihood ratios (NLR) were calculated. One hundred and twenty-one patients aged 55.5 ± 13.2 years (mean ± SD) with a body mass index of 24.6 ± 3.7 kg/m^2 were included in data analysis. The total monitoring time was 52.6 h. Thirty-four patients experienced 236 events of apnea lasting for a total of 122.2 min. The log-var apnea detection algorithm detected apnea with 92% sensitivity, 98% specificity, 46 PLR and 0.08 NLR. The performance of apnea detection in the PACU using the log-var tracheal sounds method proved to be reliable and accurate. Tracheal sounds could be used to minimize the potential risks from apnea in PACU patients.

Keywords Tracheal sounds · Acoustic monitoring · Apnea detection · Recovery from anesthesia

1 Introduction

Apnea during recovery from anesthesia in the post anesthesia care unit (PACU) [1, 2] can be associated with serious sequelae and increased morbidity and mortality if not discovered and corrected within a short period of time. The frequency and the length of periods of apnea experienced by patients in the PACU are related to the anesthetic drugs and muscle relaxants administer and to the patient's sensitivity to those anesthetics and muscle relaxants. Patients with obstructive sleep apnea syndrome (OSAS), morbid obesity, neuraxial opioid or patient-controlled analgesia (PCA) appear to be at significantly higher risk for apnea [3–7]. Late detection of apnea continues to cause severe complications, such as metabolic acidosis, hypoxia, bradycardia, and even cardiac arrest [8].

The current methods used to detect apnea in non-intubated patients after anesthesia have limitations. Visual inspection of respiratory activity is time consuming, intermittent and often ineffective for detecting significant events [9, 10]. Pulse oximetry is a reliable estimate of arterial oxygenation; however, a fall in oxygen saturation alone does not

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provide a reliable indication of the adequacy of a patient's ventilation. Early detection of hypoventilation, airway obstruction, or apnea, and the fall in arterial oxygen saturation can be delayed, especially when supplemental oxygen is administrated [11, 12]. Capnography has been found to be more reliable than pulse oxymetry in early detection of apnea or hypoventilation [13], but nasal cannulas or face masks are often not well tolerated by patients, especially not by young children [14]. Capnography sampled through a nasal cannula may be inaccurate during mouth breathing, airway obstruction, or when oxygen is administrated through the cannula [4, 15, 16]. Transthoracic impedance respiratory rate monitoring can be used to detect significant decreases in respiratory rate, which supports detection of central apnea. However, the modality is sensitive to various artifacts, such as coughing, shivering and movement, causing obstructive apnea detection to be delayed or missed while thoracic respiratory movements persist [17, 18].

We previously showed that tracheal sounds can be used to detect apnea with acceptable sensitivity and specificity [19] during sedation in healthy subjects, but the accuracy and reliability of this acoustic method for apnea detection in the PACU have not been examined. The logarithm of tracheal sounds' variance could be used as an alternative to entropy for estimating respiratory flow [20, 21], and it has advantages of lower computational cost and higher speed with acceptable precision compared to other features [22–24]. We hypothesized that tracheal sounds' variance may detect apnea with high sensitivity and specificity in patients undergoing recovery from anesthesia in the PACU.

2 Methods

After obtaining approval for the study protocol from the Human Institutional Review Board of the China Medical University and written informed consent from patients, an observational study was conducted during their PACU stay after surgery. Subjects were excluded if they had postoperative agitation, head and neck wounds or skin abnormalities which would affect sensor placement, and tracheotomy or other mechanical airway devices. The monitoring of oxygen saturation, heart rate, electrocardiogram, blood pressure and respiratory rate were applied to all the subjects as recommended by the American Society of Anesthesiologists [25]. Other monitoring and treatments were given following conventional practice, depending on the patients' state, such as patient controlled anesthesia (PCA) or opioid bolus. Facemasks (HX.O01, Kyoling, Hangzhou, China) were used to provide supplemental oxygen with 5 ~ 8 L/min flow rates.

Tracheal sounds from the patients in the supine position were acquired using a microphone (HC4015G-02L25-423, Hong Chang Electronics, Shenzhen, China) encased in a plastic bell, 25 mm in diameter. This microphone provides a flat frequency response (± 3 dB) between 100 and 5000 Hz. The bell was attached to the subject's neck using a double-stick disc (#2181 3M, St Paul, MN), just below the larynx and above the suprasternal notch (Fig. 1). The audio signals were continuously recorded by a digital voice recorder (ICD-SX734, Sony, Dongguan, China) at 44,100 Hz. Meanwhile, each subject was also fitted with a nasal cannula connected to a sleep apnea screening monitor (RS01, Contec Medical Systems, Qinhuangdao, China) to collect nasal flow pressure signals at 50 Hz. Our pilot study showed that the oxygen mask above the nasal cannula (Fig. 1) caused an enhanced amplitude of the nasal flow pressure signal, even if the patient was also mouth breathing. Thus the nasal flow pressure signals were relatively reliable and accurate for recording the patients' respiratory status in most cases. Tracheal sounds and pressure were collected throughout the PACU stay. Data from the digital voice recorder and sleep apnea screening monitor were transferred to a computer for further analysis. Both signals were processed and analyzed in Matlab R2015a (MathWorks Inc., Natick, MA).

Tracheal sounds were initially filtered using a 5th-order Butterworth filter with a passband between 150 and 800 Hz to minimize heart sounds, muscle interference and high-frequency noise (Fig. 2a). The filtered signal was segmented into windows of 20 ms with 75% overlap between adjacent windows. The logarithm of the tracheal sound variance (log-var) in each window was calculated. The values of optimum window size and overlap for segmenting the tracheal sound signal were selected based on the results of the studies on acoustical flow estimation [26]. Each patient's log-var subtracted the most negative value in the corresponding tracheal sounds data, so that the characteristic signal was converted to be positive to facilitate subsequent analyses. Because tracheal sounds and nasal flow pressure data were recorded on different devices, log-var of acoustic data were synchronized

Fig. 1 Data acquisition in the PACU

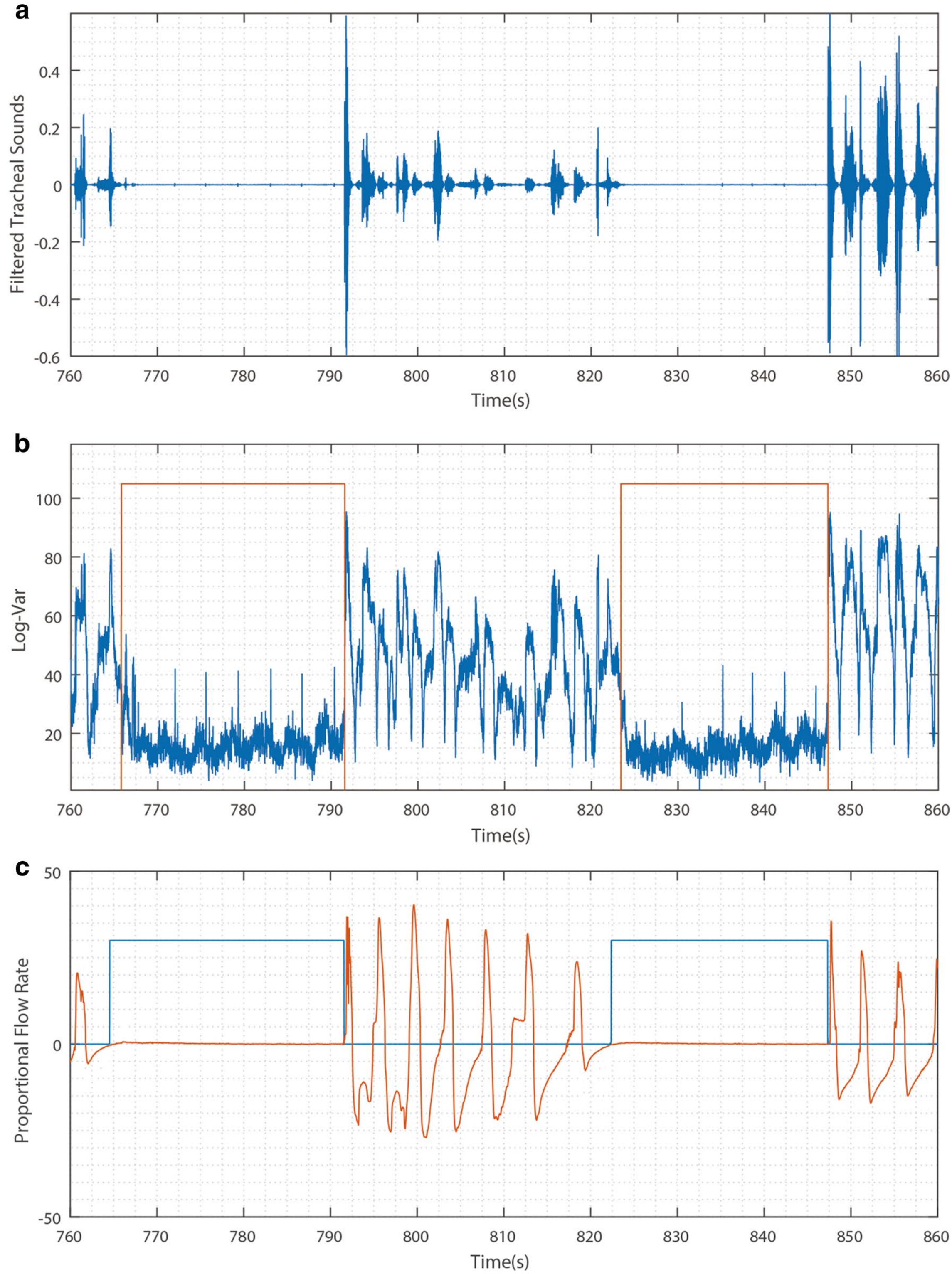

Fig. 2 **a** Filtered tracheal sounds, **b** log-var signal, the red rectangle represents apnea, **c** proportional flow rate signal, the blue rectangle represents apnea

to the nasal flow pressure signal by finding the maximal correlation coefficient when moving log-var signals in 0.02 s after the sample rate was reset to 200 Hz.

A log-var threshold that distinguished apnea from regular breathing was determined using our previous study method [19], by which (a) the log-var block was divided into 1.5 s windows, (b) the minimum value in each window was recorded, and (c) the threshold was calculated as two times the 80th percentile of all the minimum values in that block. For each patient, the log-var thresholds were found every five sequential minutes and the final block was often > 5 min in length but was included in our analysis. Using the log-var threshold, an inspiration or expiration was marked when the log-var signal crossed the threshold and lasted for at least 0.5 s [19]. Absence of inspiration or expiration for more than 15 s was considered an event of apnea. The red rectangle in Fig. 2b shows two identified apneic periods based on the log-var. The algorithm failed to detect hypopnea because low flow rate still produced tracheal sounds.

The nasal flow pressure signals from sleep apnea screening monitor were first bandpass filtered in the range of 0.1–15 Hz to remove the effects of heart beat and baseline drift, and then resampled at 200 Hz. The nasal pressure provides a signal proportional to the square of the flow rate [27]. Accordingly, the signal with a square root transformation (proportional flow rate signal) provided a more accurate estimate of flow rate and was used as a reference signal for detecting apnea, after synchronization. Figure 3 shows the filtered nasal pressure signal with and without the square root transformation. A proportional tidal volume was calculated by the integral of continuous positive value in the reference signal. For a breath to be valid, in every patient's reference signal data block, the inspired proportional volume had to exceed 10% of the maximum proportional tidal volume and the expiratory proportional flow rate had to be less than 10% of the minimum value of the reference signal at the start of exhalation and greater than it at the end of exhalation, as shown in Fig. 4. Apnea was identified within the reference signal when the time between the end of the last breath and the start of the next breath was longer than 15 s. The criterion for apnea is from our previous study [19]. The blue rectangle in Fig. 2c shows two identified apnea events based on the reference signal. For all the apnea events detected by the reference signals, a technician would conduct a manual validation by listening to the tracheal sounds and simultaneously viewing both waveforms of reference signals and the corresponding tracheal sounds. If continuous tracheal sounds existed and the technician judged it as valid breathing, we rejected this apnea event detected by reference signal. The retrospective analysis showed there were a small number of contentious events which were usually caused by displacement of the nasal cannula or complete mouth breathing without nasal breathing. This combined validation has been described previously [14, 28] and further improved the reliability of apnea detection by reference signals.

The accuracy of apnea detection from tracheal sounds was calculated by comparing it with apnea events detected by the reference method. A true positive (TP) was defined if apnea was detected from both the tracheal sounds and the reference method. A false negative (FN) was defined if apnea was detected from the reference method but not from tracheal sounds. False positive (FP) means that apnea was detected from the tracheal sounds but not from the reference method, and true negative (TN) means that apnea was

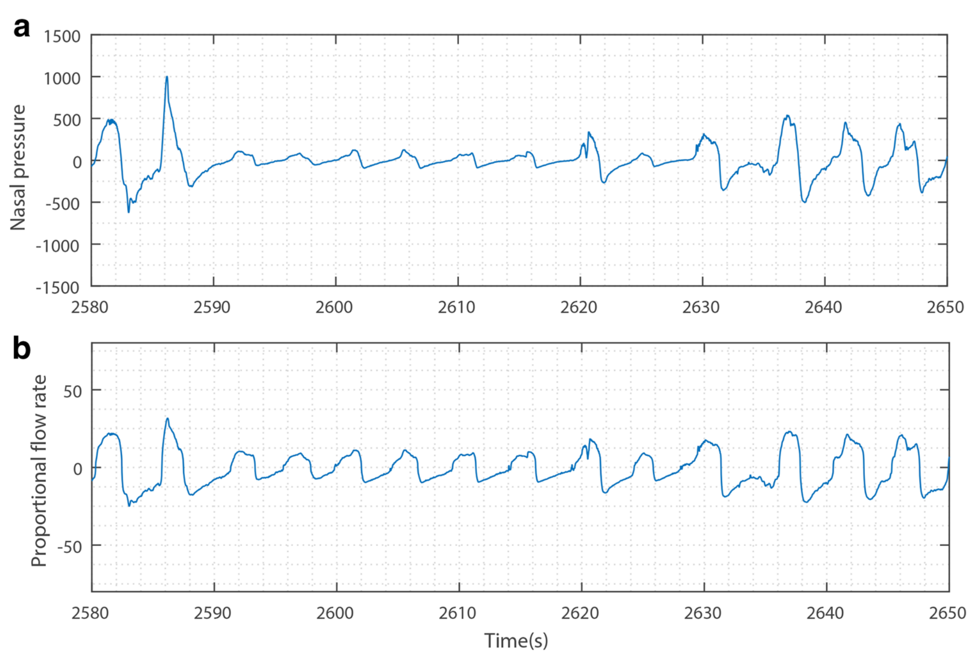

Fig. 3 **a** Filtered nasal pressure signal without square root transformation, **b** filtered nasal pressure signal with square root transformation (reference signal)

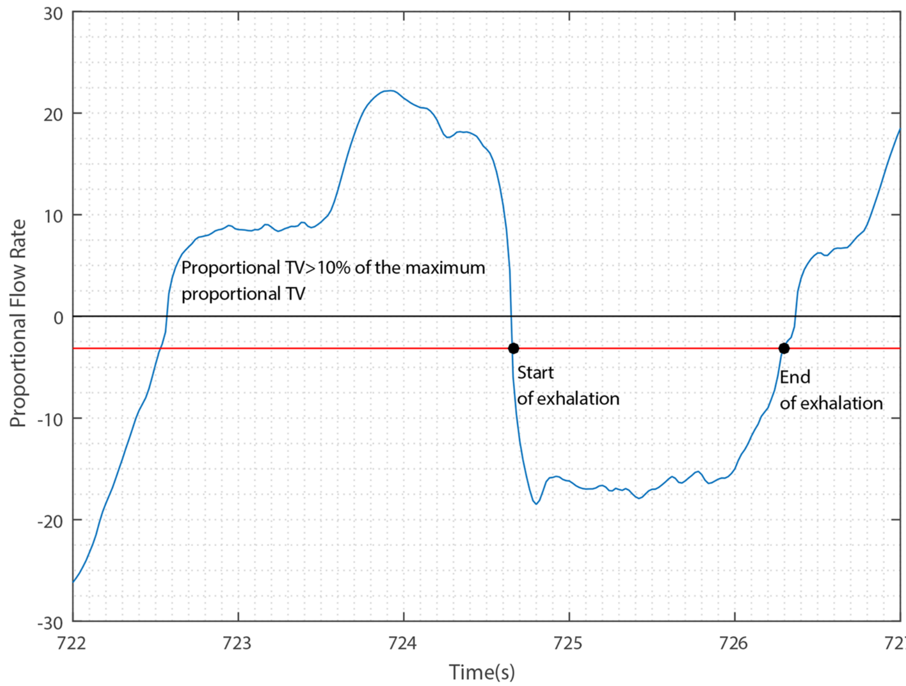

Fig. 4 Definition of a valid breath using the proportional flow rate signal: inspired proportional TV had to exceed 10% of the maximum proportional TV and the expiratory proportional flow rate had to be less than 10% of the minimum value of the reference signal at the start of exhalation and greater than it at the end of exhalation. *TV* tidal volume

neither detected from reference method nor tracheal sounds. The amount of time in which neither the acoustic apnea detection method nor the reference apnea detection method detected apnea was divided by 15 s to calculate a value for the number of TN. Sensitivity (TP/[TP + FN]), specificity (TN/[TN + FP]), positive likelihood ratios (PLR = Sensitivity/[1 − Specificity]), and negative likelihood ratios (NLR = [1 − Sensitivity]/Specificity) were calculated. The sensitivities and specificities for the patients with the same number of apnea events were calculated.

3 Results

One hundred forty-five patients were enrolled in the study. Data from 24 patients were not included due to technical error or fault of the device (n = 7), poor audio recording quality related to sensor placement (n = 9), absence of breaths detected by nasal pressure related to incorrect placement of the nasal cannula (n = 3), and data unavailable from both sensors (n = 5). Thus, 121 patients were included in the data analysis. The total monitoring time was 52.6 h. Thirty-four patients had 236 events of apnea lasting with a total of 122.2 min. The demographic information for five patients was not recorded, so Table 1 lists the demographics of the remaining 116 patients as well as the number of all patients who experienced apnea events. Table 2 shows the prevalence of apnea in different procedure locations, the presence of postsurgical analgesia and the types of anesthesia.

The log-var apnea detection algorithm had a 92% sensitivity, 98% specificity, 46 PLR and 0.08 NLR in our study.

Table 1 Demographics of 116 patients with available data and the number of all patients with apnea events detected by the reference method

	Mean (SD)	Min	Max
Number	116		
Number with apnea	34, 236 events		
M/F	51/65		
M/F with apnea	15/19		
Age, year	55.5 (13.2)	18	79
Height, cm	165.9 (7.9)	150	186
Weight, kg	67.8 (12.9)	42	102
BMI, kg/m^2	24.6 (3.7)	16.9	35

Table 3 shows that the tracheal sounds correctly detected apnea 217 of the 236 times it occurred. Meanwhile, tracheal sounds falsely reported apnea 291 times during a period that contained 11,859 nonapnea events.

Thirty–four patients with apnea were divided into 14 groups in which the patients had the same number of apnea events, and the sensitivity in each group was calculated. Figure 5 shows the calculated sensitivities. The remaining 87 patients without apnea were classified as the 15th group. The specificities of all the 15 groups were also calculated. Figure 6 shows the calculated specificities. The missed events of apnea (19 times) and false apnea alarms (219 times) were distributed in these groups and result in different sensitivity and specificity. We observed that most of the sensitivities

Table 2 Locations of procedures, postsurgical analgesia, types of anesthesia and associated events of apnea detected by the reference method

Locations of procedures	n
Thorax	12 (19%) of 63 Experienced 80 (33.9%) events of apnea
Abdomen	8 (33%) of 24 Experienced 51 (21.6%) events of apnea
Lower extremity	8 (50%) of 16 Experienced 80 (33.9%) events of apnea
Other (lumbar vertebrae, eyes, etc.)	6 (46%) of 13 Experienced 25 (10.6%) events of apnea
Postsurgical analgesia	**n**
PCIA	5 (23%) of 22 Experienced 50 (21.2%) events of apnea
PCEA	5 (25%) of 20 Experienced 25 (10.6%) events of apnea
other	24 (32%) of 74 Experienced 161 (68.2%) events of apnea
Types of anesthesia	**n**
Total intravenous anesthesia	5 (29%) of 17 Experienced 58 (24.6%) events of apnea
Intravenous anesthesia combined with inhalation anesthesia	24 (32%) of 75 Experienced 153 (64.8%) events of apnea
General anesthesia combined with epidural anesthesia	5 (21%) of 24 Experienced 25 (10.6%) events of apnea

PCIA patient-controlled intravenous analgesia, *PCEA* patient-controlled epidural analgesia

Table 3 Number of times apnea was detected by tracheal sounds and the reference method

Tracheal sounds	Reference method	
	Apnea	Normal
Apnea	217 Times (TP)	291 Times (FP)
Normal	19 Times (FN)	11,568 Times (TN)

TP true positive, *FP* false positive, *FN* false negative, *TN* true negative

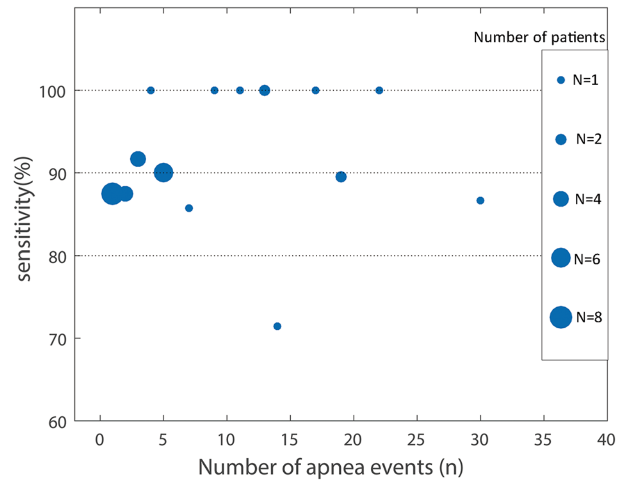

Fig. 5 Different sensitivities for the patients with the same number of apnea events

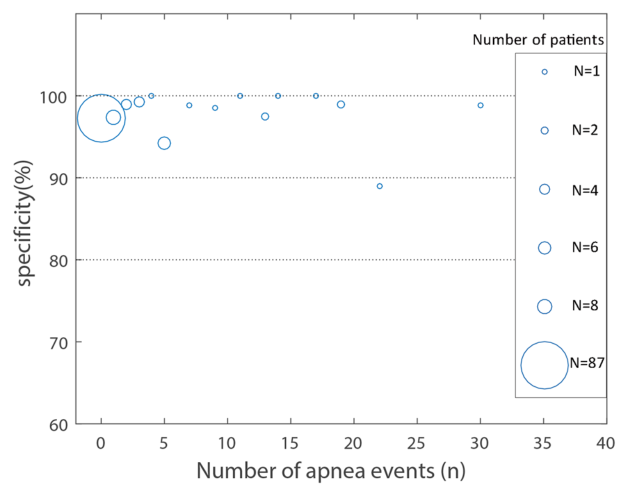

Fig. 6 Different specificities for the patients with the same number of apnea events

were between 87 and 100%, and most of the specificities ranged from 97 to 100%.

4 Discussion

Our results show that the variance of tracheal sounds can reliably detect the onset of apnea in PACU patients with high sensitivity (92%) and specificity (98%), thereby potentially indentifying patients at risk for the sequelae associated with apneic events.

Different acoustic methods of respiratory monitoring have been developed in recent years [14, 28, 29]. However, most of these studies focused on the detection of respiratory rate and failed to indicate pauses in ventilation rapidly because respiratory rate needs to be averaged over some time interval. With the increasing prevalence of obstructive sleep apnea syndrome (OSAS) and the use of post-operative opioids, it is crucial to monitor not just respiratory rate, but the adequacy of ventilation. Ramsay et al. [28] detected apnea with the lower sensitivities of 81% and 62%, respectively, using acoustic monitoring (RAS-125c, Masimo, Irvine, CA, USA) and capnometry in the PACU, but the study included only 21 instances of apnea that occurred across only 33 subjects. Our study included more events of apnea from a larger number of patients (236 instances of apnea that occurred across the 121 patients) as well as a description of how the apnea events were distributed, so that the performance of apnea detection can be assessed more accurately.

The Masimo product used a piezo-electric film as a transducer on the side of the neck rather than a microphone encased in a plastic bell on the tracheal (just below the larynx and above the suprasternal notch). This makes it subject to low frequency vibration and results in a lower signal-to-noise ratio. Functioning in the similar mechanism as stethoscope, the plastic bell we used dampened ambient noise. Although the Masimo does have the advantage of being easily applied, it did not work well in an acoustically noisy environment without a noise-cancellation feature. The Masimo device also might rely heavily on the pulse-oximeter to detect apnea. Our method further improved the detection of adverse respiratory events so that the patients' potential injuries could be preventable with this better monitoring and timely response to apnea [30].

The nasal flow pressure has previously been used as a standard signal for monitoring respiratory rate in related research [17]. It is more well tolerated by PACU patients than pneumotachography which requires a tight-fitting mask. The nasal cannula is also typically used for oxygen delivery. Due to the non-linear characteristics of the nasal pressure signal (proportional to the flow rate squared) [27], the signal underestimates low flow rates and could result in the misdiagnosis of apnea when some valid shallow breaths appear or nasal breathing is combined with mouth breathing. A square root transformation of the nasal pressure signal allows for an improved estimate of flow rate and minimizes this problem. Using a nasal pressure signal with the square root transformation is well known in polysomnography for scoring respiratory events in sleep [31]. The inspired proportional volume and the expiratory proportional flow rate threshold used in our study ensure that the reference signals annotate the majority of apnea and nonapnea events properly even if the timing of apnea onset and resolution might change slightly with the threshold variation. Just as with the definition of apnea (a cessation of breath longer than 15 s), the thresholds chosen may also affect the results, albeit negligibly.

5 Limitation

Although we explored the optimal placement location of the plastic bell in our pilot study, inaccurate placement or unsecure attachment of the bell by the data collector at the beginning of our experiment resulted in poor quality of tracheal sounds for some patients. Poor quality tracheal sounds could not reflect the breath trend and the sounds could not even be heard by the technician. We just excluded these tracheal sounds from analysis and didn't provide a solution to alert this invalid signal at the beginning of collection. In future studies, an algorithm to evaluate the quality of tracheal sound signals could be developed to help the user adjust placement of the bell during monitoring if needed.

Although the plastic bell dampened part of ambient noise, tracheal sounds monitoring may fail to detect apnea when the noise penetrated the bell and was detected as a normal breath when actual apnea appeared. Persistent noise may raise the log-var threshold and result in false apnea alarms. A better bell material to dampen the environment noise is likely necessary. An adaptive noise cancellation device would also be a good addition to the system.

Our algorithm failed to distinguish loud snoring during severe airway obstruction from normal snoring or breathing. Tracheal sounds combined with a nasal thermistor which is associated with the patient's ventilation can resolve this issue and improve the sensitivity further when severe airway obstruction produces apnea or hypopnea. The real-time performance of log-var threshold was not evaluated because the threshold was based on retrospective analysis of 5-min epochs. Some optimized algorithm based on log-var should be measured in a prospective real-time study.

6 Conclusion

Our results suggest that tracheal sounds reliably and accurately detects apnea in patients recovering from anesthesia in the PACU. This acoustic method for apnea monitoring is not affected by supplemental oxygen and is more well tolerated than monitoring via a nasal cannula or face mask. This monitoring method can help minimize the risks of adverse respiratory events of the patients, and decrease the perceived workload of PACU staffs which might potentially further improve patients' safety.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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