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Agreement between respiratory rate measurement using a combined electrocardiographic derived method versus impedance from pneumography

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ABSTRACT

Background: Impedance pneumography (IP) is the current device-driven method used to measure respiratory rate (RR) in hospitalized patients. However, RR alarms are common and contribute to alarm fatigue. While RR derived from electrocardiographic (ECG) waveforms hold promise, they have not been compared to the IP method. Purpose: Study examined the agreement between the IP and combined-ECG derived (EDR) for normal RR (≥12 or ≤20 breaths/minute [bpm]); low RR (≤5 bpm); and high RR (≥30 bpm). Methodology: One-hundred intensive care unit patients were included by RR group: (1) normal RR ($n = 50$; 25 low RR and 25 high RR); (2) low RR ($n = 50$); and (3) high RR ($n = 50$). Bland-Altman analysis was used to evaluate agreement. Results: For normal RR, a significant bias difference of −1.00 + 2.11 (95% CI −1.60 to −0.40) and 95% limit of agreement (LOA) of −5.13 to 3.13 was found. For low RR, a significant bias difference of −16.54 + 6.02 (95% CI: −18.25 to −14.83) and a 95% LOA of −28.33 to - 4.75 was found. For high RR, a significant bias difference of 17.94 + 12.01 (95% CI: 14.53 to 21.35) and 95% LOA of −5.60 to 41.48 was found. Conclusion: Combined-EDR method had good agreement with the IP method for normal RR. However, for the low RR, combined-EDR was consistently higher than the IP method and almost always lower for the high RR, which could reduce the number of RR alarms. However, replication in a larger sample including confirmation with visual assessment is warranted.

Introduction

In hospitalized patients, abnormal respiratory rate (RR) (e.g., tachypnea, bradypnea) is often the first indication of impending respiratory arrest and/or the need for rescue intubation [1–4]. Visual assessment of RR is insufficient because this measure is not obtained frequently nor with a high degree of accuracy. Therefore, early recognition of respiratory compromise can be delayed and/or missed. In hospital settings that utilize electrocardiographic (ECG) monitoring, such as critical care and step down units, impedance pneumography (IP) has been incorporated into these systems for continuous RR monitoring.

For the IP method, the algorithm that derives RR uses alternating electrical currents measured on the torso [5,6]. While the IP method uses the ECG lead wires and skin electrodes to deliver alternating currents, ECG waveforms (i.e., P-wave, QRS, T-wave) are not used to calculate the RR. The major advantages of the IP method are that it is safe and simple to use and is integrated into current ECG monitoring devices. However, signal interruptions (i.e., poor skin electrode contact, skin electrodes fall off), as well as patient movement and cardiac artifact effect the accuracy of IP RR [7,8]. In addition, the hardware components of the IP method (e.g., lead wires/cables) can be sources of IP measurement error [9]. As a result, the IP method is prone to frequent RR alarms that contribute to alarm fatigue in clinicians [7,9–13].

In one comprehensive study in 461 ICU patients ($n = 77$ beds),161,931 RR alarms (i.e., high and low parameter limit and apnea) were found during the one-month study period or 68 RR alarms/bed/

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day [7]. While the RR alarms were not annotated in this study (i.e., true versus false), the investigators found that the IP respiratory waveform was often flat in patients who were known to be breathing adequately (e.g., no respiratory arrest or need for intubation). Therefore, while the IP method has important advantages for RR assessment in hospitalized patients, the data show that IP RR measurements are prone to false alarms, which limits the value of this technology to identify patients with respiratory compromise.

Given the problems with IP generated RR, researchers are exploring alternative methods to measure RR using ECG waveforms (i.e., QRS and R-to-R intervals) [14]. While the ECG-derived (EDR) method is not currently available for use in the hospital setting, this method has numerous advantages [14]. For instance, like IP, the EDR method is non-invasive; uses already existing data from bedside ECG monitors; and RR assessments can be done continuously [15]. One study showed that because ECG QRS amplitude changes are highly correlated with tidal volume changes during breathing they may be more suitable than IP for calculating RR [14]. In addition, the ECG derived method has been used to identify abnormal respirations associated with sleep disordered breathing [16–21]. However, similar to the IP method, the EDR method is prone to signal quality issues, device failure, and/or patient movement. In addition, the EDR method is less reliable in older patients due to the following factors: a decline in respiratory sinus arrhythmia (RSA), which is used in the EDR method; age related arrhythmias (e.g., atrial fibrillation); and the use of medications that effect heart rate and rhythm (e.g., beta-blockers, antiarrhythmics) [14]. A method that requires evaluation is one that combines both IP and ECG signals along with the myogram. This combination may improve the accuracy of algorithm-based RR assessment.

While visual assessment (VA) of RR is the non-invasive gold standard method, a great deal of interest exist in device driven methods for hospital-based monitoring because RR changes can occur quickly and could be missed by using VA alone [22]. The VA method can interrupt a nurse's workflow because they must stop care activities and carefully count full breaths for one minute. In addition, VA of RR can be difficult in patients who are talking, not able to follow instructions and/or cooperate.

In a prior study examining VA of RR, RR was often estimated, guessed, omitted, or simply copied from a previous assessment [23]. In another study, nurses reported intentionally or unintentionally omitting RR assessments over 90% of the time [24]. Finally, in a study that examined 62 patients with 1597 unique vital signs recorded, only one RR assessment was documented per day, while multiple recordings of blood pressures (5/day); heart rate (4.4/day); and temperature (4.2/day) were documented (all $p < 0.001$) [25].

Only four studies have compared VA, IP, and EDR assessment of RR [26–29]. Importantly, none of these studies compared all three methods in the same patient [22]. In the three studies that compared the VA and IP methods [26,27,29], the upper and lower limits of agreement (LOAs) between the two methods were extremely poor.

Other studies have evaluated the EDR method but did not include confirmatory VA. One study found that RR algorithms that use ECG waveform data performed better than RR algorithms that use only an IP signal [15]. In a second study, three different algorithm-based RR methods were compared to RRs obtained using an air flow sensor [14]. The three algorithm-based approaches included: an EDR only method; an electromyogram method; and a RSA method. The RR accuracy ranged from 80% to 90% depending on the performance measure used in this study. Of note, these authors concluded that a combination of these different methods, rather than one, may improve the overall performance of RR assessment.

Given the importance to RR assessment and the identified challenges associated with the VA and IP methods, a need exists to evaluate alternative methods to objectively measure RR in hospitalized patients. An alternative approach to the limitations identified for the individual algorithms discussed above, would be to create an algorithm that combines all of the available physiologic signals (i.e., IP, oxygen saturation [SpO2], ECG and the myogram), to create a "combined-EDR method." Recent work from our research team has evaluated the accuracy of an ECG only method to detect abnormal breathing associated with Cheyne-Stokes respirations. In one study that included hospitalized cardiac patients ($n = 90$) and a group of healthy community based participants ($n = 100$), it was found that patients with acute coronary syndrome had 7.3 times more Cheyne-Stroke respiration episodes (>3 consecutive cycles of hyperpnea/hypopnea with apnea) as compared to healthy community-based adults [19]. In a separate study that included 461 ICU patients, patients who had a higher rate of Cheyne-Stroke respirations (mean number/h = 1.19 ± 1.12) had a higher frequency of cardiorespiratory arrest when compared to ICU patients with lower rates of Cheyne-Stokes respirations (mean number/h = $0.02 + 0.02$; $p = 0.001$) [30].

In the current study, we build on this work by examining the agreement between the IP method and a combined-EDR method in a group of adult ICU patients. The purpose of this study was to examine the RR agreement between the IP and a combined-EDR method for: (1) normal RR (≥12 or ≤ 20 bpm); (2) low RR (≤5 bpm); and (3) high RR (≥30 bpm).

Materials and methods

Research design and setting

This study is a secondary analysis of data from the University of California, San Francisco (UCSF) Alarm Study, detailed methods were published previously [7]. In brief, the UCSF Alarm study was an observational study designed to examine the total number of alarms generated from bedside physiologic monitors during a one-month period (March 2013). Data were collected from three adult ICUs (i.e., cardiac [16 beds]; medical/surgical [32 beds]; and neurological [29 beds]). Each bed was equipped with a Solar 8000i bedside monitor (version 5.4 software, GE Healthcare, Milwaukee, WI). The study used a data capture system to collect all available physiological signals and alarms from the bedside monitor. The physiologic data passed securely through the hospital's Enterprise network to a secure server in our research lab for off-line analysis. For this study, we utilized the following physiologic data: IP, SpO2 and ECG waveforms. The study was approved by the Institutional Review Board (IRB) with a waiver of signed patient consent because physiologic monitoring is done as part of standard care and the data were analyzed retrospectively.

Sample

The primary study collected data from 461 consecutive ICU patients. For the current study, we randomly selected 50 patients who had one or more low RR IP parameter limit alarms (≤5 bpm) and another 50 patients who had one or more high RR IP parameter limit alarms (≥30 bpm). These parameter limit alarms were selected based on the current alarm configuration used in our bedside ICU monitors (described below). From the sample of 100 patients, we randomly selected a subgroup of 25 patients from each group (i.e., 25 patients with low RR parameter limit alarms and 25 patients with high RR parameter limit alarms) for the normal RR comparisons. A normal RR was identified prior to the IP RR limit alarm (i.e., low or high RR). While we attempted to identify "normal" RRs (i.e., between 12 bpm and 20 bpm) using this approach, a small subset of the ICU patients were consistently tachypneic (i.e., >20 bpm) because of their acute illness. Therefore, we used a clean IP RR signal prior to a low or high RR alarm for the normal RR comparisons.

In addition to the RR data we collected the following variables from the electronic health record: demographic (i.e., age, gender, and race) and clinical characteristics (i.e., BMI, current smoker, impaired cognitive status, tremor); ICU type (i.e., cardiac, medical/surgical, neurological); use of mechanical ventilation; and mean ICU monitoring time. These variables were selected because of their potential impact on IP RR [27,31,32].

IP method

To derive RR using the IP method, a drive-and-measure circuit is established that delivers two out-of-phase AC-coupled currents into a combination of ECG lead wires and their corresponding skin electrodes [8,33]. During inspiration, as the chest expands, resistance to the flow of the electrical current increases which increases impedance. Alternatively, during expiration, as air leaves the lungs impedance decreases. The difference in the amplitude of the injected current during inspiration (chest expands; impedance rises) and expiration (chest recoiles: impedance falls) is displayed as an IP waveform on the bedside physiologic monitor. The manufacture of the bedside monitor used in this study adds a "marker," or artificial flag, on the IP waveform so that clinicians can identify inspiration (upward flag) and expiration (downward flag). In addition to the IP waveform, a numeric RR value is displayed on the bedside monitor.

The bedside monitor used in this study, uses either lead I or lead II to measure the IP RR. Therefore, when lead I is selected, the AC signal is applied to the right arm and left arm electrodes. Whereas the right arm and left leg electrodes are used if lead II is selected for IP RR. The IP ECG lead (i.e., I or II) is a pre-determined setting in the bedside monitor. However, the leadcan be changed by the user based on whether the patient is a chest or an abdominal breather. The default IP ECG lead used in our ICUs is lead II. As mentioned previously, while ECG lead wires and skin electrodes are used to measure an IP RR, the ECG waveforms are not used. However, the IP signal can be disrupted by motion artifact and or ECG lead failure (i.e., broken or frayed), poor skin electrode contact, or the skin electrode(s) fall off.

Combined-EDR method

The algorithm for the combined-EDR method was created by biomedical engineers in the UCSF Center for Physiologic Research. This algorithm uses the IP waveform, the plethysmograph from the oxygen saturation sensor (SpO2), ECG signals and the myogram to derive RR. Below we describe in more detail the signals used in the combined-EDR method.

ECG signals used for RR detection

The combined-EDR algorithm uses all seven of the available ECG leads from the bedside monitor including leads: I, II, III, aVR, aVL, aVF and one V lead, which is V1 at our hospital. The combined-EDR algorithm uses changes in R-to-R intervals to identify RR. Breathing causes slight changes in heart rate (i.e., increased heart rate with inspiration; decreased heart rate with expiration) that can be detected as RSA. While RSA is easily observed in young healthy people, the heart rate tends to become more fixed with age and co-morbidities (e.g., heart failure, diabetes) [14,34]. Therefore, using only R-to-R intervals to measure RR is not sufficient for accurate and reliable RR calculations. Therefore, in addition to the R-to-R intervals, the literal QRS area, or the sum of all of the QRS complexes from all available ECG leads, is used. For example, during inspiration and expiration the heart moves relative to the ECG skin electrodes on the body surface, which are at fixed locations on the chest. The amplitude (height) and width (duration) of each waveform that make up the QRS complex (i.e., Q, R, and S waves) are measured and used in the combined-EDR algorithm. Finally, the combined-EDR method uses the myogram from the ECG skin electrodes on the torso. During inspiration and expiration both chest muscle and diaphragm effort are measured from the skin electrodes during breathing.

Additional physiologic signals for RR detection

In addition to the ECG features and myogram signal described above, the combined-EDR method incorporates the IP and SpO2 signal. The combined-EDR algorithm generates an RR by examining and combining all of these features. A good quality signal from at least two of the aforementioned parameters (ECG, myogram, IP and Sp02) must be present for the combined-EDR algorithm to generate a RR.

Data acquisition for comparing the IP versus combined-EDR methods

IP data

The IP RR data from the bedside physiologic monitors were stored as Standard for the Exchange of Product Data (STEP) or STP files. The STP files were converted into binary files and exported into the Continuous ECG Recording Suite (CER-S software program,Amps LLC, New York, NY). The CER-S software allowed for qualitative assessment of the IP waveforms at the time that comparisons were done between the IP versus combined-EDR methods. To optimize the workflow in the CER-S tool the following steps were taken: multi-day recordings were formatted in 24-h periods from midnight to midnight; data were compressed using a loss-less proprietary algorithm, which varied between a three and four-fold rate, depending on the input signals; and all of the data were de-identified. Fig. 1 illustrates a screen shot of the CER-S software tool that was used to identify the IP RR for comparisons with the combined-EDR method.

Combined-EDR data

The physiologic signals (i.e., IP, SpO2, ECG [seven leads], and the myogram) were processed with the combined-EDR algorithm. The entire ICU monitoring period was processed and a combined-EDR RR was generated every 30 s. These data were exported into Microsoft Excel (2021 version, Microsoft Corporation, Redmond Washinton) as a comma separated value (.csv) file in order to make comparison between RRs generated by the IP and combined-EDR method. The IP RR data (normal, low, and high RRs) identified in the CER-S software tool and the corresponding time of the combined-EDR RR were used for the comparisons. The times for the comparisons between the IP and combined-EDR methods were within one-minute of each other. Two reviewers independently collected the RR data. The reviewers met weekly and overall inter-rater agreement was 95%.

Data analysis

Descriptive statistics were generated for each of the RR groups. The groups were compared on demographic, clinical characteristics, ICU type and use of mechanical ventilation. Data are expressed as means and standard deviations and percentages. Scatter plots were generated to evaluate the relationships between the IP and combined-EDR RRs. In addition, for each RR group, the agreement between the two methods (IP versus combined-EDR) was evaluated using Bland-Altman analysis [35]. This approach included plots of the mean difference in RR between the two methods against the average of the two measurements. In the case of strong agreement, the mean difference between the two methods is expected to be 0 or close to 0. An advantage of a Bland-Altman analysis is that it can uncover measurement bias (i.e., a significant slope on the regression line of the scatter plot) related to the underlying true RR in the event that one of the two methods was systematically worse at accurately capturing values at either end of the range of all RRs.

The Bland-Altman analysis reports the estimated difference between the two measurements with 95% limits of agreement (LOA) around the estimate (mean difference of $\pm$1.96 SD) and a test of bias in the form of ordinary least of square (OLS) regression on these estimates. Statistically significant differences were noted at a p-value of $<$0.05. Descriptive analyses were performed using SPSS version 27 (IBM Corporation, Armonk, NY). The Bland-Altman analysis was performed using R version 4.0.0 and BlandAltmanLeh package v0.3.1 statistical software [35–37].

Results

Demographic and clinical characteristics

The demographic and clinical characteristics, ICU type and use of mechanical ventilation by RR group are presented in Table 1. The time differences between the two RR methods used for comparison was

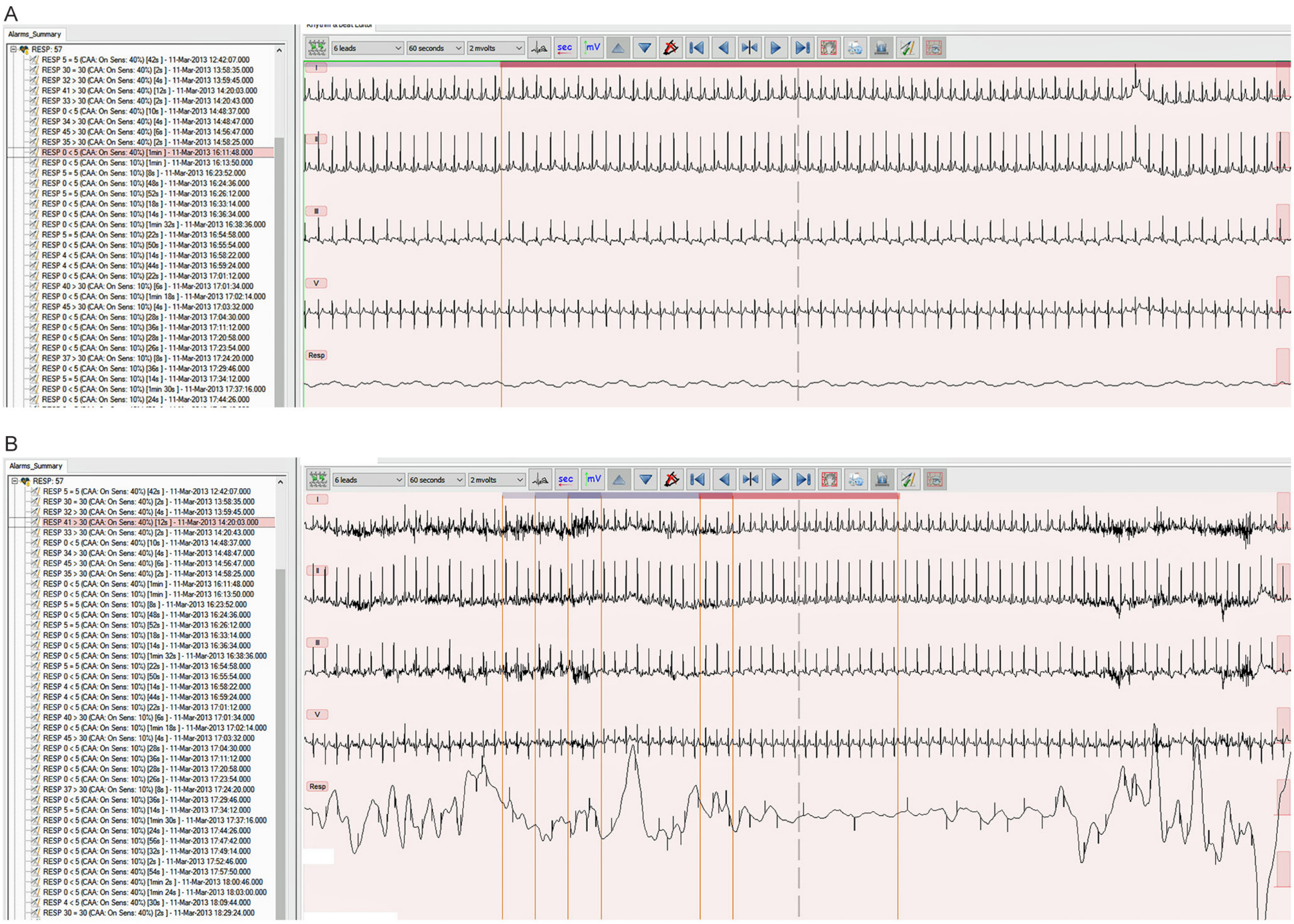

Fig. 1. A and B. Illustrates the continuous ECG recording suite (CER-S) software program used to compare the impedance pneumography (IP) respiratory rate (RR) to the combined-electrocardiographic (EDR) method. The IP waveform is labeled as Resp in the figures.

A. The left side of the figure shows several IP RR parameter limit alarms (low and high) in an intensive care unit patient. The highlighted IP alarm is for a low parameter RR alarm (RESP $0 < 5$; where $0 =$ RR and $5 =$ the parameter limit alarm setting). The panel to the right of the alarm is a one-minute tracing of ECG signals (leads I, II, II and V1) and the IP waveform (Resp) for the selected IP alarm. Note that the ECG signal in lead II, which is used by the IP algorithm, is clean. However, the IP waveform is flat therefore, the RR of 0, likely due to poor skin electrode contact, that is sufficient for an ECG signal but not the IP algorithm, or shallow breathing.

B. The left side of the figure shows several IP RR parameter limit alarms (low and high) in an intensive care unit patient. The highlighted IP alarm is for a high parameter RR alarm (RESP $41 > 30$; where $41 =$ RR and $30 =$ the parameter limit alarm setting). The panel to the right of the alarm is a one-minute tracing of ECG signals (leads I, II, II and V1) and the IP waveform (Resp). At the beginning and end of the IP tracing, motion artifact and 60-cycle interference in lead II is illustrated. Based on the IP algorithm, the result is a high RR alarm. Note that the IP waveform improves somewhat when the artifact and 60-cycle interference are no longer present (middle). The flags are applied by the vendor's algorithm to denote inspiration (upward) and expiration (downward) during breathing.

<40 s ± 1 s. These variables were examined by RR type (i.e., normal, low, and high) and are summarized below.

Normal RR (between 12 and 20 bpm)

The mean age of the 50 patients in the normal RR group was 60.14 (±18.01) years, 52% were male, and 66% were white (Table 1). Forty percent had documented cognitive impairment, 18% were current smokers, 42% had mechanical ventilation, and 40% were admitted to the neurological ICU.

Low RR (≤5 bpm)

The mean age of the 50 patients in the low RR group was 61.80 (±16.89) years, 56% were male, and 60% were white. In this group, 28% had cognitive impairment, 10% were current smokers, 50% had mechanical ventilation, and 36% were admitted to the medical-surgical ICU.

High RR (≥30 bpm)

The mean age of the 50 patients in the high RR group was 60.86 (±16.13) years, 58% were male, and 62% were white. In this group, 48% had cognitive impairment, 24% were current smokers, 36% had mechanical ventilation, and 42% were admitted to the neurological ICU.

Bland Altman analysis

The results of the Bland Altman analysis are presented in Table 2. Scatter plots and Bland-Altman plots are shown in Fig. 2A–C. These figures illustrate the distribution and agreement between the two methods for normal, low, and high RR.

Normal RR (between 12 and 20 bpm)

For normal RR, a significant bias difference of −1.00 ± 2.11 (95% CI −1.60 to −0.40) and LOA of −5.13 to 3.13 were found (Table 2). The LOA showed that the RR were within three and five bpm. Fig. 2A shows the scatter plot and Bland-Altman analysis for the normal RR comparisons. The regression line through the points was not significant ($p = 0.088$). The Bland Altman plot indicates close agreement between the two methods for normal RR.

Low RR (≤5 bpm)

For low RR, a significant bias difference of −16.54 ± 6.02 (95% CI: −18.25 to −14.83) and a 95% LOA of −28.33 to −4.75 were found (Table 2). As illustrated on the scatterplot (Fig. 2B), the combined-EDR RR was always higher than the IP RR. Note that the points on the

Table 1
Demographic and clinical characteristics of 100 intensive care patients by respiratory rate (RR).

Characteristics	Normal RR (≥12 to ≤ 20 bpm)	Low RR (≤5 bpm)	High RR (≥30 bpm)
	n = 50	n = 50	n = 50
Demographic characteristics			
Age (mean ± SD, in years)	60.14 ± (18.01) n (%)	61.80 ± 16.89 n (%)	60.86 ± 16.13 n (%)
Sex			
Male	26 (52.0)	28 (56.0)	29 (58.0)
Female	24 (48.0)	22 (44.0)	21(42.0)
Race			
Asian	6 (12.0)	8 (16.0)	7 (14.0)
Black/African American	5 (10.0)	6 (12.0)	8 (16.0
White	33 (66.0)	30 (60.0)	31 (62.0)
Unknown or decline	6 (12.0)	6 (12.0)	4 (8.0)
Clinical characteristics			
BMI (mean ± SD, kg/m^2)	26.72 ± 4.73	26.84 ± 4.83	29.50 ± 9.79
Current smoker	9 (18.0)	5 (10.0)	12 (24.0)
Documented cognitive impairment	20 (40.0)	19 (28.0)	24 (48.0)
Tremor	3 (6.0)	2 (4.0)	5 (10.0)
Intensive care unit type			
Cardiac (16 beds)	13 (26.0)	16 (32.0)	11 (22.0)
Medical-Surgical (32 beds)	17 (34.0)	18 (36.0)	18 (36.0)
Neurological (29 beds)	20 (40.0)	16 (32.0)	21 (42.0)
Mechanical ventilation	21 (42.0)	25 (50.0)	18 (36.0)

Abbreviation: BMI = body mass index; bpm = breaths per minute; IQR = interquartile range; kg = kilogram; m^2 = meter squared; RR = respiratory rate; SD = standard deviation.

Bland-Altman plot are essentially distributed in two lines. This pattern is seen because nearly all of the IP values were RRs of 0 or 5, with the exception of two single points with a measure of 4. The regression line was significant (−1.26; 95% CI -1.62 to −0.89; $p < 0.05$).

High RR (≥30 bpm)

For high RR, a significant bias difference of 17.94 ± 12.01 (95% CI: 14.53 to 21.35) and 95% LOA of −5.60 to 41.48 were found (Table 2). Fig. 2C shows the scatter plot and Bland-Altman plot for high RR comparisons. As illustrated in the scatterplot, the combined-EDR RR was always lower with the exception of one comparison. A test of a regression line through the points did not indicate a significant slope ($p = 0.87$). Fig. 3 illustrates the one outlier patient who had an IP RR of 30 bpm and a combined-EDR RR of 50 bpm. The IP RR appears to be accurate despite motion artifact. However, it is not clear which of physiologic signals used in the combined-EDR RR algorithm was driving the RR. However, the frequent premature ventricular complexes seen throughout the tracing are a likely source.

Discussion

This study is the first to evaluate, in a group of ICU patients, the level of agreement between two algorithm-based methods to measure RR, the IP method and a novel combined-EDR method that uses an algorithm that combines signals from the IP, SpO2, ECG waveforms and the myogram. Good agreement was found between the two methods for normal RR. An inverse relationship was found between the two methods for both the low and high RR comparisons.

For normal RR, the upper and lower LOA were within three to five bpm, which is clinically acceptable. Agreement between the two RR methods was found for patients who were both tachypneic and bradypneic. Figs. 4 A and B are examples of IP and ECG tracings from two patients in our study, one with tachypnea (33 bpm) and one with bradypnea (9 bpm). Based on our findings, it is reasonable to suggest that the IP and combined-EDR methods are comparable not only when measuring RR within the normal range (i.e., between 12 and 20 bpm) but in patients with tachypnea and bradypnea. However, because we did not simultaneously assess RR using VA method, these findings warrant confirmation using this gold standard. Despite this limitation, based on our findings for normal RR, albeit in a small sample of ICU patients, we were able to make comparisons with some level of confidence between the IP and combined-EDR method for both low and high RRs.

For low RRs, compared to the IP method the combined-EDR method was consistently higher. This finding is consistent with prior studies that show that the majority of low IP RRs are false [7,38] primarily due to low frequency signals that saturate the ECG leads with noise and fail to capture the impedance signal [39]. As illustrated in Fig. 1A, low frequency IP signals can increase the number of false low RRs [40,41]. In addition, shallow breathing can be misinterpreted by the IP method as a low RR and contribute to the number false low RR alarms [41]. Several studies have examined why low RR occurs when using the IP method. In one study, cardiac oscillations (i.e., "small waves produced by heartbeats that are superimposed on the pressure and flow signals at the airway opening") thus, interfering with the IP signal and led to an increased number of false low RRs [38]. In healthy people, several factors can impact the IP signal including: hemodynamic properties [42]; RSA [43]; blood pressure [44]; stroke volume [45]; pulmonary vascular resistance [43]; pulmonary blood flow [46]; and lung volume [47]. These factors are attenuated in patients with cardiac and/or respiratory diseases, which are common in hospitalized patients. Moreover, the IP signal can be effected by body position changes and/or talking [1,6,27,48]. Accurate and reliable identification of low RR is extremely important in hospitalized patients who are susceptible to bradypnea because of the administration of medications that compromise breathing (e.g., sedatives, opioids), sleep disordered breathing [49,50], or acute respiratory compromise [4,19,51]. The combined-EDR algorithm, that uses multiple physiologic signals to derive RR, appears to be an improvement over the IP method. However, the combined-EDR method requires further validation against the VA method in a larger sample.

When comparing the IP method to the combined-EDR method for high RR, in nearly every comparison the combined-EDR RR was lower. Fig. 5 illustrates an outlier patient with an IP RR of 83 bpm caused by motion and cardiac artifact. This example supports previous studies that identified that both motion [8,9,39] and cardiac artifact, due to aortic blood flow picked up by the IP signal, results in an increased number of false high RR readings [42,52]. Because the combined-EDR algorithm uses a combination of several different physiologic signals this method appears to minimize this problem. With one exception, the RR derived using the combined-EDR were consistently lower than the IP method. The one exception was a patient with frequent abberantly conducted beats with a wide QRS. This finding suggests that the combined-EDR algorithm may warrant modifications to accurately assess high RR in patients with intermittent wide QRSs. However, our data suggest that overall the combined-EDR method may reduce the number of false

Table 2
Mean difference and limits of agreement for normal, low and high respiratory rate comparing impedance pneumography to the combined-electrocardiographic derived method.

Patient group	Bias Mean (SD)	95% CI of the bias	95% LOA Lower, Upper	Regression Test (p-value)
Normal RR	−1.00 (2.11)	−1.60 to −0.40	−5.13 to 3.13	0.088
Low RR	−16.54 (6.02)	−18.25 to −14.83	−28.33 to - 4.75	−1.26; 95% CI -1.62 to −0.89; $p < 0.05$*
High RR	17.94 (12.01)	14.53 to 21.35	−5.60 to 41.48	0.87

Abbreviations: CI = confidence interval; LOAs = limits of agreement; RR = respiratory rate; SD = standard deviation.

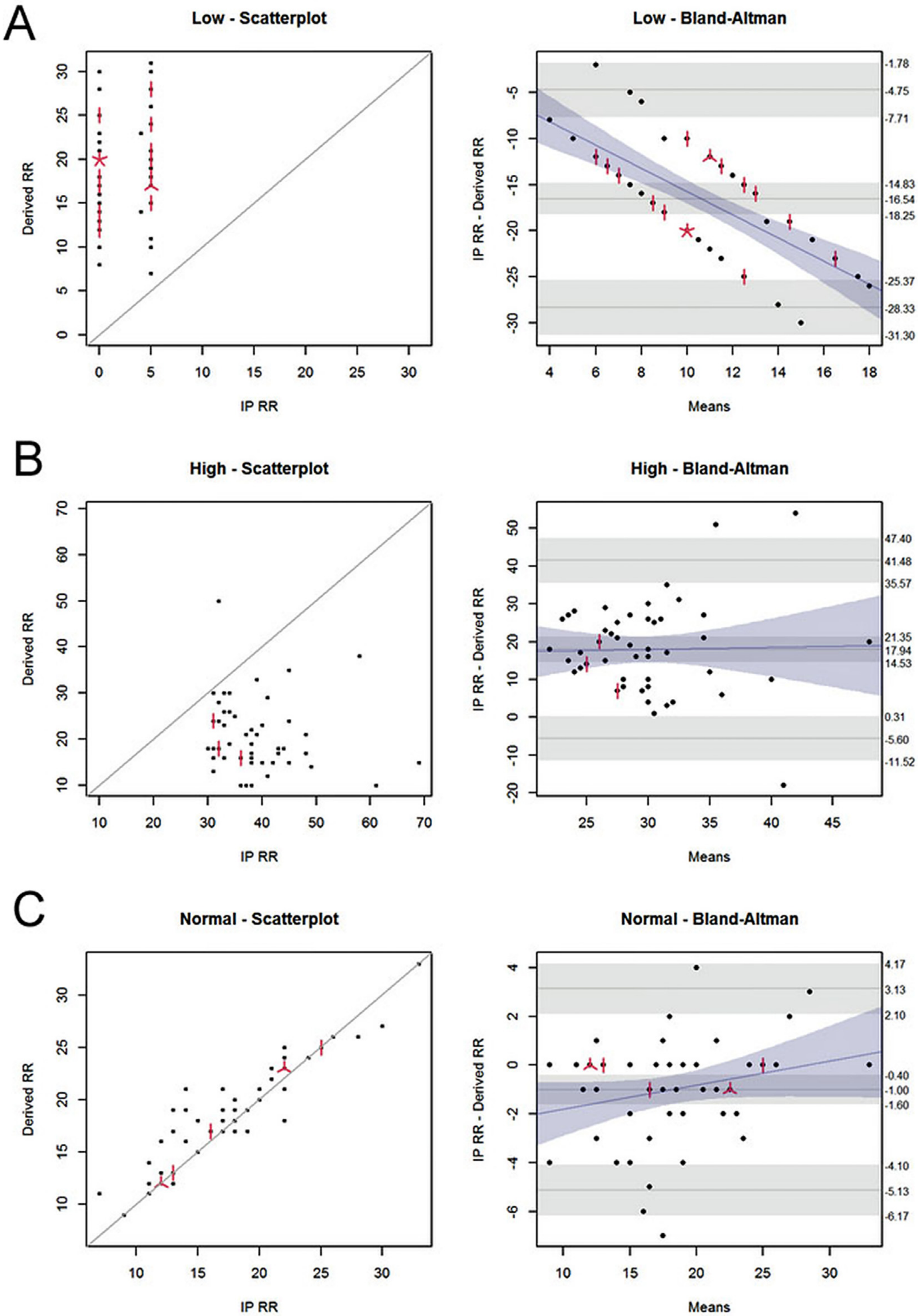

Fig. 2. A, B, C. Scatterplots (left) and Bland-Altman plots (right) for normal, low, and high respiratory rate (RR) that compare impedance pneumography (IP) to the combined-electrocardiographic derived-respiration (combined-EDR) method. The heavier dashed lines in the Bland-Altman figures represent the mean difference (middle line) and the upper and lower limits for 95% of the data. The lighter dashed line is the 95% confidence interval (CI) for each of these lines. The red lines are sunflower plots and show when more than one value occurs at this location. For example, a three-armed sunflower plot indicates that three individual values occured at this one location.

high RR alarms associated with motion and/or cardiac artifact. Future studies need to determine whether refinements in the combined-EDR algorithm are needed to account for potential ECG and/or physiologic signal confounders.

A noteworthy finding from our study is the number of patients with a RR above the physiologic upper limit of "normal" (i.e., >20 bpm). An examination of the normal RR comparisons, that showed good agreement between the IP and combined-EDR methods, found 17 of 25 patients (68%) with a RR >20 bpm. This finding highlights that tachypnea is a common problem in ICU patients. However, this finding warrants confirmation using VA and capnography (end tidal CO2) the non-invasive and device driven gold standard methods, respectively. If

Fig. 3. Example of a mismatch of respiratory rate (RR) between the impedance pneumography (IP) and the combined-electrocardiographic (EDR) method. Shown is a one-minute tracing of ECG leads I, II, III, V1 and the IP waveform (Resp). The IP method determined a RR of 30 breaths per minute (bpm) and the combined-EDR determined a RR of 50 bpm. Note that despite 60-cyle interference in lead II, which the IP used to calculate RR, the IP signal is clean suggesting good skin electrode contact. The combined-EDR RR of 50 is likely due to the frequent abberantly conducted beats (lead II and III), which effected the QRS width used in this method.

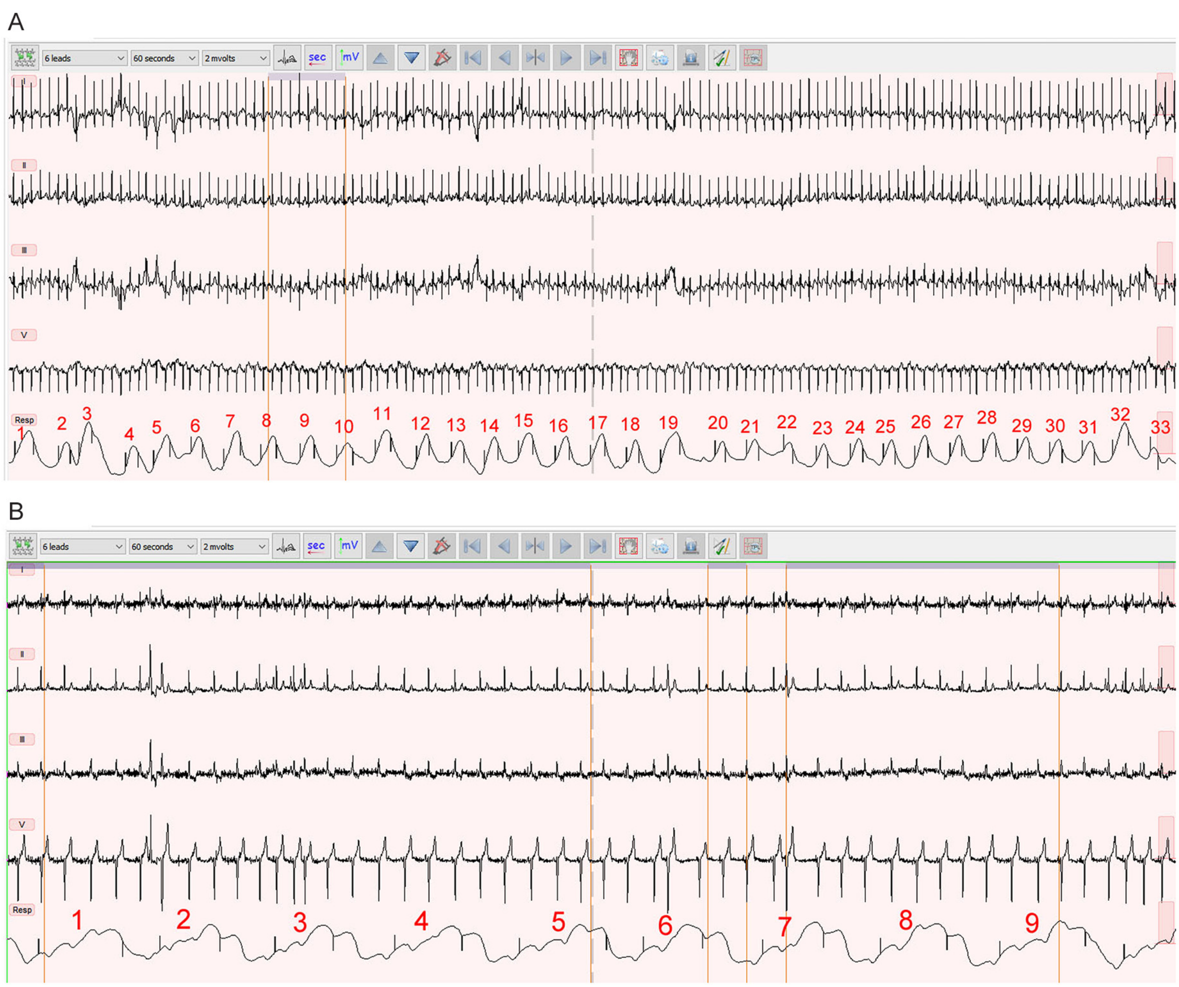

Fig. 4. Illustrates the respiratory rate (RR) measured using impedance pneumography (IP) in two different intensive care unit patients during tachypnea (A) and bradypnea (B). Shown are one minute time periods with electrocardiographic (ECG) leads I, II, II, and V1 and the IP waveform (Resp). The IP waveform has an upward flag during inspiration and a downward flag during expiration.
A. Patient with an IP RR of 33 breaths per minute (bpm). The combined-EDR method RR is 33 bpm. The patient's heart rate is 150 beats/min, which when combined with the tachypnea suggests this patient is in acute distress.
B. Patient with an IP RR of 9 bpm. The combined-EDR method RR is 9 bpm. While the IP waveform is not as smooth as seen in A (above), the upward and downward flags are present. This patient's heart rate is 60 beats/min, with pre-mature atrial complexes and a short run of supra-ventricular tachycardia.

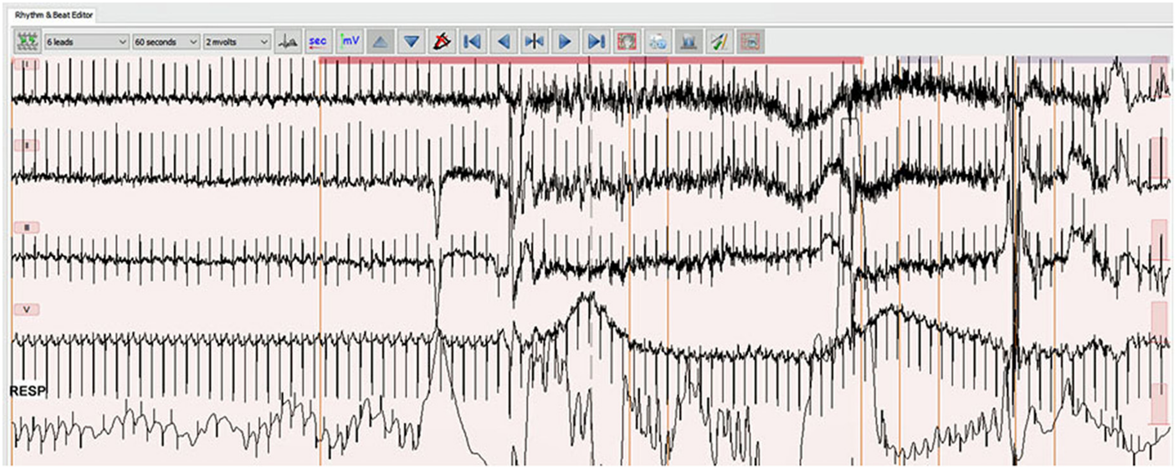

Fig. 5. Illustrates a high respiratory rate (RR) measured using impedance pneumography (IP) in an intensive care unit patient. The IP RR is 83 breaths per minute (bpm), the combined-electrocardiographic RR is 15 bpm. Shown is a one-minute time period with ECG leads I, II, II, and V1 and the IP waveform (RESP). The initial IP waveform is likely reading a high RR due to cardiac artifact (see upward flags and downward flags on IP waveform) that is then disrupted by motion artifact.

confirmed, this finding has important implications both clinically (true tachypnea) and when setting high RR parameter alarms, that are commonly set at >30 bpm to decrease the number of RR alarms. Setting the high RR parameter alarm above >30 bpm may miss clinically important respiratory distress.

Limitations

Several limitations warrant consideration. While we provide new information on the agreement between the IP RR method and a novel multi-physiological signal algorithm for RR measurement, we did not use a gold standard method (i.e., visual assessment [non-invasive], or capnography [device driven]) to compare the two methods. In addition, because we used only one monitoring vendor, our findings may not be generatable to other monitoring manufacturers. The study's retrospective design did not allow us to evaluate the patient scenario and/or alarm adjustments made by clinicians, that would add important context to our findings. In addition, we were unable to reliably identify the dates and times when a patient was on a ventilator during our RR comparisons. Future research should evaluate data on RR from ventilators as another comparator. Lastly, because some of our ICU patients were intubated and/or comatose, comparisons between the two methods in non-ICU patients is warranted. Despite these limitations, this study is the first to evaluate the use of a novel physiologic-based RR algorithm to derive RR. Given that these data exist in current bedside monitors, this approach could be easily integrated into existing monitoring systems and potentially decrease alarm fatigue due to frequent RR alarms.

Conclusions

While confirmation of our findings is warranted, our data suggest that the combined-EDR method is comparable to the IP method to derive normal RR. For low RR, the combined-EDR method was consistently higher than the IP method. Calculating low RR using the IP method may be influenced by low frequency signals and lead to inaccurate RR. However, low RR can occur with shallow breathing, which would be of clinical significance in hospitalized patients at risk for respiratory compromise. By using multiple physiologic signals, more accurate low RR may be detected with the combined-EDR method. The combined-EDR RR was almost always lower than high IP RR. False high RRs, using the IP method, caused by motion and/or cardiac artifact are common and may lead to alarm fatigue in clinicians. However, we found RRs with good agreement between the two methods often exceeded the upper limit of normal (i.e., <20 bpm), suggesting tachypnea is common among ICU patients. This finding is important, because it is common practice for hospitals to use a default alarm limit setting of ≥30 bpm in an effort to minimize RR alarms. Our finding suggests that true tachypnea may be missed by using this default setting. This study should be replicated in a larger sample, in both ICU and non-ICU patients, and include confirmation with visual and device driven gold standard methods.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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