Title

A Comprehensive Evaluation of Respiratory Type Alarms during Electrocardiographic (ECG) Monitoring in the Intensive Care Unit and a Comparison of Respiratory Rate between an ECG Derived Method and Impedance Pneumography

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A Comprehensive Evaluation of Respiratory Type Alarms during Electrocardiographic (ECG) Monitoring in Intensive Care Unit and a Comparison of Respiratory Rate between an ECG Derived Method and Impedance Pneumography

by

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DISSERTATION

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DEDICATION

Dedicated to the Memory of My Dad, Samuel Wilberforce Kwasi Boakye, and to My Mother, Georgina Nhyarkoa Osarfo (Kantanka) for the Life I Breath, and for Who I Have Become!

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"Meda mo ase, Onyankopon nhyira mo bebereii" (God, Abundantly Bless You All)

Abstract

A Comprehensive Evaluation of Respiratory Type Alarms during Electrocardiographic (ECG) Monitoring in the Intensive Care Unit and a Comparison of Respiratory Rate between an ECG Derived Method and Impedance Pneumography

Linda Kyeremateng Bawua

Continuous monitoring of respiratory rate (RR), especially in the ICU, is important to identify patients with respiratory compromise. Currently, there are two methods used to assess RR, visual assessment (VA) and impedance pneumography (IP). While VA is easy to use, RR assessments are intermittent, time-consuming, and often inaccurate. The IP method, while continuous, is plagued with alarms, which can lead to alarm fatigue in clinicians. Electrocardiographic (ECG) derived RR methods, or EDR, have been examined but have not been validated for use in the hospital setting.

This dissertation was designed to examine RR assessment using the three methods identified above. Three overall aims were studied, including: (1) a systematic review of the literature describing the strengths and limitations of the three methods (VA, IP, and EDR); (2) an evaluation of the number and types of RR alarms (i.e., parameter and apnea) in 461 ICU patients and the association of RR alarms to demographic, clinical characteristics, and supportive therapies; and (3) an evaluation of RR agreement between the IP method and a novel combined-ECG derive (combined-EDR) method in 100 ICU patients.

Chapter #2: Of the 78 studies identified in the systematic review, full manuscripts for 23 studies were reviewed and four studies were included in this review. Given the paucity of research and the fact that no studies have compared all three methods in the same patients, no definitive conclusions can be drawn about the accuracy of these three methods. Chapter #3: RR parameter alarms (high $\geq$30 breaths per minute [bpm] or low $\leq$5 bpm) and apnea ($\geq$20 seconds of no breathing) were examined in 461 ICU patients. These parameters were selected because

it was the hospital's standard default parameter alarm limits in all the ICUs at our hospital. A total of 159,771 RR type alarms over 48,000 hours of monitoring occurred (67 RR alarms/bed/day). The majority of the alarms (82.5%; n=131,827) were high parameter alarms. RR alarm occurrence rates were associated with: the type of ICU ($p<0.01$); mechanical ventilation ($p<0.01$); and the lack of a ventricular assist device, or pacemaker ($p<0.01$). Male gender was associated with low ($p<0.01$) and apnea ($p<0.05$) alarms. Chapter #4: This study was designed to examine the agreement between the IP and combined-EDR method for normal RR; low RR ($\leq$5 breaths per minute (bpm); and high RR ($\geq$30 bpm) in 100 ICU patients. For normal RR, a significant bias difference -1.00 $\pm$ 2.11 (95% CI -1.60 to -0.40) and LOA of -5.13 to 3.13 was found between the two methods. For low RR, a significant bias difference of -16.54 $\pm$ 6.02 (95% CI: -18.25 to -14.83) and a 95% LOA of -28.33 to - 4.75 were found. For high RR, a significant bias difference of 17.94 $\pm$ 12.01 (95% CI: 14.53 to 21.35) and 95% LOA of -5.60 to 41.48 were found. The combined-EDR method had good agreement with the IP method for measuring normal breathing. Whereas the combined-EDR method was consistently higher than low IP RR and almost always lower than high IP RR. This study should be replicated in a larger sample and include confirmation with VA.

The overall findings of this dissertation research show that there are very few studies that have examined the three RR methods. For the IP method, high parameter RR alarms are the most common type of alarm. Occurrence rates were associated with the type of ICU, mechanical ventilation and the lack of a ventricular assist device, or pacemaker. Male gender was associated with low parameter and apnea ($p<0.05$) alarms. These data suggest that the combined-EDR method is comparable to the IP method with regards to normal RR, was consistently higher than low IP RR, and almost always lower when comparing high RR. This dissertation adds to scientific knowledge regarding RR alarms using the IP method. However, further research is needed to test the combined-EDR method to the gold standard VA method to determine the accuracy of this method.

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LIST OF ABBREVIATIONS

(AC)	Alternating Current
(ANOVA)	Analysis of Variance
(BMI)	Body Mass Index
(BPM)	Breaths per minute
(BP)	Blood Pressure
(CCU)	Critical Care Unit
(CER-S)	Continuous Electrocardiographic Recording Suite Software
(CI)	Confidence Interval
(CINAHL)	Cumulative Index to Nursing and Allied Health Literature
(CSM)	Criterion Standard Measurement
(CTVS)	Cardiothoracic and Vascular Surgery
(ECG)	Electrocardiograph
(ED)	Emergency Department
(EDR)	Electrocardiographic Derive Respiration
(EKG)	Electrocardiograph
(ICU)	Intensive Care Unit
(IHR)	Instantaneous Heart rate
(IP)	Impedance Pneumography
(LA)	Left Arm
(LL)	Left Leg
(KG)	Kilogram
(LOA)	Limits of Agreement
(M^2)	Meter Squared
(OLS)	Ordinary Least of Square

LIST OF ABBREVIATIONS

(RA)	Right Arm
(RAM)	Respiratory Amplitude Modulation
(RC)	Respiratory Compromise
(RESP)	Respiration
(RL)	Right Leg
(RN)	Registered Nurse
(RR)	Respiratory Rate
(RSA)	Respiratory Sinus Arrythmia
(SD)	Standard Deviation
(STP)	Standard for the Exchange of Product Data (STEP)
(STEP)	Standard for the Exchange of Product Data
(UCSF)	University of California San Francisco
(US)	United States
(VAD)	Ventricular Assist Device
(WI)	Wisconsin

CHAPTER 1

INTRODUCTION

Chapter 1

Introduction to the Dissertation

Respiratory rate (RR), an essential indicator of physiological state, is a vital sign that, when abnormal, is associated with clinical deterioration in hospitalized patients.[1, 2] While visual assessment (VA) is the non-invasive standard of care used to assess the RR and breathing characteristics (i.e., depth, effort, skin color), studies show that this method is plagued with inaccuracies because clinicians often omit, repeat, or even guess a patient's RR.[3-7] In addition, VA of RR is performed intermittently (e.g., every 30 minutes with vital signs), which means that acute changes can be missed. Alternative methods using non-invasive device-driven techniques, such as impedance pneumography (IP) and Electrocardiographic (ECG) -Derived Respiration (EDR) + myogram, have been examined.[8, 9] However, only the IP method is currently available in the hospital setting. Importantly, the IP method is riddled with frequent alarms.[10, 11] In one study, a total of 161,931 RR type alarms were recorded during a one-month period in 77 ICU beds (79 alarms/bed/day).[11] While one could argue these may have been true alarms the investigators noted that in many of the alarms the IP waveform was flat, and the alarms occurred in patients who were not experiencing acute respiratory distress. These data illustrate that IP RR alarms are a significant source of alarm burden for clinicians and thus, contribute to alarm fatigue (i.e., desensitization and/or unsafe alarm adjustments).[9, 12, 13]

Background and Significance

A change in a patient's RR indicates the body's reaction to a physiologic disturbance and is a mechanism the body uses to maintain homeostasis.[14] According to the Respiratory Compromise Institute[15] *respiratory compromise* (RC) is defined as "a potentially life-threatening state of unstable respiratory health, which can occur across the care continuum – in the operating room, in the post-anesthesia care unit, the general care floor or in out-patient care facilities. It is a multifaceted disease state in which there is a high likelihood of decompensation into respiratory failure or death, but in which specific interventions (enhanced monitoring and/or therapies) might prevent or mitigate decompensation".(para. 2)

Respiratory compromise is an umbrella term use to describe acute respiratory distress/insufficiency, respiratory failure, and/or arrest. Of note, 60% of cardiopulmonary arrests that are associated with RC are preventable.[16] A RR of $\geq$ 27 breaths per minute (bpm) is the most important predictor of cardiac arrest. Fifty percent of patients with RR > 24 bpm experience severe life-threatening events and 21% of patients with RR of $\geq$29 will die.[6] Respiratory compromise increases a patient's mortality rate by over 30%. In addition, the length of hospital and intensive care unit (ICU) stays are three times longer for patients who experience RC.[17, 18,] Notably, nearly 20% of respiratory arrests associated with RC are potentially preventable. This unfortunate situation provides an opportunity for researchers to examine the accuracy of device driven methods to assess RR with the goal of identifying RC and improving patient outcomes.[19] Based on findings from multiple research studies,[17, 18] the Centers for Medicare and Medicaid Services proposed that RC be a national patient safety indicator for use by the Hospital Inpatient Quality Reporting Programs.

Respiratory compromise ranks fifth among acute unanticipated conditions that leads to high hospital costs.[16] Respiratory compromise is the second leading avoidable safety event in hospitalized patients; is one of the top five conditions leading to increased hospital costs; and is the third most rapidly increasing inpatient cost each year.[16] It ranks third in being associated with the most rapidly increasing costs and is among the five conditions with highest growing hospital costs for Medicare-covered stays in 2010.[16] Total per-patient hospital costs for patients with RC were four times higher than for patients without RC. In a 2017 report, the Department of Health and Human Services reported that $7.8 billion was spent on RC in U.S. hospitals, which was based on data from 2007, therefore, these costs are likely to be much higher now.[16]

Given the significant economic costs, morbidity and mortality associated with RC, immediate evidence-based solutions are needed. Research should focus on both preventive strategies and improvements in monitoring methods (ideally continuous) that are aimed at early identification and management of RC in hospital patients. The immediate identification of patient deterioration associated with RC could reduce patient morbidity and mortality, as well as hospital costs.[15, 16]

Despite the high prevalence and serious consequences of RC in hospitalized patients, visual RR assessment is the most neglected and inadequately measured vital sign.[5, 6] In clinical practice, VA of RR is performed with the patient at rest and preferably without them being aware that the measurement is being performed. The nurse is expected to count the rise and fall of the patient's chest for a full 60 seconds and note several other respiratory characteristics (e.g., depth, effort, skin color).[21-23] However, this best practice is not performed on a routine basis. Instead, the requisite systematic assessment of RR is often omitted, guessed, or missed [3]. This situation places patients at increased risk for missed RC events because subtle and/or acute changes are not identified in a timely manner.

Focus of this dissertation research

In hospital units that use continuous ECG monitoring for heart rate and arrhythmia identification, the IP method is used to measure RR continuously. Using the ECG skin electrodes on the body's surface, the IP method measures thoracic impedance during inspiration and expiration. Advantages of the IP method include that it is non-invasive, uses existing ECG skin electrodes and lead wires and continuously measures RR. However, a significant disadvantage of the IP method is that it is plagued with alarms,[10, 11] which negatively impacts IP as a reliable method for identifying RC. Another non-invasive technique that has been studied is the EDR method. Unlike the IP method the EDR uses ECG waveforms (i.e., QRS, R-to-R intervals) and the myogram to derive RR.[8, 9, 24] While several research studies using the EDR method have been published[8, 9, 24] this method has not been introduced into the hospital setting. In addition, this method has not been evaluated for agreement with the IP method; thus, it is not known if this method would improve RR assessment.

While the IP method has been used in hospitals for years, its sensitivity is low.[9] In addition, the IP method generates a high number of parameter (high and low RR) and apnea alarms. In a one-month study that included 461 consecutively enrolled ICU patients, there were a total of 161,931 IP respiratory type alarms (i.e., parameter high/low and apnea).[11] The RR alarms accounted for 6% of the over 2.5 million total number of alarms.[11] However, this study did not annotate the respiratory alarms as true versus false or report on the specific types of respiratory alarms (i.e., apnea, high, low respiratory rate). Hence, both of these questions (true/false, type) remain unanswered.

Therefore, this dissertation research was designed to addresses the gaps in knowledge regarding IP generated alarms. For this dissertation research, three types of IP RR alarms were examined (i.e., parameter violation high/low and apnea). The alarms examined were based on the default settings used in the ICU bedside physiologic monitors. A low parameter alarm was $\leq$5 bpm, a high parameter alarm was $\geq$30 bpm, and an *apnea* alarm was defined as cessation of breathing for > 20 seconds. In addition to RR type alarms, to date there has not been a study that has described whether demographics (i.e., age, sex, ethnicity), clinical characteristics (i.e., body mass index [BMI], altered cognitive status, tremor, current smoker), supportive therapies (i.e., mechanical ventilation, ventricular assist device [VAD], pacemaker), and/or primary ICU diagnosis are associated with RR parameter (i.e.,$\leq$5 bpm $\geq$30 bpm) and/or apnea (i.e., cessation of breathing $\geq$20 seconds) alarms. While several of these factors have been found to be associated with false ECG arrhythmia alarms,[9, 25-26] it is not known whether these same associations exist for RR alarms. A better understanding of the specific types of RR alarms and patient and/or clinical characteristics associated with RR alarms could provide valuable information to help guide alarm reduction strategies to reduce alarm fatigue in nurses. These data could also help guide future RR algorithm development to improve the accuracy of device-driven RR methods.

Another gap in knowledge that this dissertation research was designed to address is an evaluation of the agreement between the IP method and a new algorithm that combined the IP signal, ECG waveforms and the myogram (Combined-EDR). Our research team has explored an EDR method using only ECG waveforms (QRS and R-to-R intervals) and the myogram to detect Cheyne-Stokes respirations in healthy adults, hospitalized patients with acute coronary syndromes admitted to a telemetry unit, and ICU patients.[24, 27] In this dissertation we build on this research by evaluating a new algorithm that our group has created that combines the IP waveform, ECG waveforms and the myogram, or a “combined-EDR method.” We hypothesized that RR using the combined-EDR method will be equivalent to the IP method for normal, low, high RR. Our algorithm is based on our prior work and others that suggests that the combination of multiple physiologic signals for RR is more accurate than an algorithm that uses only one signal.[9, 28]

Purpose

Therefore, this dissertation was designed to examine RR type alarms generated with the IP method in a cohort of ICU patients and examine the agreement of the IP method to a combined-EDR method. The three subsequent chapters of this dissertation are entitled: (1) A review of the literature on the accuracy, strengths, and limitations of visual, thoracic impedance, and electrocardiographic methods used to measure respiratory rate in hospitalized patients; (2) High parameter alarms are the most frequent respiratory type alarm during impedance pneumography in the intensive care unit ; and (3) Agreement of respiratory rate measurement between a combined electrocardiographic derived method and impedance pneumography
A brief description of the study and the Specific Aims for each chapter are detailed below.

Chapter 2 is a systematic review of studies using prespecified inclusion and exclusion criteria and each study was evaluated using standardized measures. The review compared the accuracy, strengths, and limitations of RR using VA to IP and EDR. The first paper reports on findings from a systematic review with four studies.[29-32] undertaken using prespecified inclusion and exclusion criteria; each study was evaluated using standardized measures. The review compared the accuracy, strengths, and limitations of visual assessment (VA) of respiration to two methods that use physiologic data, namely impedance pneumography (IP) and electrocardiographic-derived respiration (EDR).

Chapter 3 is a secondary data analysis in 461 ICU patients. The Specific Aims of this study were: to examine respiratory rate (RR) alarms by type and duration and for associations with patients' demographics and clinical characteristics in critically ill patients on a bedside ECG monitor

Chapter 4 is a secondary data analysis in 100 ICU patients. The Specific Aims of this study were: to examines the agreement of RR measurement between a combined-EDR method and impedance pneumography. The purpose was to compare the agreement between the IP and Combined-EDR methods for "normal" RR, low RR (≤5 bpm; and high RR (≥30 bpm).

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CHAPTER 2

A REVIEW OF THE LITERATURE ON THE ACCURACY, STRENGTHS, AND LIMITATIONS OF VISUAL, THORACIC IMPEDANCE, AND ELECTROCARDIOGRAPHIC METHODS USED TO MEASURE RESPIRATORY RATE IN HOSPITALIZED PATIENTS

ABSTRACT

Background: Respiratory rate (RR) is one of the most important indicators of a patient's health. In critically ill patients, unrecognized changes in RR are associated with poorer outcomes. Visual assessment (VA), impedance pneumography (IP), and electrocardiographic-derived respiration (EDR) are the three most commonly used methods to assess RR. While VA and IP are widely used in hospitals, the EDR method has not been validated for use in critically ill patients. In addition, little is known about the accuracy of these methods compared to one another. The purpose of this systematic review was to compare the accuracy, strengths, and limitations of VA of RR to two methods that use physiologic data, namely IP and EDR.

Methods: A systematic review of the literature was undertaken using pre-specified inclusion and exclusion criteria. Each of the studies was evaluated using standardized criteria.

Results: Of the 78 studies identified, full manuscripts for 23 studies were reviewed, and four studies were included in this review. Three studies compared VA to IP and one study compared VA to EDR. In terms of accuracy, when Bland-Altman analyses were performed, the upper and lower levels of agreement were extremely poor for both the VA and IP and VA and EDR comparisons.

Conclusion: Given the paucity of research and the fact that no studies have compared all three methods in the same patients, no definitive conclusions can be drawn about the accuracy of these three methods. Given the clinical importance of accurate assessment of RR, additional research is warranted with rigorous designs to determine the accuracy of these methods and acceptable clinically meaningful levels of agreement.

Key Words: accuracy, electrocardiography, hospitalized patients, impedance pneumography, respiratory rate, sensitivity, specificity, visual assessment.

INTRODUCTION

Assessment of respiratory rate (RR) is often neglected when vital signs are obtained in hospitalized patients, which is problematic given that unrecognized changes in RR are associated with worse patient outcomes,[1-4] including increases in cardiopulmonary arrest and in-hospital mortality.[5-9] An abnormal RR is observed in a wide range of both acute and chronic conditions.[10] Therefore, early detection of changes in RR and abnormal breathing characteristics (e.g., depth, use of accessory muscles, skin color) can be used to determine a patient's health status; aid in the selection of appropriate treatments; and determine when a patient is ready to transition from a high to a sub-acute level of care or discharge from the hospital. The assessment and documentation of vital signs in hospitalized patients have been noted to be deficient.[6, 11] Of the four vital signs (i.e., RR, heart rate, blood pressure, temperature), RR is the one that is most frequently missing in the medical record, even when the patient's primary diagnosis is respiratory-specific.[6] Reasons cited include the length of time required to obtain this measure and the interruptions created in workflow efficiency.[2, 12] In some unstable patients, dynamic fluctuations in RR are even more significant than changes in systolic blood pressure or heart rate, which suggests that RR may be a better indicator of physiologic instability.[6, 11]

Assessment of RR in Hospitalized Patients

In hospitalized patients, abnormal RR (e.g., tachypnea, bradypnea) are indicators of respiratory instability, respiratory compromise, and often the first indication of impending respiratory arrest and/or the need for rescue intubation.[5, 6, 8] However, identifying these acute changes can be delayed and/or missed if RR is not obtained often and with a high degree of accuracy. Therefore, assessing RR at more frequent intervals and more accurately may lead to earlier detection of clinical deterioration and appropriate intervention(s) to improve patient outcomes. To achieve this goal, the ideal method to assess RR would be accurate, sensitive, specific, non-invasive, and affordable; use currently available physiologic data; and easily be integrated into clinical care environments with minimal disruption. Current World Health Organization recommendations state that measurement of RR should include a 60-second visual count, or auscultation for the number of breaths taken, because it is the most reliable method and noted that no other gold standard measure exists.[13] While visual assessment (VA) of RR is recommended, several hospital-based studies found that RR is often not assessed, and even when recorded in the health record, it is often inaccurate.[2, 6, 14] Surprisingly, even among patients whose primary diagnosis is respiratory, assessment of RR is often not accurate.[6, 15-17]

Several challenges specific to the hospital setting make accurate RR assessment challenging. For example, nurses report that the VA of RR is one of the most challenging nursing tasks.[2, 12] Another study found that clinicians believe that this time-consuming procedure does not provide useful clinical information, especially when RR is challenging to obtain (e.g., agitated or uncooperative patients).[14] In addition, the VA of RR can be interrupted by conversations or other distractions. These obstacles and clinicians' opinions about the clinical utility of carefully measuring RR have contributed to the above-outlined problems and highlight how continuous and non-invasive methods may improve RR assessment.

Purpose Statement

The purpose of this literature review is to compare the accuracy, strengths, and limitations of VA of RR to two methods that use physiologic data, namely impedance pneumography (IP) and electrocardiographic-derived respiration (EDR). The next sections of this paper describe each of these methods.

Visual Assessment (VA)

Visual assessment of RR is performed by asking a patient to lie still and refrain from talking. Then, the clinician counts the number of times the chest rises and falls for a full minute.[18] In addition to counting the number of respirations, this method involves assessing the patient's skin and mucous membranes for color, moisture, temperature, and breathing characteristics (e.g., depth, nasal flaring, use of accessory muscles). This method requires concentration and can be difficult if a patient cannot follow instructions and/or cooperate. While RR is a critical determinant of a patient's current physiologic state,[5-7] VA of RR is often estimated, guessed, or omitted altogether.[19] In one study,[20] the nurses surveyed reported intentionally or unintentionally omitting RR assessment >90% of the time. In another study,[11] of 62 patients with 1,597 unique vital signs recorded, only one reading per day of RR was recorded compared to 5.0 for blood pressure; 4.4 for heart rate; and 4.2 for temperature (all $p<0.001$). Incorrect RR readings (low or high) can occur during routine patient activities such as talking, turning, or moving in bed.[21] Finally, in some cases, clinicians reported that they simply copy a previous RR rather than do a VA.[19]

Impedance Pneumography (IP)

Evaluation of electrical impedance in body tissues is a common technique that uses variability in tissue volumes to measure the resistance of alternating currents (AC) as electricity travels through a given material.[22] Measurement of impedance is used in several body composition assessments (e.g., body fat, muscle mass).[22] In the hospital setting, the IP method uses the same skin electrodes to measure both the ECG and RR. It should be noted that while ECG lead wires and skin electrodes are used for the IP evaluation of RR, ECG waveforms are not used to calculate RR. Rather, the ECG device (through lead wires attached to skin electrodes) directs a very small amount of electrical current into the patient's body, that is measured as electrical impedance.[23, 24]

Depending on the manufacturer, one or two of the limbs leads or a combination of two are used to detect amplitude differences of the injected current (Figure 2.1). During inspiration, as the chest expands, resistance to the flow of an electrical current increases, which increases impedance. Alternatively, during expiration, impedance decreases as air leaves the lungs. To derive RR using the IP method, a drive-and-measure circuit is established that delivers two out-of-phase AC-coupled currents onto a combination of electrodes.[23, 25]

A series of resistors and capacitors send a very low amplitude current into the patient's chest via the ECG lead wires.[23, 25] Given that the AC is minimal, patients do not experience any adverse effects, or experience any sensations associated with the injected current. A computer algorithm within the bedside ECG monitor generates both a numeric RR (breaths/minute) and a respiratory waveform. The waveform has an upward flag on the inspiratory wave and a downward flag on the expiratory wave. An accurate IP waveform is shown in Figure 2.2 (2A)

Several caveats warrant consideration regarding the IP method. For example, the best lead(s) to obtain an accurate RR in a person who is an abdominal breather are typically lead II and/or lead III.[25] These two ECG leads make sense for this application because lead II is obtained using the right arm and left leg electrodes and lead III is obtained using the left arm and left leg electrodes; thus, thoracic changes associated with abdominal breathing are most noticeable using these two leads. However, if a patient is in an upright position, or a chest breather, a more accurate ECG lead for RR detection may be lead I, which uses the right arm and left arm electrodes. For this reason, the ideal IP algorithm for hospitalized patients should use a combination of multiple ECG leads to derive the most accurate RR. However, few IP algorithms use multiple ECG leads, or have the ability to adjust automatically to changes in body position.[26] Lastly, regardless of which ECG lead is used for RR detection, any one of these ECG leads can be contaminated with motion artifact, a disconnected lead, or inaccurate lead placement, making the IP method prone to inaccurate RR measurement (Figures 2.2), 2B and 2C.[24]

Electrocardiographic-Derived Respiration (EDR)

The graphic display of the heart's electrical activity provided by the ECG can be used to estimate RR. The EDR method uses the ECG waveforms recorded from the lead wires placed on a patient's chest to detect even minor waveform alterations during breathing.

These minor waveform alterations are generated by changes in both lung volume and the heart's position relative to the ECG leads on the body's surface.[27-29] Unlike IP, the EDR method uses only the patient's ECG waveforms to derive RR. The EDR algorithms typically use direct assessments of the respiratory-influenced features described above over a series of ECG signals.[29-31] Several different algorithms are used to estimate RR from single and/or multi-lead ECG waveform morphologies.[32-34] Two of these algorithms (i.e., respiratory sinus arrhythmia [RSA], respiratory amplitude modulation [RAM]) are discussed in more detail below.[29]

EDR method using RSA – During inspiration and expiration, the heart rate slightly increases and then decreases. This phenomenon is referred to as RSA and is depicted in Figure 2.3 [29] The amount of respiratory oscillation differs from person to person and varies depending on the rate of an individual's breathing (e.g., tachypnea, bradypnea).[35] Because the response of the heart's peripheral arteries to changes in respiration is responsible for rapid changes in instantaneous heart rate variability (IHR), a computation of IHR and its inverse (R-R interval) can be used to derive the rhythm of an individual's respiration.[29]

EDR method using RAM – This algorithm takes advantage of anatomic movements related to respiration that affect the ECG. First, the heart's apex extends towards the abdomen as it stretches during inspiration and simultaneously the diaphragm moves downward.[30] Second, during exhalation the diaphragm recoils to aid in emptying the lungs and squeezes the heart's apex toward the sternum. During these processes, compared to a reference vector, the angles of the electrical and cardiac vectors are altered. These alterations exert a modifying influence on the amplitude of the ECG signals that are used to identify respirations.[36] Recently, the RAM algorithm was simplified using total (peak-to-trough) QRS amplitude in a single lead.[29] This modified process includes the following steps: 1) detection of QRS complexes; 2) measurement of the total QRS amplitude; 3) exclusion of outliers (e.g., noise and artifacts); 4) interpolation of the EDR values, and 5) separation of the waveform with a band-pass filter as suited for the range of rates anticipated.[29]

METHODS

For this review, a systematic literature search was conducted using the following databases: PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science, and the Cochrane Library. Keywords used for the database searches included: *adult(s)*, *respiration(s), RR measurement, manual, visual, ECG or EKG derived, impedance, thoracic pneumography, and hospital setting*. These terms were combined in strings using the Boolean operands “OR” and “AND” to specifically focus on studies that compared different methods to assess RR.

Studies were included if they met all of the following criteria: (a) included adult patients; (b) were a clinical trial or a comparative study that evaluated hospitalized patients; (c) compared VA of RR to IP and/or EDR; (d) were published between January 2000 and August 2020; and (e) were published in English.

The search strategy yielded 3,607 studies identified in PubMed, 21 in CINAHL, 16 in Web of Science, and 11 in the Cochrane Library (Figure 2.4). An additional 48 studies were found in Google Scholar. After duplicates and papers not directly relevant to the topic were removed, the abstracts from 78 studies were evaluated. Of these 78 studies, full manuscripts for 23 studies were reviewed. After eliminating studies that did not meet our pre-specified inclusion criteria, four studies are included in this systematic review. Of these four studies, 3 (75%) compared VA to IP[37-39] and 1 (25%) compared VA to EDR.[40]

The findings from this review are summarized in Table 2.1. Standardized criteria were developed to review the two groups of studies. Across both groups of studies, information was obtained on the author, year, purpose, study design, sample characteristics, study procedures and analysis methods, main findings, and strengths and limitations.

RESULTS

Results of the Studies that Compared VA to IP

Description of the studies

All of the studies that compared the VA and IP methods were cross-sectional descriptive studies.[37-39] These studies were conducted in the United States, India, and Denmark. Sample sizes ranged from 50[37, 38] to 159.[39] Of the two studies that reported mean age,[37, 39] the grand mean age was 45.6 years. Across three of these studies,[37-39] the grand mean percentage of females was 46.7%.

Description of the study procedures

In all three studies,[37-39] nurses' VA of RR was used for comparative purposes. In two of these studies,[38, 39] research staff were trained to provide an additional VA of RR that was used as the criterion standard measure. IP measures were captured using a cardiac monitor[37, 39] or a Sensium Vitals wireless patch.[38]

Description of the methods used to assess the accuracy of VA to IP

Across these three studies,[37-39] the analytical methods used to assess VA's accuracy compared to IP were extremely variable. In two studies,[37, 39] paired analyses were done to evaluate variability between or among the measures. In one study,[39] sensitivity and specificity analyses were done for bradypnea and tachypnea. In two studies,[38, 39] Bland-Altman analyses were performed.

Summary of major findings

The results of the comparative findings between the VA and IP methods were highly variable depending on the analytic method used. In one study,[39] when comparative methods were used (e.g., analysis of variance), variability in the RR obtained by nurses using VA was lower than for either the criterion standard or IP measures. In the other study,[37] no differences were found using paired t-tests between the VA and IP methods. However, in both studies that used Bland Altman analyses,[38, 39] the upper and lower levels of agreement (LOA) between the two methods were extremely poor.

Results of the Study that Compared VA to EDR

Only one study was found that compared the VA and EDR methods (Table 2.1).[40] In this descriptive correlational study, VA of RR in 377 critically ill patients was done by one of eight unit nurses. EDR was obtained using a BT16 – piezoelectric belt for 5 minutes after admission. Using paired t-tests, significant differences in RR were found between the two methods. In addition, using Bland Altman analyses, the LOAs between the two methods were poor. Of note, visual inspection of the scatter plots determined that RR obtained using VA centered around rates of 18, 20, and 22 breaths per minute. In contrast, the RR obtained using EDR were more variable.

DISCUSSION

While designed to be a systematic review that compared the accuracy, strengths, and limitations of VA, IP, and EDR methods to measure RR, only four studies were identified.[37-40] Of note, none of these studies compared all three methods in the same sample of patients. The remainder of this discussion will provide a synthesis of the findings; discuss the strengths and limitations of the three methods; and suggest directions for future research.

One of the limitations of the current studies was the choice of the “gold standard” or reference group that was used for comparative purposes. While all four studies used VA by nurses to determine RR,[37-40] it is well known that these results are not standardized and as noted in one study,[38] were not normally distributed and were prone to having even numbers reported (e.g., 18, 20). In the two IP studies that used trained researchers to perform VA of RR for comparative purposes,[38, 39] the findings are inconclusive. A major limitation of these two studies is that the training procedures for the research staff to ensure inter-rater reliability were not described.

An equally important consideration in the evaluation of the comparability of methods is the choice of statistical tests. Three of the four studies used the Bland-Altman analysis to evaluate for agreement between VA of RR and the IP[38, 39] and EDR[40] methods. Compared to the calculation of a correlation coefficient, the Bland-Altman analysis describes the agreement between two quantitative measures by constructing LOA. These statistical limits are calculated using the mean and the standard deviations of the differences between the two measurements.[41] However, it should be noted that only a clinician, who will use the test results, can determine whether the LOA are or are not acceptable.[42] In all three studies, [37-39] the upper and lower LOA between VA and the IP and EDR methods were very poor.

Several study limitations contribute to these significant discrepancies including relatively small sample sizes, lack of inter-rater reliability assessments, cross-sectional designs, and heterogeneity in patient samples. Given the clinical need to have accurate counts of RR in critical care settings,[1, 2, 4] additional research is warranted on the use of both the IP and EDR methods. Future studies need to develop rigorous research protocols that included: training and evaluation of the inter-rater reliability of the research staff who perform the VA of RR; power calculations to determine appropriate sample sizes; pre-specified criteria for acceptable LOA; conducting experiments to determine acceptable and clinically meaningful LOA for various clinical conditions (e.g., tachypnea, bradypnea, normal RR); and a critical evaluation of outliers (e.g., changes in patient's position during data collection).

As noted in the Introduction, accurate, real time assessments of RR, that use physiologic data and are integrated into the critical care environment, may contribute to earlier detection of clinical deterioration.[1-4] Given the paucity of evidence, the remainder of this discussion will describe the advantages and disadvantages of the VA, IP, and EDR methods to improve the earlier detection of deleterious changes in RR (see Table 2.2). While VA is easy to perform, does not require any additional equipment, involves human interaction, and allows a clinician to evaluate a number of breathing characteristics (e.g., depth, skin color), it is not the ideal method for critically ill patients. For example, VA is time consuming and prone to numerous omissions [16, 20]. In addition, inaccurate measurements can occur because of environmental distractions and patient movement.[8, 14, 22] However, the major limitation in the critical care setting is that because VA of RR is done at prescribed intervals (e.g., every 30 minutes), dynamic changes in RR are missed.

The major advantages of the IP include that it is safe and simple to use; it is available in cardiac monitors; and it provides a continuous measurement of RR. However, signal interruptions and patient movement can affect the characteristics of the respiratory waveform and subsequent calculation of RR.[23, 43] An example of this limitation is found in a study that reported 161,931 unique RR type alarms (i.e., RR parameter high/low, or apnea) from adult patients in the intensive care unit that used IP in their bedside monitors.[43] As shown in Figure 2.5, a large proportion of the alarms were found to have flat RR waveforms in patients who were known to be breathing adequately, were not in respiratory arrest, and/or were on a ventilator.

The number of false alarms generated using the IP method is problematic because it interrupts nursing workflow unnecessarily and compounds the alarm fatigue problem. Another limitation of the IP method is that the various components of the impedance device (e.g., wires, skin electrodes and cables) can be sources of measurement error.[44] Of note, while the IP method is widely accepted, in one review,[44] it was noted that non-respiratory motion and cardiac artifact can influence the accuracy of the readings.[44]

While not as well studied in the clinical setting, the EDR method has numerous advantages.[40] Like the IP method, it is non-invasive, it provides continuous assessment of RR, which means acute alterations in RR are easily detected. In addition, the EDR algorithm could be added to existing bedside monitors to extract respiratory waveforms from the ECG signal.[35] With this method, the detection and measurement of QRS complexes are comparatively impervious to noise and muscle artifact, making it an ideal waveform to use to derive RR.[29, 45] In addition, compared to IP, direct measurements of QRS amplitude are more highly correlated with tidal volume and the amplitude displacement caused by the rise and fall of chest movement, which may be more suitable for the identification of RR.[29]

In terms of limitations, similar to the IP method, device failure can occur. In addition, EDR measurement can be affected by the natural age-related decline in RSA, as well as arrhythmias (e.g., atrial fibrillation) and the effects of medications that affect heart rate and rhythm.[29] Finally, patient movement can cause artifacts and lead to inaccurate assessments of RR. While this method holds promise, additional research is warranted that compares the accuracy of VA, IP and EDR in the same sample of critically ill patients.

Limitations of this review

The primary limitation of this review is the paucity of research on this topic. Given that only three studies compared the VA and IP methods[37-39] and only one compared VA to EDR,[40] no definitive conclusions could be drawn about the accuracy of these continuous device driven methods. In addition, given the paucity of the research and heterogeneity of the small number of studies included, a meta-analysis could not be performed.

CONCLUSIONS

Given the importance of accurate and frequent RR assessment in the fast-paced critical care environment, methods that take advantage of available physiologic data are warranted. Given the promise, but limitations of both the IP and EDR methods, future research needs to focus on making refinements to these algorithms and/or developing new algorithms that are easily integrated into existing physiologic devices used in the critical care environment. The use of a combined approach that utilizes the strengths of both IP and EDR may provide more precise and accurate results.[29] However, the optimal approach to combining these methods warrants additional investigation. Future studies need to include diverse patient populations with a variety of clinical conditions and employ the most robust analytic methods. This line of scientific inquiry will result in a clinically useful method to detect dynamic and acute changes to RR in critically ill patients who may require interventions to avert untoward outcomes.

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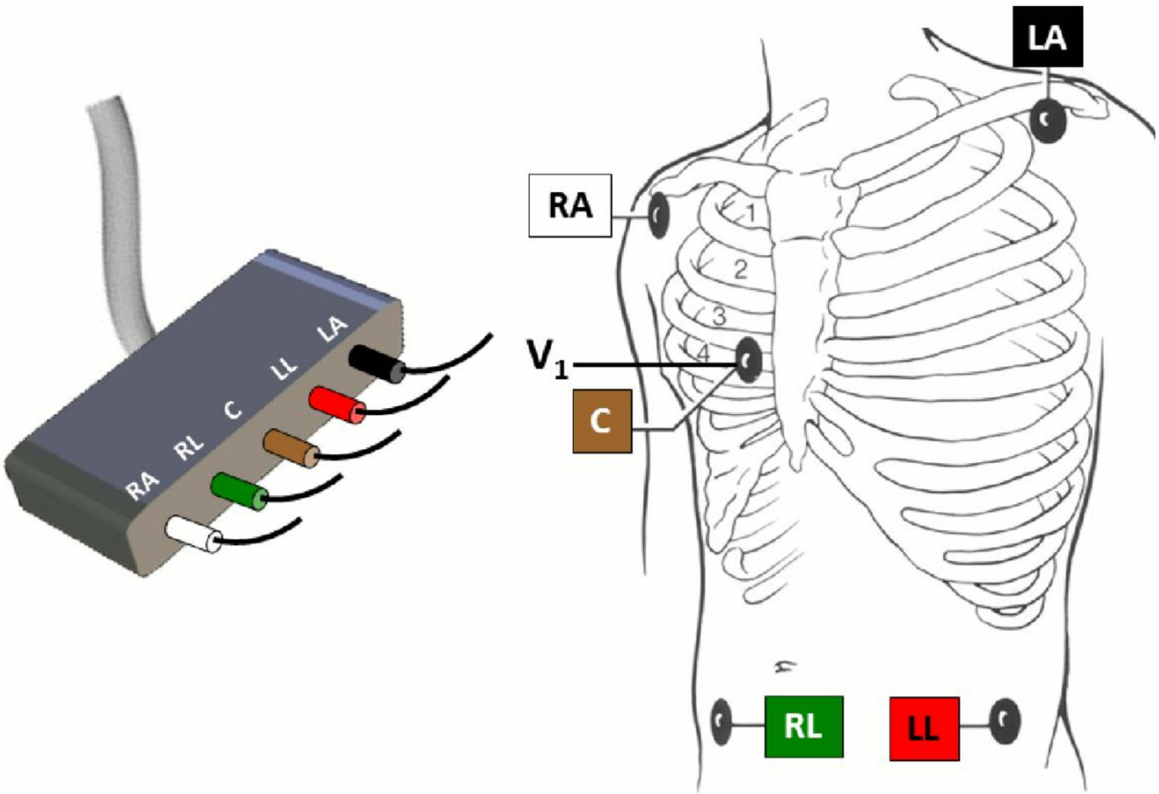
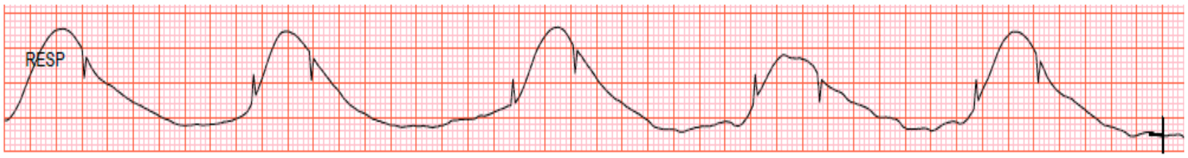


Figure 2.1 An Illustration of how electrocardiographic (ECG) limb leads I, II, and III are obtained using skin electrodes placed on the right arm (RA), left arm (LA) and left leg (LL). Impedance respiration is typically generated using one or two of these ECG leads using the bedside monitor. A single chest (C) electrode is shown that is routinely placed in the V1 position for in-hospital arrhythmia monitoring and the right leg (RL) electrode, that is required to record lead V1. Lead V1 is not used for deriving respirations. Figure from Drew et al., PloseOne doi:10.1371/journal.pone.0110274.g003.[43]

2A.



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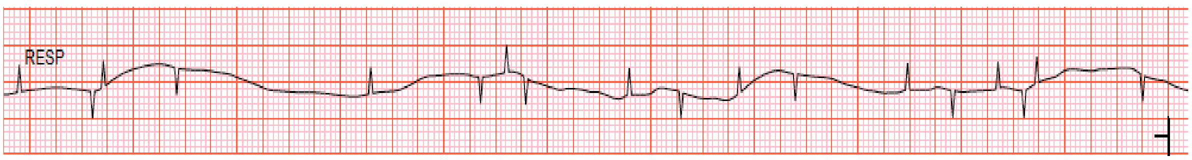

2C.

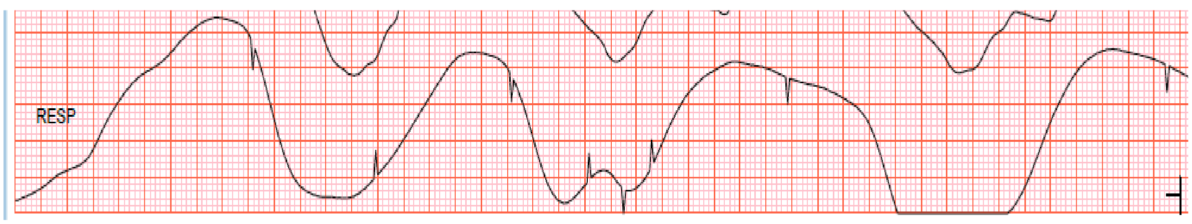

Figure 2.2 Accurate (2A), inaccurate (2B), and motion artifact (2C) respiratory waveforms using the impedance pneumography (IP) respiration method.
2A. Normal respirations are generated from a 10 second IP waveform. Note the upward flag on the inspiratory waveform and the downward flag on the expiratory waveform.
2B. Inaccurate respiratory rate from a 10 second IP waveform recording. Note that occurrence of indistinguishable waveforms that are indicative of inspiration and expiration and the random flags throughout the tracing.
2C. An illustration of an IP waveform during motion artifact. Note that flags are present on the tracing. However, not all of the flags coincide with inspiration or expiration.

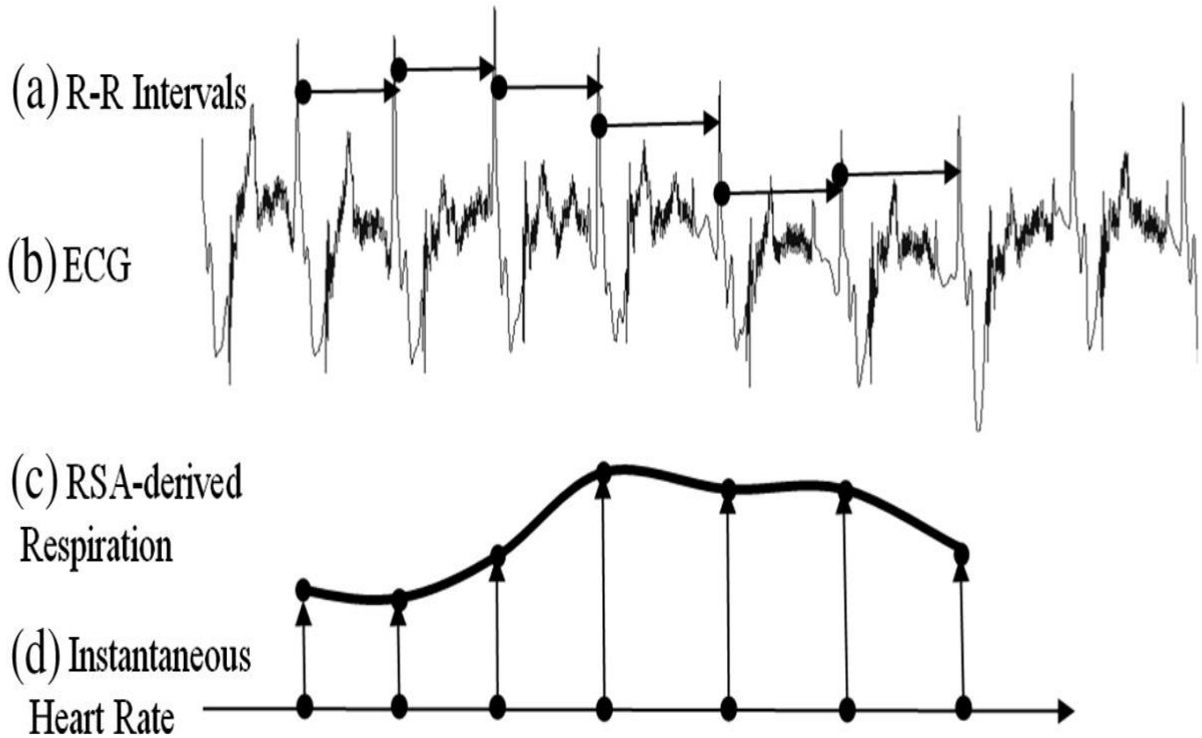

Figure 2.3 An illustration of a respiratory sinus arrhythmia (RSA) derived respiratory rate (a and b), which uses varying R-R intervals (horizontal arrows) from QRS complexes on the electrocardiogram (ECG). Note that the circles and arrowheads of the horizontal arrows de-note the QRS complexes. The inverse of the R-R intervals is shown as vertical arrows (d), that are exaggerated for illustration. A heart rate is computed, which is used as amplitude knots for cubic spline interpolation to create the RSA-derived respiration waveform (c). Reprinted with permission from the journal.[29]

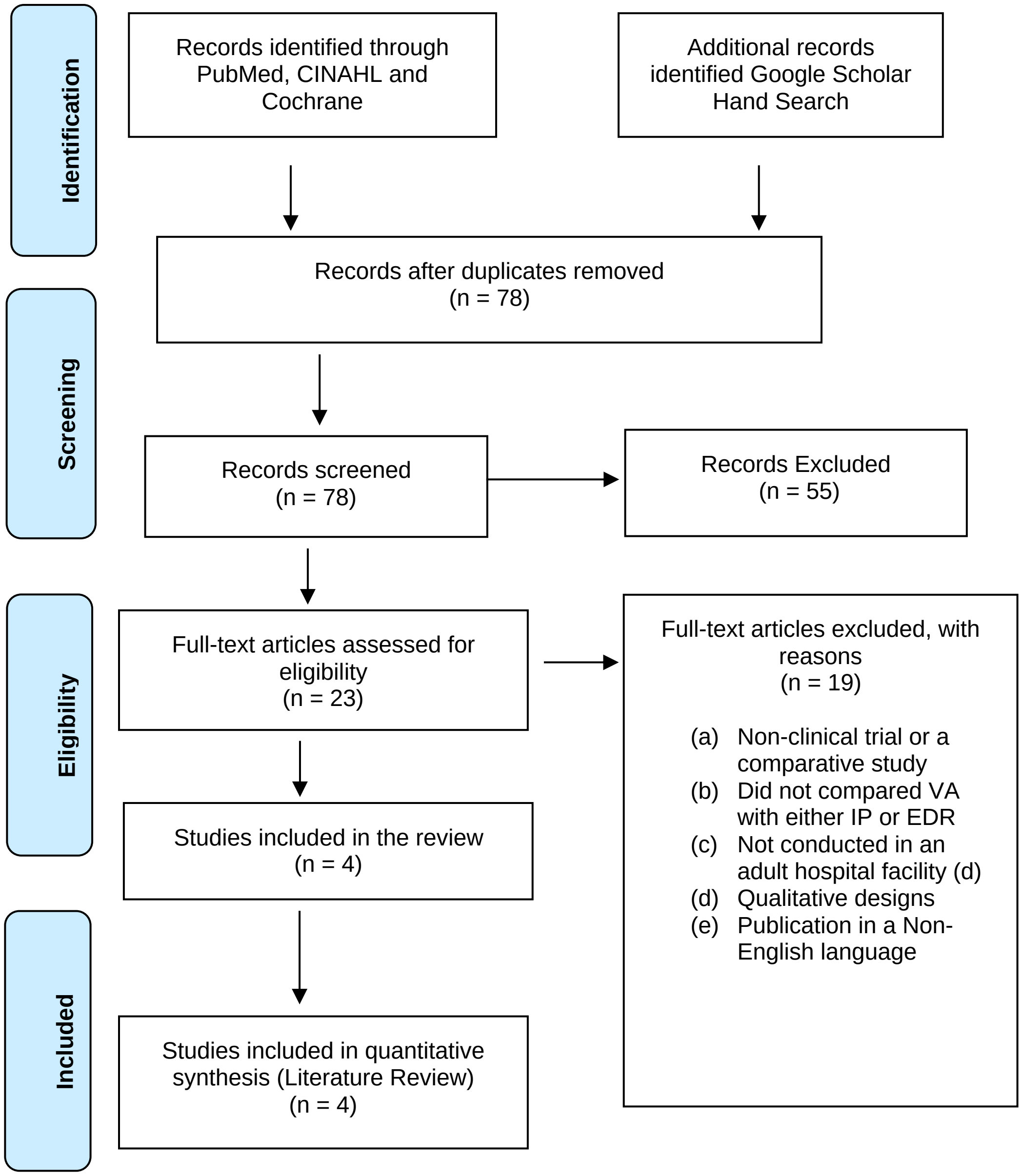

Figure 2.4 A diagrammatic representation of the literature search strategy using the PRISMA format.[46]

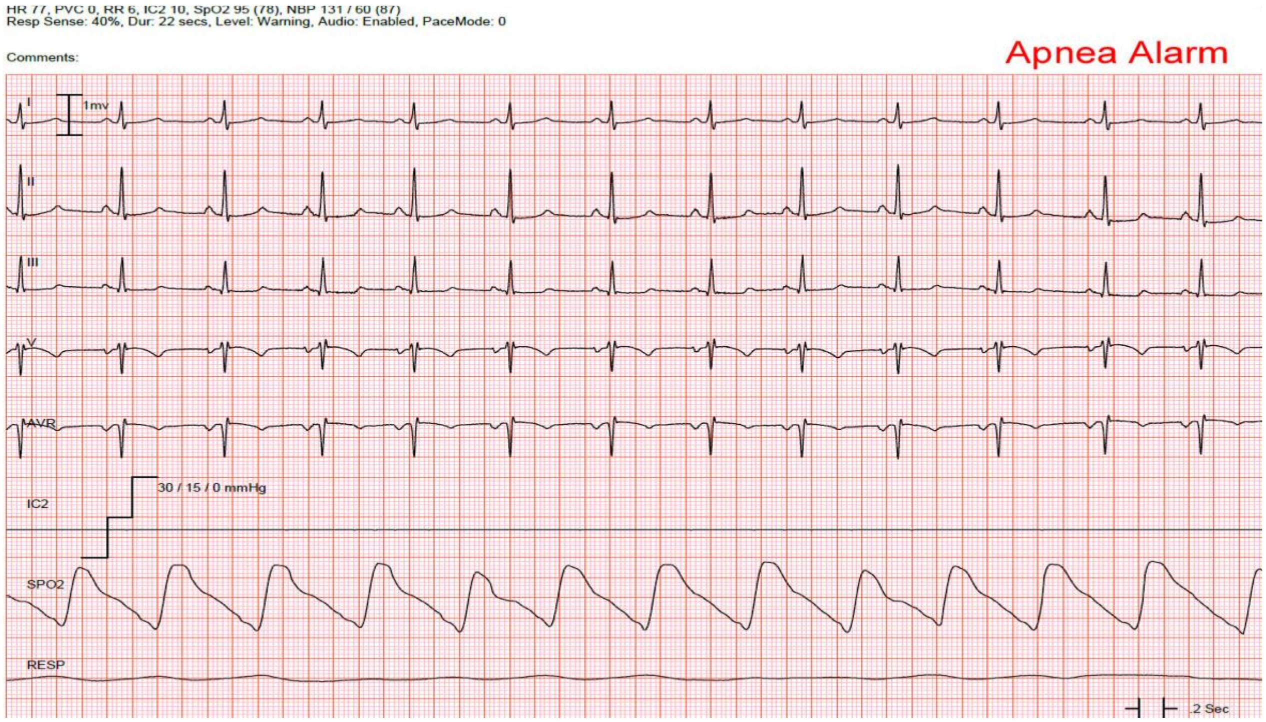

Figure 2.5 False apnea alarm in an intensive care unit patient measured using the impedance method. The respiratory waveform (bottom waveform labeled ‘‘RESP’’) is essentially a flat line. Therefore, respiratory rated calculated using the impedance method alarmed for apnea. The monitor default setting for apnea is cessation of breathing for >20 seconds. However, this patient was not in acute respiratory distress at the time of this alarm. Note at the top of the alarm tracing is an erroneous respiratory rate (RR) of 6 breaths per minute, yet the oxygen saturation measure from the Sp02 probe is 95%.

Table 2.1 – Summary of the findings from studies that compared respiratory rates (RR) identified using visual assessment (VA), impedance pneumography (IP), and/or electrocardiographic derived (EDR) methods.

Author, Year, Country, Purpose, Setting, and Study Design	Sample Characteristics	Study Procedures and Methods of Data Analysis	Main Findings	Strengths and Limitations
VA compared to IP				
Author: Lovett et al., 2005 Country: USA Purpose: Measure the variability and accuracy of triage nurses' measurements of RR relative to criterion standard measurements and Evaluate the variability and accuracy of electronic measurements of RR recorded using a cardiac monitor equipped with transthoracic impedance (IP). Setting: urban teaching ED Design: Cross-sectional	Sample size: 159 consecutive patients who presented to the ED Age (years) 18-29 = 34.0% 30-39 = 22.6% 40-49 = 14.5% 50-59 = 8.8% 60-69 = 7.5% 70-79 = 5.7% 80-89 = 1.3% NR = 5.7% Mean Age = 39.41 Female = 50.9% Hispanic = 41.5% White = 46.5%	Description of study procedures: Triage nurses' measurements of RR were recorded from the medical record RAs were trained in standardized methods to collect criterion standard measurements of RR. RAs observed respirations and auscultated RR at a single location for one minute. When auscultation could not be performed, observed RR was used in the analyses. RR using the IP method was captured at 60-second intervals. Data analysis: Variability – was estimated by calculating the SD of each of the measures. Differences among the nurse, RA, and IP measures were evaluated using ANOVA. Sensitivity and specificity of triage nurses versus IP were cross-tabulated measures against criterion standard measurements of respiratory values: Low = <12 breaths per minute Normal = 12-20 breaths per minute High = >20 breaths per minute Bland Altman analyses were done that compared for –	Variability for triage nurses' measurements of RR (3.3) was significantly lower than for IP (4.1) and criterion standard (4.8, p<.01). Variability for IP measure was significantly lower than for criterion standard measure (p<.05) Accuracy of detecting bradypnea and tachypnea - neither triage nurses nor IP measures of RR were accurate in detecting bradypnea or tachypnea Bradypnea (<12 breaths/min) Nurse versus criterion measure ▪ Sensitivity = 0.00 (0.00-0.35) ▪ Specificity = 1.00 (0.97-1.00) IP versus criterion measure ▪ Sensitivity = 0.25 (0.07-0.59) ▪ Specificity = 0.98 (0.94-0.99) Tachypnea (>20 breaths/min) Nurse versus criterion measure ▪ Sensitivity = 0.38 (0.25-0.53) ▪ Specificity = 0.84 (0.75-0.90) IP versus criterion measure ▪ Sensitivity = 0.40 (0.28-0.55) ▪ Specificity = 0.86 (0.78-0.92) Agreement between triage nurses and criterion measure of RR was poor (95% limits of agreement -8.6 to 9.5) Agreement between IP and criterion measure of RR	Strengths ▪ Data collected in an ED during triage ▪ The criterion reference standard used for comparison ▪ Use of Bland Altman analyses Limitations ▪ The majority of the patients were less than 39 years of age ▪ Triage nurses were aware that their assessments of RR were being collected ▪ Criterion measure of RR was obtained after the triage visit, not simultaneously with triage nurses' assessment of RR ▪ No inter-rater reliability estimates were done with the RAs

		a) triage nurses RR to criterion standard RR and b) criterion standard RR to IP rates Agreement Bias 95% limits of agreement	was poor (95% limits of agreement -9.9 to 7.5) Systematic bias was small for triage nurses' measurements of RR (+0.0) and electronic measurements of RR (-1.2).	
Author, Year, Country, Purpose, Setting, and Study Design	Sample Characteristics	Study Procedures and Methods of Data Analysis	Main Findings	Strengths and Limitations
Author: Chand et al., 2014 Country: India Purpose: Examine differences between VA and electronic (IP) measurements of vital signs in cardiac patients Setting: Advanced Cardiac Centre ICU Design: Comparative study	Sample size: 50 patients admitted in CTVS-ICU and CCU CTVS-ICU = 21 (42%) CCU = 29 (58%) Mean age (Years) =55.9 Females = 49.25 (range 25-58) Females = 16% Ethnicity = NR	Description of study procedures: VA – By floor RNs IP – By the cardiac monitor Four measurements of temperature, pulse, respiration, and blood pressure were recorded at 30-minute intervals, consecutively. The measurement of each vital sign was done simultaneously. Data analysis: Paired t-test was used to evaluate for differences between the VA and IP methods The coefficient of variation was calculated to quantify the variation between the VA and IP measures	A total of 200 measurements were done using each method The mean difference in RR between the VA and IP methods was not significant (i.e., 0.015 ($\pm$1.16), p = 0.883) The coefficient of variation between the VA (26.25%) and IP (25.48%) was similar	Strengths ▪ Measurements made simultaneously Limitations ▪ Purposive sampling ▪ Type of physiologic monitor not reported ▪ Unclear if nurses were blinded to values obtained with the IP methods ▪ Small sample size ▪ Bland Altman analyses were not performed

Author, Year, Country, Purpose, Setting, and Study Design	Sample Characteristics	Study Procedures and Methods of Data Analysis	Main Findings	Strengths and Limitations
Author: Granholm et al., 2016 Country: Denmark Purpose: Evaluate the agreement between RR rates done using three methods (i.e., standardized approach, VA by ward staff, IP) Setting: Medical unit Design: Prospective, observational study	Sample size: 50 patients admitted to an acute medical unit Median age (years) = 71.5 Female = 54% Ethnicity = NR	Description of study procedures: VA - Ward staff performed all assessments as usual. Data obtained from medical record IP – Sensium Vitals wireless patch measures RR, heart rate, and axillary temperature every 2 minutes Standardized approach – Trained researchers counted the patient's RR over 60 seconds. Patients were instructed to lie still and refrain from talking Data analysis: Bland-Altman analysis used to evaluate the agreement between the methods with 95% LOA and 95% CI	Agreement between standardized VA by researcher versus IP ▪ Mean difference was 0.3 b/m (95% CI -1.4 to 2.0 b/m) ▪ Lower and upper 95% LOAs were -11.5 b/m (95% CI -14.5 to - 8.6 b/m) and 12.1 b/m (95% CI 9.2 to 15.1 b/m) respectively ▪ Large RR differences (>10 b/m) were found in three outliers (i.e., one obese patient with respiratory disease; one elderly patient with respiratory disease, atrial fibrillation, and prior cardiac surgery; one slim young patient with a non-respiratory-related infection) ▪ The mean difference after removing three outliers was -0.1 b/m (95% CI -0.7 to 0.5 b/m). Without outliers' differences were normally distributed Agreement between VA by ward staff versus IP ▪ Mean difference was 1.7 b/m (95% CI -0.5 to 3.9 b/m) ▪ Lower and upper 95% LOAs were -13.3 b/m 95% CI ▪ -17.2 to -9.5 b/m) and 16.8 b/m (95% CI 13.0 to 20.6 b/m) respectively. ▪ RR by ward staff was not normally distributed, with digit preferences of 16, 18, and 20 b/m.	Strengths ▪ One trained researcher recorded the standardized approach ▪ The single paired measurement used for each patient minimized bias caused by within-subject correlations Limitations ▪ No repeated measurements ▪ RR done by ward staff were obtained from the electronic health record, which could affect comparison with IP (i.e., inaccurate times recorded) ▪ Small sample size

VA compared to EDR				
Author, Year, Country, Purpose, Setting, and Study Design	Sample Characteristics	Study Procedures and Methods of Data Analysis	Main Findings	Strengths and Limitations
Author: Kellett et al., 2011 Country: Ireland Purpose: Evaluate for the association between VA and EDR measured RR and their relationships to in-hospital mortality Setting: Acute medical unit in a small rural hospital Design: Descriptive, correlational	Sample size: 377 acutely ill medical patients Mean age (years) - 68.3 ± 16.8 Alive = 67.9 (±17.0) Dead = 77.1 (±9.2) Sex = NR Ethnicity = NR	Description of study procedures: VA of RR was obtained by one of eight nurses on the patient's admission to the unit. Nurses were not given any instructions on how to measure or record RR. EDR: RR was obtained using a BT16/Piezoelectric belt for 5 minutes after admission. Data were transmitted to a separate computer system for subsequent analyses. Data analysis: Paired t-tests were used to evaluate for differences in RR between VA and EDR Correlation coefficients were calculated for VA versus EDR measures of RR. Bland Altman plots were done to evaluate the limits of agreement between the VA and IP measures of RR.	The mean RR measured by VA (20.9 (±4.8) breaths/min) was significantly different from that obtained by EDR (19.9 (±4.5) breaths/min), p=.004). The correlation coefficient between VA and EDR was 0.50. Visual inspection of the scatter plots illustrated that RR obtained using VA clustered around rates of 18, 20, and 22 breaths/min. The RR rates obtained using EDR were more variable. Bland Altman plots revealed that the 95% LOA between VA and EDR for RR were -8.2 and 10.3 breaths/min.	Strengths ▪ Relatively large sample size Limitation ▪ Demographic and clinical characteristics of the sample (e.g., acuity level, use of medications) were not reported ▪ Only eight nurses participated in this study, and their characteristics were not reported. ▪ Lack of standardization in the VA or RR ▪ Bland Altman plots not included in the paper

Abbreviations: b/m = breaths per minute, CTVS-ICU = cardiothoracic and vascular surgery-intensive care unit, CCU = critical care unit, CI = confidence interval, CSM = criterion standard measurement, EDR = electrocardiographic derived respiration, IP = impedance pneumography, ED = emergency department, LOA = limits of agreement, NR = not reported, PACU = post anesthesia care unit, VA = visual assessment, RN = registered nurse, RR = respiratory rate, SD = standard deviation.

Table 2.2 Comparison of the strengths and limitations of the visual assessment (VA), impedance pneumography (IP), and ECG-derived respiration (EDR) methods for assessment of respiratory rate.

METHODS	STRENGTHS	LIMITATIONS
VISUAL	Traditional method to assess RR Easy and safe to perform Breathing characteristics (e.g., depth, accessory muscles, skin color) can be assessed	Time-consuming for clinicians Numerous omissions and guessed measurements.[19] VA is a snapshot of a patient's RR at prescribed intervals (e.g., every 30 minutes). Acute changes and early identification of patient deterioration can be missed.
IP	Simpler, less time consuming than VA Safe to use Continuous measurement of RR Coherence analysis concluded that IP is more reliable than EDR[2, 3]	Studies found that the IP method was prone to erratic artifacts, false-positive readings and was sensitive to motion and cardiac artifacts.[43,49-52] A device's internal impedance, such as cables and wires, can be a source of measurement error.[44] IP can generate false positives from movement and interruptions by the examinee and affect the readings and values.[21] IP method is influenced by behaviors that occur naturally (e.g., talking, coughing)[21] IP is predisposed to signal degeneration with body position changes because the thoracic signal depends on posture, making it difficult to evaluate tidal volume.[44]
EDR	The EDR algorithm can be added to existing ECG to extract respiratory signals from the ECG signal without new transducers, devices, or accessories required for monitoring.[35] Continuous monitoring and non-invasive.[35] The sensitivity and specificity of the EDR algorithm to identify RR was high (99%/97%) in cardiac patients compared with other methods.[32] Alterations in the RR are easily detected.	RSA aspect weakens with aging, which may lead to inaccurate measurements in older individuals. Patient movement and noise can cause artifacts and lead to inaccurate values. Method lacks validation in the hospital setting. EDR measurement can be affected by the natural decline in RSA, as well as arrhythmias (e.g., atrial fibrillation) and the effects of medications that affect heart rate and rhythm.[29,32,53]

CHAPTER 3

HIGH PARAMETER ALARMS ARE THE MOST FREQUENT RESPIRATORY TYPE ALARM DURING IMPEDANCE PNEUMOGRAPHY IN THE INTENSIVE CARE UNIT

Abstract

Objective: The objectives of this study were to examine respiratory rate (RR) alarms by type and duration and for associations with patients' demographics and clinical characteristics.

Design: Secondary data analysis of a retrospective, cohort study.

Setting: Three adult intensive care units (ICU) were included: cardiac (16 beds); medical-surgical (32 beds), and neurological (29 beds) in an academic medical center.

Data Source: Impedance pneumography (IP) derived respiratory alarms from bedside electrocardiographic (ECG) monitors from 461 consecutive ICU patients during a one-month time period.

Measurements and Main Results: RR parameter and apnea alarms were configured as follows: RR parameter (high ≥30 breaths/minute [bpm] or low ≤5 bpm) and apnea (≥20 seconds of no breathing). A total of 159,771 RR type alarms were over triggered 48,000 hours of monitoring, an average of 67 RR alarms/bed/day. Parameter type alarms were more common in these ICU patients [88.2% (n= 140,975)] than apnea alarms [11.8% (n = 18,796)]. The majority of the parameter alarms (82.5%; n=131,827) were high. Using multivariate analysis, after controlling for the length of ICU monitoring, alarm occurrence rates were associated with: type of ICU unit ($p<0.01$); the use of mechanical ventilation ($p<0.01$); and the lack of a ventricular assist device or pacemaker ($p<0.01$). Male gender was associated with low parameter ($p<0.01$) and apnea ($p<0.05$) alarms.

Conclusion: Study findings highlight the high rates of respiratory alarms and suggest that these alarms contribute to the overall alarm burden. This study confirms that high parameter alarms are more prevalent in the ICU setting and that some demographic and clinical characteristics contribute to the types of alarms generated using the IP method. Attention to appropriate alarm settings, as well as patients' demographic and clinical characteristics are essential to reduce the number of RR alarms in the ICU.

INTRODUCTION

Respiratory rate (RR) measurement in the intensive care unit (ICU) is an essential component of patient monitoring that aids in early recognition of patient deterioration and is used to guide treatments (e.g., pharmacologic, mechanical ventilation).[1-3] Impedance pneumography (IP) was developed for continuous assessment of RR. When paired with electrocardiographic (ECG) monitoring of heart rate and rhythm, IP is an essential non-invasive innovation in the continuous assessment of a patients' vital signs.[4, 5] An additional feature of this method is that it generates an alarm(s) when a RR falls above or below prespecified parameters or when no breaths are detected. While RR alarms are designed to alert busy clinicians to a change in a patient's condition that may require immediate intervention, they can contribute to alarm fatigue in clinicians (desensitization or unsafe alarm adjustments), which increases the risk of missing true events.[6-8]

To date, seven studies have evaluated the number and/or types of RR alarms using IP in adult hospitalized patients.[6, 9-14] In all of these studies, data on RR alarms, as well as other types of physiologic alarms were evaluated. In the three studies that provided specific data on RR alarms,[6, 9, 10] the total number of all alarm types ranged from 835[10] to 2,558,760.[6] Reasons for this wide range may be explained by differences in the overall purpose of the studies, sample sizes, settings of care, duration of data collection, and type of monitor used.

In terms of specific types of RR alarms, the total number of apnea alarms was reported in only two studies.[10, 14] In one study,[10] of the 223 apnea alarms identified, 33% were true alarms with 2.6 apnea alarms/patient/day. In the other study,[14] of the 148 apnea alarms identified, 72.6% were true alarms with one apnea alarm per patient every 37 minutes reported. In terms of low parameter RR alarms, two studies reported ranges from 499 (28% were true alarms)[10] to 13,139 (percentage of true alarms was not reported).[9] In terms of high parameter RR alarms, in the same two studies, the reported range was between 113 (77% were true alarms)[10] and 4,104 (percentage of true alarms was not reported).[9] In another study,[6] a total of

161,931 RR parameter and apnea alarms were identified during a one month period (average 79 alarms/bed/day). Again, reasons for this wide variability in the number of alarms per day include: the duration of monitoring, total number of patients assessed, and differences in the definitions of each of the RR parameters. To date, no study has reported specifically on the number, types (parameter, apnea), and duration of RR alarms generated during IP-derived RR monitoring.

In addition to the lack of knowledge on the specific characteristics of various RR parameter alarms cited above, another unanswered question is which demographic and/or clinical characteristics influence the number of apnea, as well as low and high parameter alarms. Of the seven studies cited above that evaluated RR alarms,[6, 9-14] only one evaluated for associations between patient characteristics and apnea alarms.[14] In this study of 123 patients who underwent surgery and were monitored in the post anesthesia care unit (PACU) for approximately 101 minutes, the mean number of apnea alarms was 148 (72% true alarms). Of note, patients who had received opioids and neuromuscular relaxants had an increased frequency of true apnea. However, no associations were found between age, type of surgery, duration of anesthesia, administration of oxygen and the number of apnea alarms. Therefore, potential demographic and/or clinical characteristics associated with IP-derived RR alarms is largely unknown.

To date, no study has described RR type alarms in relationship to demographic (i.e., age, sex, ethnicity) and clinical (i.e., BMI, cognitive status, tremor, current smoker) characteristics; use of supportive therapies (i.e., mechanical ventilation, ventricular assist device, pacemaker); and/or type of ICU. Of note, several of these factors were associated with false ECG arrhythmia alarms.[6, 15-17] Specifically, age greater than 60, mental confusion, a cardiovascular diagnosis, use of mechanical ventilation, admission to a cardiac ICU, and various ECG features (i.e., bundle branch block, ventricular pacemaker, low amplitude QRSs) were associated with an increased number of false arrhythmia alarms. However, it is not known whether any of these characteristics are associated with various types of RR alarms. Of note, while the IP method does not use ECG waveforms to generate a patient's RR, the limb lead skin electrodes, typically the right arm, left arm, and/or left leg electrode, are used, which is why we hypothesize that similar demographic and clinical characteristics, and supportive therapies may be associated with RR alarms. However, because ECG waveforms are not used with the IP method, these features were not examined in this paper because they are not likely to influence IP-generated RR alarms.

In addition, it is reasonable to hypothesize that because patients who have an impaired cognitive status (confused), tremors, and/or are current smokers experiencing nicotine withdrawal may have more motion artifact during ECG monitoring, they would generate more RR type alarms. Also, devices that create either artifact, 60-cycle interference, or vibrations (i.e., mechanical ventilation, ventricular assist device, ventricular pacemaker) may interfere with the IP signal and lead to more RR type alarms. A better understanding of the aforementioned potential demographic and clinical characteristics and/or supportive therapies and their association with RR alarms may assist with the development of new algorithms to decrease the number of false alarms. In addition, while not all of these characteristics can be controlled by nurses, knowledge of them may help nurses to identify patients who are susceptible to high rates of RR alarms and allow them to intervene when possible (i.e., change skin electrodes) to ensure optimal signal quality (i.e., keeping the skin electrodes free of interference).

Given the paucity of research on the number and specific types of RR alarms that occur during continuous monitoring using the IP method, we conducted a secondary analysis of data from a group of 461 ICU patients. The purposes of this study were: (1) from a total of 159,771 RR alarms, determine the number and duration of RR parameter (i.e., $\leq$5 bpm or $\geq$30 bpm) and/or apnea (i.e., cessation of breathing for $\geq$20 seconds) alarms and (2) determine if demographic (i.e., age, sex, race) and clinical (i.e., BMI, cognitive status, tremor, current smoker) characteristics; the use of supportive therapies (i.e., mechanical ventilation, ventricular assist device, pacemaker); and/or ICU type (i.e., cardiac, medical/surgical, or neurological) were associated with the number of RR parameter and/or apnea alarms.

METHODS

Study Design

This study is a secondary analysis of data from the University of California, San Francisco (UCSF) Alarm Study. The detailed methods for this study were published elsewhere.[6] The Institutional Review Board approved the research protocol and granted a waiver of signed patient consent because physiologic monitoring is part of standard care, and the data were not used for clinical decision-making. Patient information was de-identified, and the data were processed and analyzed on an encrypted computer.

Sample and Setting

The parent study's primary aim was to identify the frequency and types of all alarms generated from bedside physiologic monitors in the ICU during a one month period.[6] For this study, only the RR type alarms are described. The cohort included 461 consecutive adult patients (>18 years of age) who were treated in one of three ICUs (i.e., 16-bed cardiac, 32-bed medical/surgical, 29-bed neurological). Patient-level data were collected from the electronic health record (EHR) and included: demographic characteristics (i.e., age, race, ethnicity, gender), length of ICU stay, monitoring time, and discharge diagnosis. In addition, clinical characteristics, that were hypothesized to increase the number of RR type alarms by affecting signal quality, were collected and included: BMI, being a current smoker (i.e., agitation from nicotine withdrawal), presence of confusion, and the presence of a tremor. In addition, information was collected on the use of devices known to cause interference and/or artifact during ECG arrhythmia monitoring (i.e., mechanical ventilation, VAD, temporary or permanent pacemaker).[6, 15, 17, 18]

Alarm Data Capture System

All 77 ICU beds were equipped with a Solar 8000i physiologic monitor (version 5.4 software, GE Healthcare, Milwaukee, WI). As shown in Figure 3.1, each bedside monitor and the central monitoring station were connected to a local CARESCAPE Gateway (GE Healthcare, Milwaukee, WI). [6] This system captured all of the physiologic waveforms (i.e., ECG, arterial blood pressure, pulse oximetry, respiration), numeric vital sign measurements, alarm parameter settings, as well as all audible and inaudible alarms. Data were passed securely from the CARESCAPE Gateway to a secure research server for off-line analyses.

Physiologic data were captured and stored using BedMasterEx software (Excel Medical Electronics, Inc, Jupiter, FL). The BedMasterEx software vendor provided a command-line software utility to extract waveform data into Extensible Markup Language (XML) files. One of the co-authors (XH) developed an application to parse the XML files; detect gaps in the data streams; identify alternations in signal channel configurations; and assemble the waveform data into multiple binary files following the publicly available format from AD Instrument (Dunedin, New Zealand). The binary files were prepared for analysis that could be done using various analytic programs (e.g., Excel, R Studio, LabChart Reader, Matlab).

Our team learned that we could not depend on the accuracy of the medical record number that was input into the bedside monitor for a given patient because of human errors at the bedside. For example, if a nurse did not discharge a patient from the bedside monitor before a new patient was admitted, the discharged patient's data were merged with the new patient’s data. Each patient’s bed transfer history was extracted from the hospital’s EHR system to solve this problem. This approach established the correct association between a patient’s medical record number and physiologic waveform data by determining a given patient's location first and then retrieving the corresponding database records by linking each patient’s bed/ICU location with date/time information.

Physiologic Monitor Data Used for Determination of RR

The bedside monitors in use during the study period recorded RR using the IP method. This non-invasive method measures thoracic changes associated with respiration from the difference in amplitude measured following the injection of a minute amount of alternating current into the patient's torso through the limb lead ECG skin electrode. As the chest expands, impedance increases, and with expiration, impedance decreases. As illustrated in Figure 3.2, an IP waveform is depicted on the bedside monitor as a respiratory waveform. In addition, the numeric RR is generated and displayed on the bedside monitor.

While seven ECG waveforms are recorded from the bedside monitor (i.e., I, II, III, aVR, aVL, aVF, and a V lead [V1 at our hospital]), the IP method does not use the ECG waveforms to determine RR. Instead, the right arm, left arm, and/or left leg electrodes are used to determine RR. The default ECG leads used to derive the IP RR are either lead I or lead II. While our hospital uses lead II as the default, nurses can change the RR lead to lead I, which is done if the patient is a chest versus abdominal breather or if frequent RR alarms and/or motion artifact occur that affect signal quality. When RR monitoring is first initiated, a brief learning period of approximately eight breaths is needed. These breaths are averaged to determine both the RR and the average amplitude of the respiratory waveform so that upward and downward flags associated with inspiration and expiration can be applied to the waveform (Figure 3.2). The monitors are configured with a 40% RR detection sensitivity. As with the ECG lead used for RR detection, the detection sensitivity can be adjusted to account for shallow versus deep breathing, artifact, and/or patient characteristics.

Data Analysis

All of the RR parameter (i.e., high and low RR) and apnea alarms that were generated during the one-month study period were analyzed. For this study, RR parameter alarms using our hospital's default settings were defined as high RR equals $\geq$30 bpm, low RR equals $\leq$5 bpm, and apnea alarms equals no breaths detected for $\geq$20 seconds. To ensure that we captured all of the RR parameter and apnea alarms and associated them with the correct patient, our research team of biomedical engineers, a Professor with ECG expertise, and two doctoral candidates performed an audit of 100 (21.7%) patients to ensure the data were accurate. Alarms were excluded if they were longer than 900 seconds (15 minutes) because these alarms were likely to occur when a patient was detached from the bedside monitor. For each patient, a summary of the total number of each type of RR alarm and the total duration in seconds were recorded.

Descriptive statistics were calculated for all of the demographic and clinical characteristics, as well as for the occurrence and duration of each type of RR alarm. Data are expressed as means and standard deviations, medians, ranges, and percentages. Associations between demographic (i.e., age, gender, and race) and clinical (i.e., BMI, current smoker, impaired cognitive status, tremor) characteristics, as well as ICU type (i.e., cardiac, medical/surgical, neurological) and use of supportive therapies (i.e., mechanical ventilation, VAD device and/or temporary or permanent pacemaker) and alarm rates were evaluated using regression models that specified a negative binomial distribution. To further describe these relationships, we included results from multivariate regression models for the number of each type of RR alarm, controlling for length of ICU monitoring time. Prior to modeling, BMI was transformed into a categorical variable using standard cutoffs for weight categories and age was considered as a categorical variable in unit increments of 10 years. Results from the multivariate regression models are reported as Incidence Rate Ratios (IRR) with 95% confidence intervals (95% CIs) for each candidate covariate with the rating period defined as the monitoring time in the ICU. Statistical significance was defined as a p-value of <0.05, using two-tailed tests for all analyses. Analyses were performed using R version 3.6 Vienna, Austria. [19]

RESULTS

Characteristics of the Total Sample

Respiratory alarm data from 461 consecutive ICU patients were reviewed, representing over 48,000 total monitoring hours from 77 ICU beds. The median monitoring time for included cases was 63 hours (interquartile range [IQR] 28 to148 hours). As shown in Table 3.1, 54.2% of the patients were male, 61.0% were white, and 43.0% had some level of cognitive impairment. The sample had a mean age of 59.6 ($\pm$17.0) years and a BMI of 28.1 ($\pm$8.2) kg/m^2. Most of the patients (42.7%) were admitted to the neurosurgical unit. In terms of treatments, 40.3% of the patients required mechanical ventilation and 7.4% had either a VAD, a temporary pacemaker, or a permanent pacemaker.

The cohort triggered a total of 159,771 respiratory type alarms. Of these alarms. 88.2% were RR parameter alarms and 11.8% were apnea alarms. Of the 140,975 RR parameter alarms, 82.5% (n=131,827) were for high parameter violations. The median number of RR parameter alarms (i.e., high and low) per patient was 114 (IQR = 45 to 286). The median number of apnea alarms per patient was 11 (IQR = 2 to 41). The median total time a patient was in an alarm per monitoring time was 40.6 (IQR = 13.5 to 113.6) minutes. Each individual alarm lasted a median of 10 (IQR = 4 to 20) seconds (Table 3.1).

Number, Type, Duration, and Characteristics of Alarm Types

For each type of RR alarm, the demographic and clinical characteristics, ICU type, supportive therapies and alarm characteristics are listed in Tables 3.2 and 3.3 Because of the high variability in the number of alarms, the median alarm values are reported and were used in the statistical analysis. Based on the univariate analysis, tremor and smoking status were not included in the multivariate model because they demonstrated weak associations ($p > 0.15$) with all of the alarm types.

High Parameter Alarms

Of the 461 patients in the cohort, 454 had at least one of the 131,827 high parameter alarms (Table 3.2). For these alarms, median ICU monitoring time was 64 (IQR = 28 to 149) hours; median number of alarms per patient was 94 (IQR = 37 to 265); median time that a patient was in this alarm was 19.6 (IQR = 6.2 to 57.7) minutes; and the median alarm duration was 8 (IQR = 4 to 18) seconds. As shown in Table 3.3, in the bivariate analysis, patients with cognitive impairment, patients on mechanical ventilation, patients without a VAD or pacemaker, and those who were in the cardiac or neurological ICUs had a higher number of high parameter alarms. After controlling for monitoring time, the only characteristic that remained significant in the multivariate analysis was being in the cardiac or neurological ICU compared to the medical surgical ICU (Table 4).

Low Parameter Alarms

Of the 461 patients in the cohort, 359 had at least one of the 9,148 low parameter alarms (Table 3.2). For these alarms, median ICU monitoring time was 73 (IQR = 43 to 182) hours; median number of alarms per patient was 6 (IQR = 1 to 21); median time that a patient was in this alarm was 2.6 (IQR = 0.2 to 18.9) minutes; and the median alarm duration was 20 (IQR = 8 to 87) seconds. As shown in Table 3.3, in the bivariate analysis, BMI, patients on mechanical ventilation, patients without a VAD or pacemaker, and those who were in the cardiac or neurological ICU had a higher number of low parameter alarms. After controlling for monitoring time, the characteristics that were significant in the multivariate analysis were: being male, being on a mechanical ventilator, not having a VAD or a pacemaker, and being in the cardiac or neurological ICU compared to the medical surgical ICU (Table 3.4).

Apnea Alarms

Of the 461 patients in the cohort, 381 had at least one of the 18,796 apnea alarms (Table 3.2). For these alarms, median ICU monitoring time was 71 (IQR = 40 to 173) hours; the median number of alarms per patient was 11 (IQR = 2 to 41); median time that a patient was in this alarm was 4.3 (IQR = 0.6 to 18.2) minutes, and the median alarm duration was 16 (IQR = 10 to 29) seconds. As shown in Table 3.3, in the bivariate analysis, patients on mechanical ventilation, patients without a VAD or a pacemaker, and those who were in the cardiac or neurological ICU had a higher number of apnea alarms. After controlling for monitoring time, the characteristics that were significant in the multivariate analysis were, being male, not having a VAD or a pacemaker, and being in the cardiac or neurological ICUs compared to the medical-surgical ICU (Table 3.4).

DISCUSSION

This study is the first to perform a detailed characterization of RR parameter and apnea alarms in a large sample of 461 ICU patients. Of the 2,558,760 alarms identified, over a one month period in the UCSF Alarm study,[6] 159,771 (6.2%) were RR alarms. This total number of alarms equates with an average of 67 RR alarms/bed/day. As expected, the duration of monitoring was associated with a higher median number of all of the IP-derived RR alarms evaluated and was controlled for in all of the multivariate analysis. The number of RR parameter alarms far exceeded the number of apnea alarms, with high parameter RR alarms accounting for 82.5% of these alarms.

Compared to the two studies that evaluated the number of RR parameter alarms,[9, 10] our rates are higher. In the study of 4,104 medical-surgical patients,[10] of the 612 RR parameter alarms identified, 113 of the high parameter and 499 of the low parameter alarms were determined to be true. In the other study of 317 general ward patients who were evaluated over 780.7 hours,[9] of the 17,243 RR alarms identified, 4,104 (24%) were high and 13,139 (76%) were low parameter alarms.[9] In this study, the vast majority of the high parameter alarms (3,404; 82%) occurred when the alarm setting was >30 bpm. However, the number of alarms decreased substantially when the alarm parameters were changed to 35 bpm (608; 15%), >40 bpm (80; 2%), and >45 bpm (12; 0.29%). Similarly, the vast majority of the low parameter alarms occurred when the alarm setting was <12 to >10 bpm (12,300; 94%) versus 0.22% when the alarm setting was <7 bpm. While our absolute number of RR parameter alarms was higher because of our longer monitoring time, our findings are consistent with those of Burgess and colleagues.[9] In our study, our high parameter alarm setting (≥30 bpm) was the most sensitive, similar to the Burgess study. Therefore, it is not surprising that we found very high rates for this particular alarm. Furthermore, our low RR parameter setting was 5 bpm, which was found to be the least sensitive setting in the Burgess et al., study. In terms of clinical characteristics, of the 461 patients with high RR parameter alarms, 42.9% had cognitive impairment. In the bivariate analysis, those patients with cognitive impairment had a median of 126 high parameter alarms compared to 77 in patients without cognitive impairment. This increased number of high parameter alarms may be related to motion artifact that disrupts the IP signal quality.

The parameter alarm settings used in our ICUs (≥ 30 bpm and ≤ 5 bpm) are consistent with the current standard of care.[20] However, based on our findings and those of Burgess et al.,[9] a high parameter alarm setting of ≥30 bpm may be too sensitive and cause high rates of false alarms with resultant alarm fatigue. Additional research is warranted to determine the optimal alarm setting to reduce the number of high parameter alarms and maintain patient safety. An equally important consideration is that the use of the IP method to detect RR is problematic. For example, the IP method can over count respirations in some patients. Figure 3.3 illustrates a patient from our study who was mechanically ventilated with positive end-expiratory pressure (PEEP) whose respiratory rate was doubled during PEEP therapy. These findings suggest that this problem cannot be solved by simply changing alarm settings and/or skin electrode.

In terms of apnea alarms, compared to two previous studies,[10, 14] our total median number of alarms (i.e., 11 per patient per day) was higher (i.e., 2.6 per patient per day true; 4.7 per patient per day false[10] and 2.7[14]). Because we did not annotate our RR alarms, comparisons of true versus false apnea alarms cannot be examined. Our apnea alarm rate is higher than that reported by Gross et al., most likely because we used a more sensitive alarm parameter (≥20 seconds versus >30 seconds).[10] Other factors that may explain differences between the two studies include: different bedside monitors; a sample from a general medical-surgical ward; and shorter total monitoring time (48,000 hours versus 1,040 hours).[10] Studies of apnea type alarms using the IP method are lacking. This omission is problematic given that respiratory compromise (RC), which is associated with both apnea and acute RR changes, increases a patient's mortality rate by over 30%. In addition, the length of hospital and ICU stays for patients with RC are three times longer than for patients without RC.[21] Therefore, a more accurate and reliable measure of apnea and RR may identify high risk patients prior to an acute RC event. Our data and that of others,[10, 14] illustrates important limitations of current IP method to evaluate RR and apnea.

The duration of alarms varied by type. Low parameter alarms had the highest median duration (20 seconds), followed by apnea (16 seconds), then high parameter alarms (8 seconds). Given that all of the alarms were of relatively short duration, this finding suggests that brief changes in the IP signal, most likely due to motion artifact or other signal quality problems caused the alarms. In the UCSF Alarm study,[6] out of the over 2.5 million alarms identified, 32% were technical alarms (i.e., artifact, lead(s) off, lead(s) fail). This finding highlights that signal quality is the most likely cause of RR alarms because the IP signal is dependent on the ECG leads (I or II). This problem may be solved by using a RR alarm delay in the configuration setting because clinically important RR changes are most likely of longer duration. Having a trend report of RR, would be even more useful to be able to identify patients with developing RC who would benefit from interventions. However, the identification of high-risk patients with the current IP RR alarm algorithm is extremely difficult because of the absolute number of alarms generated that leaves the true alarms buried among false alarms. Of note, prior studies found a reduction in ECG arrhythmia alarms by using daily skin electrode changes.[22-24] While this strategy was used with the goal of reducing false arrhythmia alarms, it is possible that this intervention may improve IP signal quality and reduce RR type alarms. However, this hypothesis warrants investigation in a future study.

The time spent in alarms varied by RR alarm type. High parameter alarms had the highest duration (19.6 minutes), followed by apnea (4.3 minutes), then low parameter (2.6 minutes). This finding suggests that nurses will spend most of their time evaluating high parameter alarms. Current IP algorithms are limited in that only one ECG lead is used (typically lead I or II), which is pre-determined as a default setting. While the nurse has the ability to change to the ECG lead used for IP measurement, these extra steps disrupt workflow and require multiple adjustments to the monitor. Algorithms that can automatically search for the best available ECG lead(s) may improve this problem.[6] In addition, the IP method used for detection of RR may be enhanced by incorporating already existing ECG waveforms. Our group and others have evaluated the use of ECG derived methods to identify abnormal respirations associated with sleep disordered breathing.[25-30] The next phase of this research will be to determine if a combined ECG RR method, that uses both IP signals and ECG waveforms, compared to the IP method improves RR detection and reduces the number RR alarms.

We hypothesized that demographic and/or clinical characteristics associated with ECG arrhythmia alarms would be associated with RR alarms. In the multivariate analysis, for all alarm types, length of ICU monitoring time was associated with a higher number of alarms. While this finding is not surprising, it highlights a susceptible group of patients who can exacerbate alarm fatigue in nurses. Alarm management strategies should incorporate an evaluation of each patient's length of stay and an evaluation of skin electrode integrity to ensure an optimal IP signal. In addition, across all three alarms, compared to a medical-surgical ICU, being in a cardiac or neurological ICU was associated with higher alarm rates. The reason for this finding is not entirely clear. In our prior studies,[6, 15, 16] cardiac ICU patients had a higher number of arrhythmia alarms, primarily due to ECG abnormalities (i.e., bundle branch block, ventricular paced rhythms and low amplitude QRSs). However, given that these ECG abnormalities would not impact the IP signal, they are not the likely source of RR alarms. The association between the neurological unit and the higher number of alarms may be related to changes in cognitive functioning in patients with neurologic conditions. Given that 42.7% of the patients in our study who were in the neurological unit had documentation of a cognitive impairment supports this hypothesis.

In terms of low parameter alarms, being male, being on mechanical ventilation, and not having a VAD or a pacemaker were associated with a higher median number of alarms. In terms of apnea alarms, being male and not having a VAD or a pacemaker were associated with a higher median number of alarms. It is worth noting that for both low parameter and apnea alarms, being male was associated with these two types of alarms that are mechanically similar (i.e., slow or no breathing). In a study of 40 healthy men and women ages 18 to 70,[31] compared to women, men accumulated more fluid in their torso after changing from a lying to a supine position due to fluid shifting from the legs to the chest cavity. Because progressive accumulation of fluid in the lungs decreases bioimpedance, the IP signal would be impacted.[32, 33] Moreover, in a study of 403 patients hospitalized for acute coronary syndrome,[32] internal thoracic impedance decreased by 16.4% (95% CI=−12.2% to −20.6%; $p<.0001$) from the baseline level prior to the onset of lung rales (i.e., an increase in fluid in the lungs). To build on this concept, that excess fluid in the lungs can impact the IP signal, several studies found that critically ill patients who are mechanically ventilated accumulate excess fluid as a result of fluid resuscitation during their acute illness.[34-36] Given these findings, excess accumulation of fluids in the thorax is a likely explanation for the association between the increased number of low parameter and apnea alarms in males and those treated with mechanical ventilation. From a clinical perspective, one has to question whether these alarms were simply due to changes in the IP signal, or whether these patients had true episodes of bradypnea and/or apnea. However, we did not annotate our alarms as true or false. Therefore, we are not able to confirm this hypothesis. Of note, the above studies may explain why patients in the cardiac ICU, who are more likely to have heart failure and associated fluid accumulation, had more low parameter and apnea alarms compared to patients in the medical-surgical ICU.

With regards to VAD and/or ventricular pacing, we hypothesized that these devices would impact the IP signal due to electrical interference, which is associated with false arrhythmia and technical alarms (artifact, lead(s) off/fail).[37]
However, we found the opposite in our study. This finding should be interpreted with caution because of the small number of patients with VADs and/or ventricular pacemakers in our sample.

We were somewhat surprised that no associations were found between BMI and any of the RR alarms. We hypothesized that a higher BMI would influence the IP signal and result in a higher number of RR alarms. This hypothesis was based on a study that found that higher BMIs altered gas exchange due to decreases in chest wall compliance[38] and that patients with higher BMIs have RR that ranged from 15.3 bpm to 21 bpm.[39-42] Given that the mean BMI in our study was in the overweight range and 60.3% of the patients were obese may explain why our hypothesized association was not supported.

Limitations

Several limitations warrant consideration. While we provide new information on the number and types of RR parameter alarms, we did not annotate for true and false alarms. Because only one vendor's monitor was used, we do not know if our findings generalize to other manufacturers. The study's retrospective design did not allow us to evaluate how alterations in alarm settings would impact the number of alarms identified. Despite these limitations, our study represents the most comprehensive evaluation of RR parameter and apnea alarms in a consecutive sample of ICU patients.

Implications for Practice and Research

This study highlights the high occurrence rates for RR parameter and apnea alarms and suggests that these alarms make a significant contribution to overall alarm fatigue. This study confirms that high parameter alarms are more prevalent in the ICU setting. In addition, it provides new information on demographic (being male) and clinical (being on mechanical ventilation, not having a VAD or pacemaker, length of ICU monitoring time, being in a cardiac or neurological ICU) characteristics that are associated with higher alarm rates. To decrease the number of RR alarms, clinicians need to evaluate the most appropriate alarm settings, as well as the demographic and clinical characteristics identified in this study. In addition, clinicians should aim to reduce the patients' length of ICU stay through vigorous and adequate management of their condition(s).

Additional research is warranted to reduce the number of RR alarms. Prospective studies are warranted that compare visual assessments of RR with those obtained using IP. In addition, bioengineers need to develop new algorithms that can be incorporated into ECG monitors with increased sensitivity and specificity to detect RR. In addition, studies are warranted that compare accuracy of the IP method to a combined method that incorporates IP with ECG waveforms and the myogram for the evaluation of RR parameter and apnea alarms. Finally, examining whether daily skin electrode changes would reduce RR alarms by ensuring optimal IP signal quality should be explored.

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Table 3.1 Demographics, clinical, and hospital characteristics and number of respiratory type alarms in 461 intensive care unit patients

Characteristics	Total sample n = 461
Demographic characteristics	n (%)
Age (mean ± SD, in years)	59.6 ± 17.0
BMI (mean ± SD)	28.1 ± 8.2
Gender	
Male Female	250 (54.2) 211 (45.8)
Race	
Asian Black/African American Native Hawaiian or Pacific Islander White Patient unable to state due to acute illness or not recorded in the EHR	76 (16.5) 35 (7.6) 8 (1.7) 281 (61.0) 61 (13.2)
Characteristics hypothesized to influence respiratory alarms	
Current smoker	71 (15.4)
Documented cognitive impairment	198 (43.0)
Tremor	36 (7.8)
Type of intensive care unit	
Cardiac (16 beds) Medical-Surgical (32 beds) Neurological (29 beds)	83 (18.0) 181 (39.3) 197 (42.7)
Use of supportive therapy	
Mechanical ventilation	186 (40.3)
Ventricular assist device or pacemaker	34 (7.4)
Median monitoring time in hours (IQR)	63 (28-148)
Total number of respiratory type alarms Parameter (high or low) High (≥30 bpm) Low (≤5 bpm) Apnea (≥20 seconds no breathing)	159,771 140,975 (88.2% of total) 131,827 (82.5% range 1 – 5852) 9,148 (6% range 1 – 455) 18,796 (11.8% or total) (range 1 – 1208)
Median monitoring time per patient (IQR)	63 (28-148) hours
Median number of total alarms per patient (IQR)	136 (55-349)
Median number of parameter alarms (high and low) per patient (IQR)	114 (45-286)
Median number of apnea alarms (IQR)	11 (2 - 41)
Median time a patient was in alarms (IQR) per monitoring time	40.6 (13.5 - 113.6) minutes
Median duration of alarms (IQR)	10 (4-20) seconds

Abbreviations: BMI = body mass index; EHR = electronic health record; bpm = breaths per minute; IQR = interquartile range; SD = standard deviation; VAD = ventricular assist device

Table 3.2 Demographics, clinical, and hospital characteristics of the intensive care unit patients who had one or more apnea or parameter type alarms.

Characteristics	Patients with a high RR parameter alarm (≥30 bpm) n = 454	Patients with a low RR parameter alarm (≤ 5 bpm) n = 359	Patients with any apnea alarm (no breaths for ≥20 seconds) n = 381
Demographic Characteristics			
Age (years, mean (SD)	59.5 (16.9)	59.4 (16.8)	59.5 (17.0)
BMI (kg/m^2, mean (SD)	28.1 (8.2)	27.9 (7.3)	27.7 (7.2)
Gender (n (%))			
Male	245 (54.0)	200 (55.7)	217 (57.0)
Female	209 (46.0)	159 (44.3)	164 (43.0)
Race (n (%))			
Asian	72 (15.9)	52 (14.5)	60 (15.7)
Black/African American	34 (7.5)	30 (8.4)	31 (8.1)
Native Hawaiian or Pacific Islander	52 (11.5)	40 (11.1)	42 (11.0)
White	267 (58.8)	214 (59.6)	223 (58.5)
Patient unable to state due to acute or not illness or not recorded in the EHR	29 (6.4)	23 (6.4)	25 (6.6)
Characteristics Hypothesized to Increase Respiratory Type Alarms			
Current smoker (n (%))	69 (15.2)	60 (16.7)	59 (15.5)
Documented cognitive impairment (n (%))	196 (43.2)	169 (47.1)	177 (46.5)
Tremor (n (%))	36 (7.9)	30 (8.4)	33 (8.7)
Intensive care unit type (n (%))			
Cardiac (16 beds)	82 (18.1)	70 (19.5)	73 (19.2)
Medical surgical (32 beds)	176 (38.8)	134 (37.3)	144 (37.8)
Neurological (29 beds)	196 (43.2)	155 (43.2)	164 (43.0)
Supportive Therapies			
Mechanical ventilation, n (%)	176 (38.8)	158 (44.0)	167 (44.0)
Ventricular assist device or pacemaker	33 (7.3)	27 (7.5)	32 (8.4)
Median ICU monitoring time in hours (IQR)	64 (28-149)	73 (43-182)	71 (40-173)
Total number of alarms	131,827 (82.5%)	9,148 (6%)	18,796 (11.8%)
Median number of alarms (IQR)	94 (37-265)	6 (1-21)	11 (2-41)
Median time in alarms (IQR, minutes)	19.6 (6.2-57.7)	2.6 (0.2-18.9)	4.3 (0.6-18.2)
Median duration of alarms (IQR, seconds)	8 (4-18)	20 (8-87)	16 (10-29)

Abbreviations: BMI = body mass index; bpm = breath per minute; ICU = intensive care unit; EHR = electronic health record; IQR = interquartile range; kg = kilograms; m^2 = meters squared; SD = standard deviation.

Table 3.3 Occurrence of high and low parameter and apnea alarms by demographic and clinical characteristics and supportive therapy and intensive care unit type.

Characteristic	n	Median number of high RR parameter alarms (≥30 bpm)	p-value	Median number of low RR parameter alarms (≤5 bpm)	p-value	Median number of apnea alarms (≥20 bpm)	p-value
Age							
18 - 34	42	75 (31 - 169)	0.07	6 (0 - 21)	0.33	11 (2 - 29)	0.58
35 - 49	86	80 (20 - 318)		6 (1 - 26)		10 (1 - 42)	
50 - 64	138	120 (37 - 305)		5 (1 - 24)		13 (3 - 50)	
65 - 79	136	83 (42 - 247)		6 (1 - 16)		10 (2 - 41)	
80+	59	127 (51 - 236)		4 (1 - 16)		12 (2 - 38)	
Sex							
Male	250	88 (34 - 263)	>0.99	6 (1 - 20)	0.18	12 (3 - 41)	0.06
Female	211	97 (38 - 265)		5 (1 - 22)		9 (1 - 42)	
BMI (kg/m^2)							
<25	181	81 (35 - 205)	0.67	6 (1 - 16)	0.02*	10 (3 - 30)	0.13
25 - 30	131	95 (39 - 230)		4 (1 - 18)		11 (2 - 44)	
30+	144	130 (40 - 328)		7 (1 - 30)		14 (2 - 54)	
Race							
White	269	94 (35 - 260)	0.65	6 (1 - 20)	0.50	12 (2 - 42)	0.63
Non-White	192	96 (38 - 282)		5 (1 - 22)		11 (2 - 40)	
Smoking status							
Current smoker	71	97 (34 - 324)	0.92	4 (1 - 14)	0.15	8 (2 - 27)	0.28
Non-smoker	390	94 (38 - 245)		6 (1 - 22)		12 (2 - 43)	
Cognitive impairment							
Yes	198	126 (43 - 344)	<0.001*	8 (1 - 28)	0.30	18 (4 - 54)	0.11
No	263	77 (35 - 198)		4 (0 - 16)		7 (1 - 30)	
Tremor							
Yes	36	143 (65 - 302)	0.56	6 (1 - 16)	0.46	11 (4 - 32)	0.18
No	425	92 (37 - 264)		5 (1 - 21)		11 (2 - 42)	
Mechanical ventilation							
Yes	178	146 (51 - 483)	<0.001*	14 (4 - 42)	<0.001*	25 (7 - 64)	<0.001*
No	283	73 (34 - 196)		2 (0 - 10)		6 (1 - 26)	
VAD or pacemaker							
Yes	34	191 (66 - 622)	<0.001*	6 (2 - 20)	0.18	19 (3 - 42)	0.03*
No	427	92 (37 - 247)		6 (1 - 21)		11 (2 - 41)	
Intensive care unit							
Cardiac	83	150 (44 - 488)	<0.001*	6 (1 - 21)	<0.001*	21 (3 - 60)	<0.001*
Medical surgical	181	95 (37 - 206)		4 (0 - 16)		8 (1 - 39)	
Neurological	197	84 (37 - 230)		8 (2 - 41)		12 (2 - 35)	

Abbreviations: BMI = body mass index; bpm = breath per minute; EHR = electronic health record; IQR = interquartile range; kg = kilograms; m^2 = meters squared; RR = respiratory rate; VAD = ventricular assist device * Tukey's honestly significance difference post hoc analysis for low RR; BMI (<25) - (30 +) differ at p=0.018. No difference between BMI of (< 25) - (25-29) p=0.82; and (25-29) - (30 +) p=0.13

Table 3.4 Multiple regression analysis for number of respiratory parameter (high and low) and apnea alarms among intensive care unit patients.

Characteristic	B (SE)	p-value	IRR	95% CI	p-value
High Respiratory Rate Parameter Alarms (≥30 bpm)					
Monitoring time in ICU (hours)	0.75 (0.05)	<0.001*	-	-	
Age (units of 10 years)	0.06 (0.03)	0.07	1.06	1.00 - 1.12	
Male	0.08 (0.11)	0.44	1.09	0.88 - 1.34	
BMI (kg/m^2, reference = <25) 25 – 30 30+	 0.06 (0.12) 0.14 (0.12)	 0.62 0.26	 1.06 1.15	 0.83 - 1.37 0.90 - 1.47	
Cognitive impairment	0.17 (0.12)	0.14	1.19	0.94 - 1.50	
Mechanical ventilation	-0.01 (0.12)	0.96	0.99	0.79 - 1.26	
Ventricular assist device or pacemaker	-0.16 (0.22)	0.48	0.86	0.57 - 1.34	
Unit (Reference = Medical Surgical) Cardiac Neurological	0.48 (0.17) 0.31 (0.11)	0.004* 0.008	1.62 1.36	1.17 - 2.24 1.08 - 1.70	0.0002* 0.012*
Low Respiratory Rate Parameter Alarms (≤5 bpm)					
Monitoring time in ICU (hours)	0.47 (0.06)	<0.001*	-	-	
Age (units of 10 years)	-0.04 (0.04)	0.36	0.96	0.88 - 1.04	
Male	0.38 (0.15)	0.01*	1.46	1.09 - 1.96	
BMI (kg/m^2, reference = <25) 25 – 30 30+	 -0.08 (0.18) 0.21 (0.18)	 0.64 0.22	 0.92 1.23	 0.65 - 1.31 0.87 - 1.75	
Cognitive impairment	0.13 (0.16)	0.45	1.13	0.83 - 1.56	
Mechanical ventilation	0.48 (0.17)	0.005 *	1.62	1.16 - 2.27	
Ventricular assist device or pacemaker	-1.06 (0.31)	0.001*	0.35	0.19 - 0.67	
Unit (Reference = Medical Surgical) Cardiac Neurological	 0.96 (0.23) 0.56 (0.16)	 <0.001* <0.001*	 2.60 1.76	 1.67 - 4.16 1.26 - 2.43	 0.0001* 0.004*
Apnea (≥20 seconds of no breathing)					
Monitoring time in ICU (hours)	0.50 (0.06)	<0.001*	-	-	
Age (units of 10 years)	0.02 (0.04)	0.58	1.02	0.94 - 1.12	
Male	0.41 (0.15)	0.005 *	1.51	1.13 - 2.03	
BMI (kg/m^2,Reference = <25) 25 - 30 30 +	 0.00 (0.18) 0.21 (0.17)	 >0.99 0.22	 1.00 1.24	 1.00 - 1.04	
Cognitive impairment	0.33 (0.17)	0.05	1.40	1.02 - 1.91	
Mechanical ventilation	0.24 (0.17)	0.17	1.27	0.93 - 1.77	
Ventricular assist device or pacemaker	-0.75 (0.31)	0.02 *	0.47	0.26 - 0.91	
Unit (Reference = medical surgical) Cardiac Neurological	 0.91 (0.23) 0.51 (0.16)	 0.001* 0.002*	 2.46 1.66	 1.59 - 3.89 1.19 - 2.29	 <0.0001* 0.0025*

Abbreviations: BMI = body mass index; bpm = breath per minute; CI = confidence interval; ICU = intensive care unit; EHR = electronic health record; IQR = interquartile range; IRR = incident rate ratio; kg = kilograms; m^2 = meters squared; SD = standard deviation; SE = standard error. *Tukey's honestly significance difference post hoc analysis. For high RR alarms: No difference between neuro and medical-surgical; cardiac and neuro differ at p = 0.02; cardiac and medical-surgical differ at p<0.01; For Low alarms and Apnea RR: There are no differences between Medical-Surgical and Neurological unit but Cardiac and neurological is different at p<0.01; p = 0.0025.

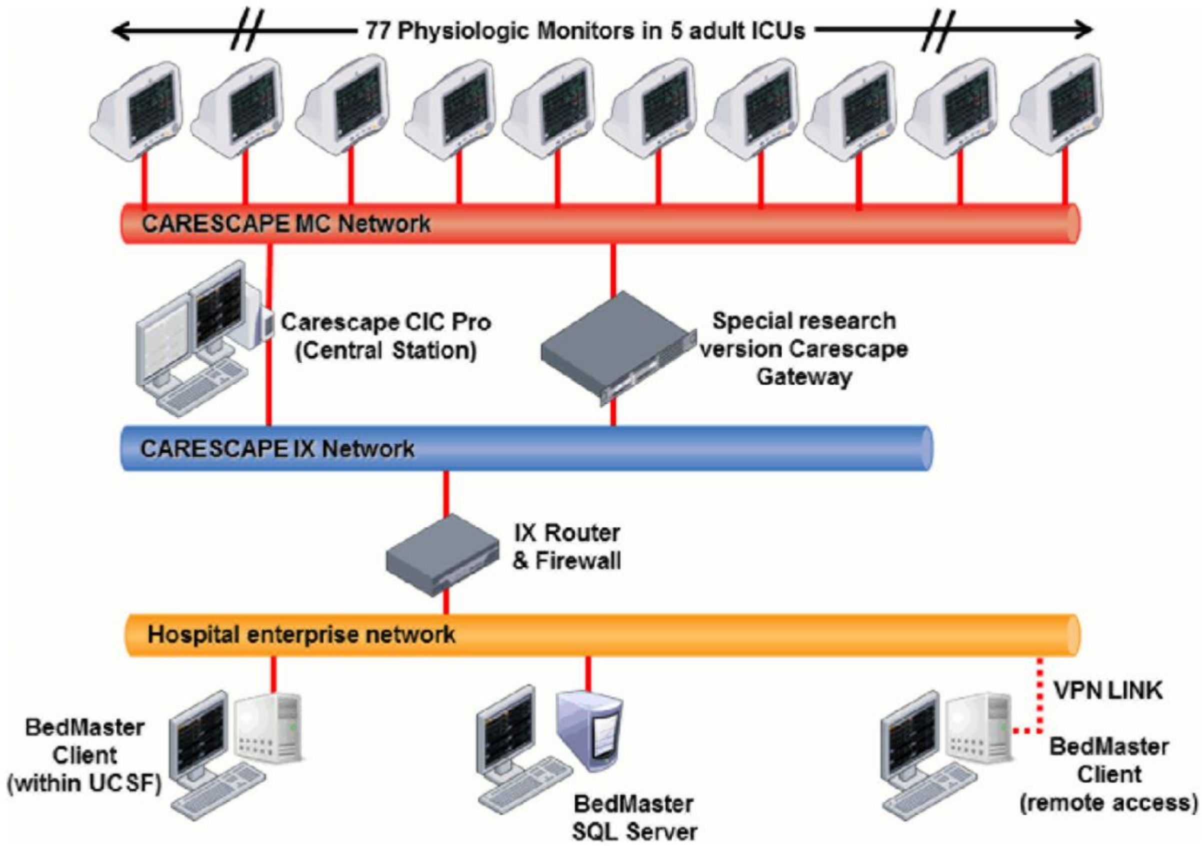

Figure 3.1 Hospital infrastructure used to capture and store all physiologic monitor waveform and alarm data automatically. Permission: reprinted with permission from [6] doi:10.1371/journal.pone.0110274.g002

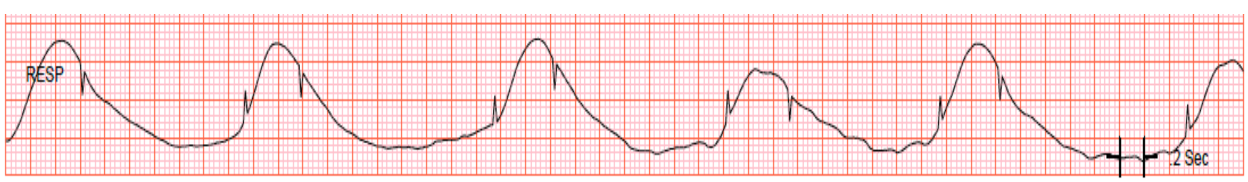

Figure 3.2 Impedance pneumography (IP) respiratory waveform (RESP) generation. Note the upward flag on the inspiratory waveform and the downward flag on the expiratory waveform, which denotes a single breath.

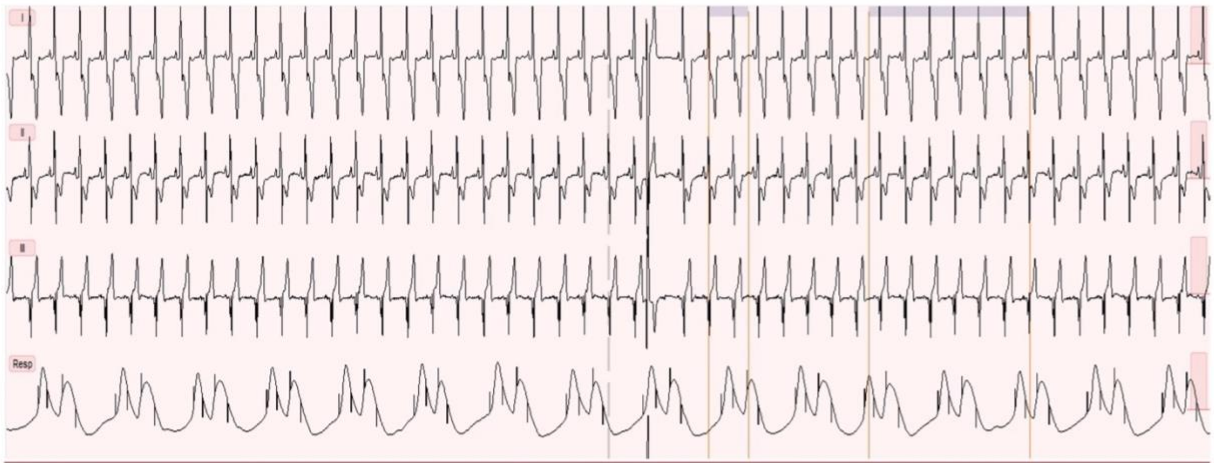

Figure 3.3 Illustrates double counting of respiratory rate (RR) in an intensive care unit patient treated with mechanical ventilation and positive end-expiratory pressure (PEEP). Shown are leads I, II, III and the RESP (respiratory) waveforms. Note the second RR just after the ventilator breath caused by PEEP, which doubles the RR in this patient from 16 breaths per minute to 32 breaths/minute.

CHAPTER 4

AGREEMENT OF RESPIRATORY RATE MEASUREMENT BETWEEN A COMBINED ELECTROCARDIOGRAPHIC DERIVED METHOD AND IMPEDANCE PNEUMOGRAPHY

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 using IP method, contributing to alarm fatigue in clinicians. While newer RR algorithms that use electrocardiographic features (i.e., QRS, heart rate and myogram) hold promise, they have not been compared to the IP method.

Purpose: This study was designed to examine the agreement between the IP and combined-electrocardiographic derived respiration (combined-EDR) method for normal RR; low RR ($\leq$5 breaths per minute (bpm)); and high RR ($\geq$30 bpm).

Methodology: This secondary analysis used data from the University of California, San Francisco (UCSF) Alarm Study. A total of 100 intensive care unit (ICU) patients were included and were distributed by RR group as follows: (1) normal RR (n=50 patients; 25 from the low RR group and 25 from high RR group); (2) low RR (n=50 patients); and (3) high RR (n=50 patients). Bland-Altman analysis was used to evaluate the agreement between the two methods.

Results: For normal RR, a significant bias difference -1.00 $\pm$ 2.11 (95% confidence interval [CI] -1.60 to -0.40) and limits of agreement (LOA) of -5.13 to 3.13 was found between the two methods. For low RR, a significant bias difference of -16.54 $\pm$ 6.02 (95% CI: -18.25 to -14.83) and a 95% LOA of -28.33 to - 4.75 were found. For high RR, a significant bias difference of 17.94 $\pm$ 12.01 (95% CI: 14.53 to 21.35) and 95% LOA of -5.60 to 41.48 were found.

Conclusion: The combined-EDR method had good agreement with the IP method for measurement of normal breathing. However, for the low RR, the combined-EDR method was consistently higher than the IP RR. For the high RR, the combined-EDR method was always lower than the IP RR. This study should be replicated in a larger sample and include confirmation with visual assessment (VA).

Key words: impedance pneumography; electrocardiographic derived respiratory rate; respiratory rate; intensive care unit; physiologic monitoring

INTRODUCTION

Impedance pneumography (IP) is the current device-driven method that is used to measure respiratory rate (RR) in hospitalized patients.[1] Abnormal RR (e.g., tachypnea, bradypnea) are indicators of respiratory instability, respiratory compromise, and often the first indication of impending respiratory arrest and/or the need for rescue intubation in hospitalized patients.[2-5] However, identifying these acute changes can be delayed and/or missed if RR assessments are not obtained often and with a high degree of accuracy. Therefore, assessing RR at more frequent intervals and more accurately may lead to earlier detection of clinical deterioration and appropriate intervention(s) to improve patient outcomes. To achieve this goal, the ideal method to assess RR should be continuous, accurate, sensitive, specific, non-invasive, and affordable. The use of physiologic data that can detect respiration signals, that is already collected in hospitalized patients, would offer important advantages since these data could be easily integrated into existing clinical care devices.

The algorithm used for the IP method is based on the ratio of alternating electrical currents measured using electrocardiographic (ECG) lead wires and skin electrodes on the torso. Of note, the IP method does not use ECG signals for RR calculation, it only uses the lead wires and skin electrodes to deliver the alternating currents used for the IP method. The major advantages of the IP method include that it is safe and simple to use and is integrated into current physiologic monitoring devices. However, signal interruptions (i.e., poor skin electrode contact, skin electrodes fall off), patient movement and cardiac artifact can affect the accuracy of IP RR.[6, 7] In addition, the various components of the IP method (e.g., lead wires, cables) can be sources of IP measurement error.[8] As a result, the IP method is prone to frequent RR alarms that contribute to alarm fatigue in clinicians.[6, 8-12] In one comprehensive study in 461 ICU patients (n=77 beds),161,931 RR alarms (i.e., high and low parameter and apnea) were found during the one-month study period or 79 RR alarms/bed/day.[6] While the alarms were not annotated in this study, 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, no 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 problematic, 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 interval).[13] While the EDR method is not currently available for use in the hospital setting, this method has numerous advantages.[13] For instance, like IP, the EDR method is non-invasive; uses already existing data from bedside ECG monitoring devices; and RR assessments are done continuously.[14] One study showed that because ECG QRS amplitude changes were highly correlated with tidal volume changes during breathing, they may be more suitable for calculating RR.[13] The EDR method has been used to identify abnormal respirations associated with sleep disordered breathing.[15-20] 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 was found to be 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).[13] What has not been tested, is a method that combines all of these signals (i.e., ECG, IP, and the myogram), which together may improve the accuracy of RR assessment.

While visual assessment (VA) of RR is the gold standard method, a great deal of interest exists in device driven methods, like IP and EDR, for hospital-based monitoring because RR changes can occur quickly and could be missed by using VA alone. The VA method can interrupt nurse's workflow because they must stop care activities and carefully count full breaths for one minute, which can be difficult in patients who are talking, not able to follow instructions and/or cooperate. One study found that inaccurate RR readings were measured during routine patient activities such as talking, turning, or moving in bed.[21]

In a prior study of VA of RR,[22] RR was often estimated, guessed, omitted, or simply copied from a previous assessment.[22] In another study,[23] nurses reported intentionally or unintentionally omitting RR assessments over 90% of the time. In another study that examined 62 patients with 1,597 unique vital signs recorded,[24] only one RR assessment was recorded per day, while multiple recordings of blood pressures (5/day); heart rate (4.4/day); and temperature (4.2/day) were documented (all $p<0.001$).[24]

Surprisingly, only four studies have compared VA, IP, and EDR assessment of RR.[25-28] Importantly, none of these studies compared all three methods in the same patient. In the three studies that compared the VA and IP methods,[25, 26, 28] the upper and lower limits of agreement (LOAs) between the two methods were extremely poor. In the only study that compared the VA and EDR methods,[27] significant differences in RR were found between the two methods. In addition, using Bland Altman analyses, the LOAs between the two methods were poor. The scatter plots showed that VA RR centered around RR of 18, 20, and 22 breath per minute (bpm). In contrast, the EDR RR were more variable. These findings suggest that VA of RR cluster around “normal” values that clinicians commonly use. In contrast, the EDR method captured dynamic RR variations, which suggest that the EDR method may be more reliable.

Other studies have evaluated the EDR method. One study found that the IP method had 95% LOAs that were within –5.6 to 5.2 bpm with a bias of -0.2 bpm. The authors noted that for four of the algorithms evaluated, those that used ECG waveform data performed better than the IP only algorithm.[14] In a second study,[13] three different RR methods were compared to RRs using an air flow sensor. The three approaches included: an EDR only method; an electromyogram method; and an RSA method. The accuracy of determining RR ranged from 80% to 90% depending on the performance measure used in this study. Of note, the authors concluded that a combination of these different methods may improve the overall performance of RR assessment.[13]

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. While the EDR method, which relies on the R-to-R intervals, appears to be an improvement over IP, this method lacks accuracy in older patients because of its dependence on heart rate variability, which tends to be fixed in older adults. In addition, this method is less reliable in patients with atrial fibrillation and those taking certain cardiac medications (e.g., beta-blockers). Hence, because hospitalized patients have many of these characteristics, the generalizability of an ECG only method may be limited.

An alternative approach to the limitations identified for the individual algorithms discussed above,[13, 14] would be to create an algorithm that combines all of the available physiologic signals (i.e., IP, ECG and the myogram), to create a “combined-EDR method.” Recent work from our research team has evaluated the accuracy of this method to detect Cheyne-Stokes respiration in healthy adults, hospitalized patients with acute coronary syndromes, and ICU patients.[18, 19] In one study, periodic breathing ($\geq$3 consecutive cycles of hyperpnea/hypopnea without apnea) and Cheyne-Stroke respirations ($\geq$3 consecutive cycles of hyperpnea/hypopnea with apnea) were compared between healthy community-based adults and patients hospitalized with a cardiac diagnosis. Of the hospitalized cardiac patients, those with acute coronary syndrome had 1.6 times more periodic breathing episodes and 7.3 times more Cheyne-Stroke respiration episodes than healthy community-based participants.[18]

In the current study, we build on this work by examining agreement between the IP method and a combined-EDR method in a group of adult ICU patients. The purpose of this study, in a group of 100 ICU patients were to: (1) examine agreement between the IP and combined-EDR method for normal RR; (2) examine agreement between the IP and combined-EDR method for low RR ($\leq$5 bpm); and (3) examine agreement between the IP and combined-EDR method for high RR ($\geq$30 bpm). These parameters were used because they were the standard default alarm settings for all the intensive care units in our hospital and wanted to evaluate the standard our research aim with the standard practice at the facility.

METHODS

Research Design and Setting

This study is a secondary analysis using data from the University of California, San Francisco (UCSF) Alarm Study, the methods of which have been published.[6] Briefly, 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 the following physiologic data from each ICU monitor: all available waveforms (e.g., ECG, arterial BP, central venous pressure, intracranial pressure, SpO2); vital signs (e.g., heart rate, non-invasive BP, RR); alarm settings (i.e., crisis, warning, advisory and technical); as well as audible and inaudible alarms. The physiologic data passed securely through the hospital's Enterprise network via a research network (CARESCAPE Gateway; GE Healthcare, Milwaukee, WI) to a secure server in our research lab for off-line analysis. 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.

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 IP parameter alarms (< 5 bpm) and another 50 patients who had one or more high IP parameter alarms (> 30 bpm). The parameter alarms were selected based on the current alarm configuration used in our bedside ICU monitors. From this sample of 100 patients, we randomly selected a subgroup of 25 patients from each group (i.e., 25 patients with low parameter alarms and 25 patients with high parameter alarms) for the normal RR comparisons. While we use the term “normal” breathing it should be noted that in some of these ICU patients their RR was consistently tachypneic (i.e., >20 bpm). Therefore, a normal RR (i.e., >12 bpm and < 20 bpm) could not be used for comparisons.

IP Method

Evaluation of electrical impedance in body tissues is a common technique that measures variability in tissue volume based on the measurement of resistance of alternating currents (AC) as electricity travels through a given material.[29] In the hospital setting, the IP method uses skin electrodes placed on the torso for ECG monitoring. It should be noted that while ECG lead wires and skin electrodes are used for the IP method, the ECG waveforms are not used to calculate RR. Rather, the ECG device (through lead wires attached to skin electrodes) directs a very small amount of electrical current into the patient’s body to measure electrical impedance.[7, 30] Depending on the manufacturer, one or two of the limb leads are used to detect amplitude differences of the injected current.[31]

During inspiration, as the chest expands, resistance to the flow of an electrical current increases, which increases impedance. Alternatively, during expiration, impedance decreases as air leaves the lungs. 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 electrodes.[7, 31] The difference in amplitude of the injected current during inspiration (chest expands; impedance rises) and expiration (impedance falls) is displayed as an IP waveform on the bedside physiologic monitor. This computer algorithm puts an artificial flag on the IP waveform when inspiration is identified (upward flag) and a downward flag when expiration is identified. In addition to the IP waveform, a numeric RR value is displayed on the bedside monitor.

Combined-EDR Method

The combined-EDR method was created by biomedical engineers in the UCSF Center for Physiologic Research. The algorithm uses all of the following signals to derive a RR: ECG waveforms; IP signals; and the myogram. The following features are used to calculate the RR, namely: (1) *R-to-R intervals,* (2) *the QRS area,* (2) *the ECG baseline*, (3) the IP *waveform,* (4) the *plethysmograph from the oxygen saturation sensor (SpO_2),* and (5) *the myogram*. At least two of these parameters, with high quality signals, must be present for the combined-EDR method to generate a RR.

ECG signals: The algorithm uses *R-to-R interval changes*. Breathing causes slight changes in heart rate that can be detected as RSA (i.e., increased heart rate with inspiration; decreased heart rate with expiration). While RSA is observed in young healthy people, the heart rate tends to become more fixed, thus less variable, with age and co-morbidities (e.g., heart failure, diabetes).[13, 32] 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,* that is, the sum of all of the QRS complexes from all available ECG leads is used. Breathing causes slight changes in the QRS morphology (width and amplitude) that can be used for RR assessment. For example, during inspiration and expiration the heart moves relative to the ECG skin electrodes on the body surface, that are at fixed locations on the chest. The amplitude (height) and width (duration) of each waveform that make up each QRS complex (i.e., Q, R, and S wave) are measured and used in the algorithm.

In addition to these ECG features, the combined-EDR method incorporates the IP and $Sp0_2$ waveforms as well as the myogram signal. The latter uses the ECG skin electrodes during inspiration and expiration to measure both chest muscle and diaphragm effort during breathing. The combined-EDR algorithm examines all of these features simultaneously to generate a RR. Therefore, it is important to note that in the absence of a good quality signal from any two of the aforementioned parameters, a combined-EDR RR will not be generated.

Data Acquisition for IP versus Combined-EDR Method Comparisons

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 same time that comparisons were done between the IP and combined-EDR methods. To optimize the workflow in the CER-S tool, the following steps were taken: multi-day recordings were formatted in 24-hour periods from midnight to midnight; data were compressed using a loss-less proprietary algorithm, which varied between three and four-fold rate, depending on the input signals; and all of the data were de-identified. As mentioned above, the IP parameter alarms for the low and the high RR analyses were compared to the combined-EDR RR. Figure 4.1(a and B) illustrates a screen shot of the CER-S software tool that was used to identify the IP RR parameter alarms for comparison with the combined-EDR method.

Combined-EDR Data: Physiologic data signals from the primary study (i.e., ECG, IP signal, SpO_2, myogram) were processed with the combined-EDR algorithm. The entire ICU monitoring period was processed and a combined-EDR RR was generated every 30 seconds. These data were exported into a common separated value (.csv) file in order to perform the comparisons of RR between the two methods. The de-identified IP RR data (normal, low, and high RRs) were viewed in the CER-S software tool and the corresponding times of the combined-EDR RR were used for the comparisons. Both RR values were required to be within two minutes of each other. Two reviewers independently collected the data. The reviewers met weekly to compare their results and overall inter-rater agreement was $\geq$95%.

Data Analysis

Descriptive statistics were generated for each of the RR groups. For each group, the agreement between the two methods was evaluated using Bland-Altman analysis.[33] 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 RR.

The Bland-Altman analysis reports the estimated difference between the two measurements with 95% LOAs around the estimate (mean difference of ±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 v.27 (IBM Corporation, Armonk, NY). The Bland-Altman analysis was performed using R v4.0.0 and BlandAltmanLeh package v0.3.1 statistical software.[33-35]

RESULTS

Demographic and Clinical Characteristics

The demographic and clinical characteristics of the groups are presented in Table 4.1. The time differences between the two RR measurements that were used for comparison was <40 seconds for 90% of the data. The results for each type of RR that were compared: (1) normal RR; (2) low RR; and (3) high RR are summarized below.

Normal RR: The average age of the 50 patients in the normal RR group (Table 4.1), was 60.14 (±18.01) years, 52% were male and 66% were white. Forty percent had documented cognitive impairment, 18% were current smokers, 42% had mechanical ventilation, and 40% were admitted to the neurological ICU. Their median monitoring time (IQR) was 1.11 (0.23 – 29.13) hours.

Low RR: 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. Their median monitoring time (IQR) was 1.52 (0.33 – 10.67) hours.

High RR: 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. The median monitoring time (IQR) was 0.99 (0.18 – 29.1) hours.

Bland Altman Analysis

The results of the Bland Altman analysis are presented in Table 4.2. The Bland-Altman analysis examined the agreement between the two RR methods by estimating the mean difference and producing 95% LOAs.[33] The scatter plots and Bland-Altman plots are shown in Figure 4.2 (A, B, and C), that illustrate the distribution and agreement between the two methods for normal, low, and high RR.

Normal RR: For normal RR, a significant bias difference of -1.00 + 2.11 (95% CI -1.60 to -0.40) and 95% LOA of -5.13 to 3.13 were found (Table 4.2). The LOA showed that the RR were within three and five bpm. Figure 4.2 (2A) shows the scatter plot and Bland-Altman analysis for 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: For low RR, a significant bias difference of -16.54 + 6.02 (95% CI: -18.25 to -14.83) and 95% LOA of -28.33 to - 4.75 were found (Table 4.2). As illustrated on the scatterplot (Figure 4.2) 2B, the combined-EDR RR was always higher than the IP RR. Note that the points on the Bland-Altman plot are essentially distributed in two lines. This pattern is seen because nearly all of the IP values for RR were 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: 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 4.2). Figure 4.2 (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 than the IP RR, with the exception of one comparison. A test of a regression line through the points did not indicate a significant slope (p=0.87).

DISCUSSION

This study is the first to evaluate the level of agreement between two algorithm-based methods to measure RR, the IP method and a novel combined-EDR algorithm that combines signals from the IP, myogram, and ECG waveforms in a group of ICU patients. Good agreement was found between the two methods for the normal RR. An inverse agreement was found between the two methods for both the low and high RR comparisons. For low RR, the combined-EDR algorithm was consistently higher than the IP method. For high RR, the combined-EDR algorithm was consistently lower as than the IP method in all but one patient. Given the high level of agreement for normal RR, these findings suggest that the combined-EDR algorithm may be more accurate when measuring low and high RR.

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. Figure 4.3 (A and B) are examples of tracings from two patients in our study, one with tachypnea and one with bradypnea. Based on our findings, it is reasonable to conclude that the IP and combined-EDR methods are comparable when measuring RR within the normal range (12 to 20 bpm) and in a small subset of patients with tachypnea and bradypnea. However, because we did not simultaneously assess RR using VA method, these findings warrant confirmation using the gold standard. Despite this limitation, based on our findings for normal RR, albeit in a small sample of ICU patients, we were able to compare the IP to the combined-EDR for both low and high RRs with some level of confidence.

For low RRs, compared to the IP method the RR using the combined-EDR method was consistently higher. This finding is consistent with prior studies that found that the majority of low IP RRs are false[6, 36] due to low frequency signals, which saturate the ECG leads with noise and fail to capture the impedance signal.[37] As illustrated in Figure 4.1 (A), low frequency IP signals can increase the number of false IP RRs.[38, 39] In addition to low frequency signals, shallow breathing can be misinterpreted by the IP method as a low RR and contribute to false alarms.[39] Several studies have examined why low RR readings occur when using the IP method. In one study,[40] cardiac oscillations (i.e., "small waves produced by heartbeats, which are superimposed on the pressure and flow signals at the airway opening") interfered with the IP signal and led to false low RR calculations.[36] In healthy people, several factors can impact the IP signal including: hemodynamic properties,[41] RSA,[42] blood pressure,[43] stroke volume,[44] pulmonary vascular resistance,[42] pulmonary blood flow,[45] and lung volume.[46] These factors are attenuated in patients with cardiac and/or respiratory diseases, that are common in hospitalized patients. Moreover, the spatial distribution of the IP signal in the thorax is not fixed or static. Instead, it likely undergoes variations due to respiration that may affect the generation of IP respirations. Accurate and reliable identification of low RR is extremely important in hospitalized patients who are susceptible to this problem because of the receipt of medications that compromise breathing (e.g., sedatives, opioids), sleep disordered breathing, or acute respiratory compromise.[5, 18, 47] The combined-EDR algorithm, that uses multiple physiologic signals to generate a RR appears to be an improvement over the IP method. However, as with the normal RR measures examined in this study, the combined-EDR method requires further validation in a larger sample along with comparisons to VA.

When comparing the IP method to the combined-EDR method for high RR, in nearly every comparison the combined-EDR RR was lower. Figure 4.4 illustrates the outlier patient with an IP RR of 69 and a combined-EDR RR of 15 bpm. This patient provides an example of non-respiratory motion and cardiac artifact, that can influence the accuracy of IP RR.[8, 37, 41] This finding supports previous studies that identified that both motion artifact[7, 8, 37] and cardiac artifact from aortic blood flow can be measured using IP and lead to false high RR.[41, 48] Because the combined-EDR method uses a combination of several different physiologic signals (i.e., R-to-R intervals, QRS area, ECG baseline, IP waveform, Sp_2O, and the myogram) this method minimizes the number of false high RRs. Our data suggest that the combined-EDR method may substantially reduce high parameter alarms associated with motion and cardiac artifact.

A noteworthy finding from our study was the number of patients with a RR above the physiologic upper limit of “normal” (i.e., <20 bpm). The scatterplot in Figure 4.2 (2C), shows that 22 patients had a RR >20 bpm, which represent 88% of the 25 ICU patients in this group. With one exception, the combined-EDR was consistently lower than the IP method. Figure 4.5 illustrates the one outlier patient who had an IP RR of 32 and a combined-EDR RR of 50. The IP RR appears to be accurate despite motion artifact. It is not known which of the physiologic signals were driving the combined-EDR calculation of RR. However, this example suggests that the combined-EDR may calculate high RR in some patients. Future studies need to determine whether refinements are needed to the combined-EDR algorithm for high RR.

Limitations

Several limitations warrant consideration. While we provide new information on the agreement between the IP RR method and a novel multi-signal algorithm for RR measurement, we did not use the gold standard of VA to compare the two methods. Additionally, because we examined only one monitoring vendor, our findings may not generalize to other monitoring manufacturers. The study’s retrospective design did not allow us to evaluate the patient scenarios or alarm adjustments made by clinicians, that would add important context to our findings. It must also be noted that the parameters we used for our study may have been too low or high in a non-critical care setting. However, since our findings for parameter alarms were high, and suggestive of tachypnea in the ICU, a replication of the study must include the alarm parameters that are lower than our <5 and >30 bpm for the low and high RR. Despite these limitations, this study is the first to examine a novel physiologic-based algorithm strategy that uses existing data from bedside monitors to determine RR.

CONCLUSION

RR alarms are common in the ICU. In one study in 461 ICU patients, there were 161,931 RR alarms (apnea and high/low parameter) were found during the one-month study period or a total of 79 alarms/bed/day.[6] The problem that is created by the high number of alarms is that true RR events (low or high RR) go unrecognized because they are buried among false alarms. This problem is described as alarm fatigue (i.e., desensitization to alarms). In an effort to reduce alarm fatigue it is standard practice for hospitals to use wide RR parameter limits (i.e., $\leq$5 bpm and $\geq$30 bpm) as a way to reduce RR alarms. Findings from our study suggest that these settings, may miss important true RR changes that require intervention to avert respiratory compromise. While confirmation of our findings is warranted, our data suggest that the combined-EDR method is comparable to the IP method with regards to normal RR, was consistently higher than low IP RR, and almost always lower than the higher IP RR. This latter finding is of significant interest, since we found that tachypnea was common in our ICU sample.

Implications for Practice and Research

Low RR using the IP method may be influenced by low frequency signals, which can cause inaccurate low RR. However, low RR can occur with shallow breathing, which would be of clinical significance in hospitalized patients at risk for respiratory compromise. High RR, using the IP method, can be caused by cardiac artifact. However, we found RRs often exceeded the upper limit of normal (i.e., $<$20 bpm) in the ICU sample we examined, which may suggest tachypnea is common. This study should be replicated in a larger sample and include confirmation with VA.

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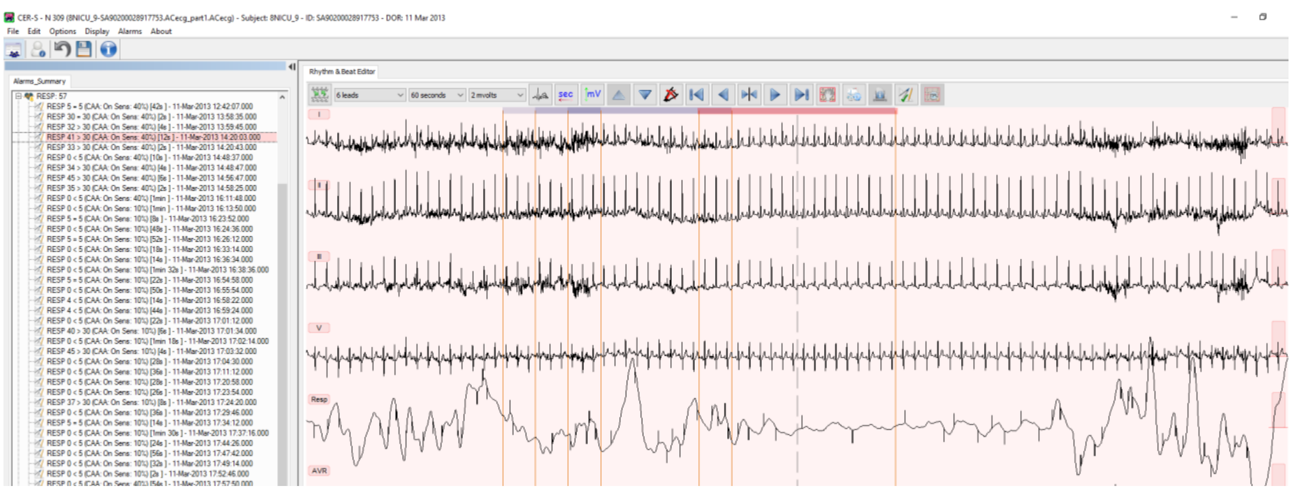
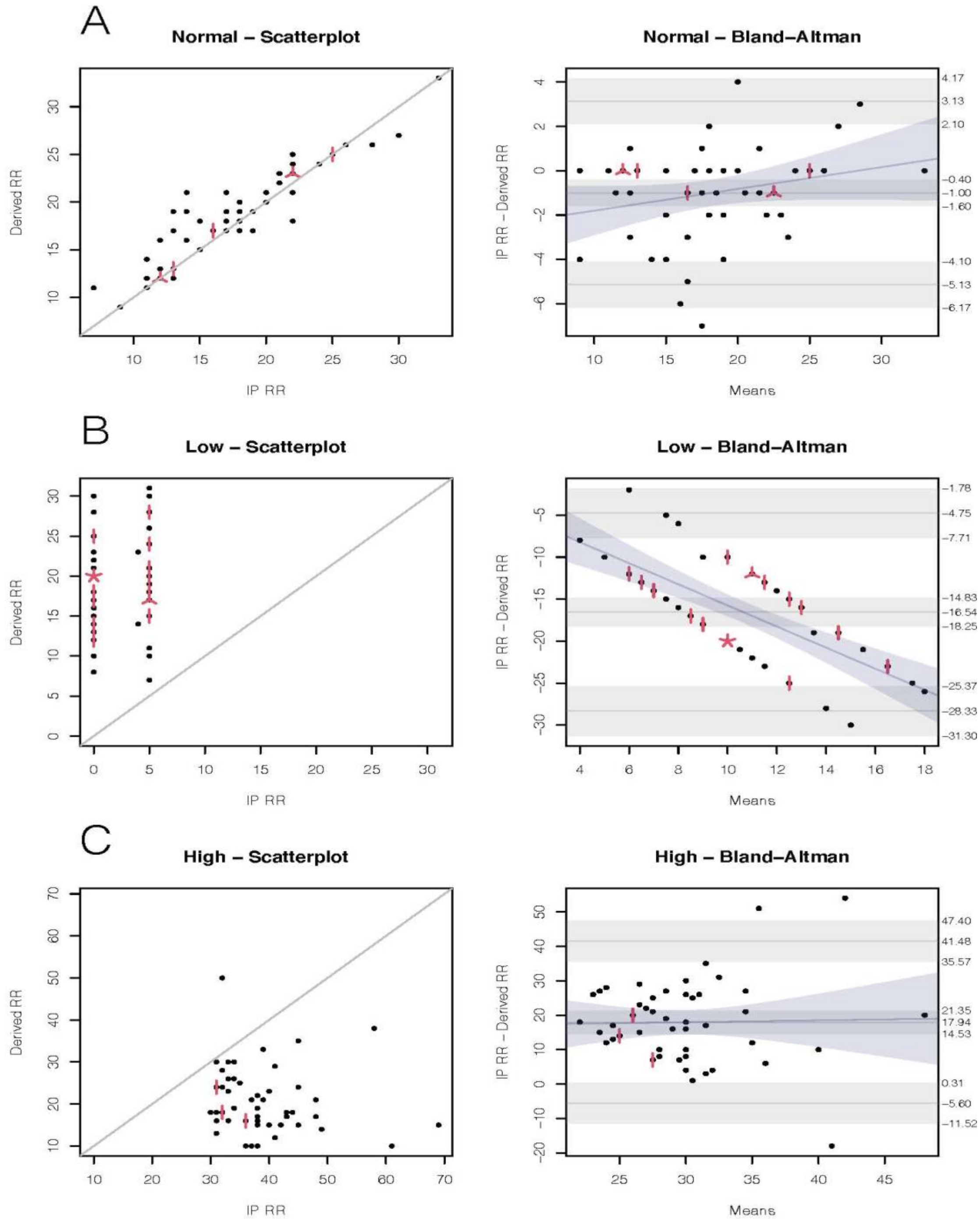
Figure 4.1 Illustrates the continuous electrocardiographic recording suite (CER-S) software program used to identify impedance pneumography (IP) respiratory rate (RR) parameter alarms for comparison to the combined-electrocardiographic derive respiration method. The IP waveform is labeled as Resp in the figures below.

A. The left side of the figure shows IP RR parameter alarms during this patient monitoring period. The highlighted IP alarm (RESP 0< 5) was for a low parameter RR alarm. The panel to the right of the alarm shows a one-minute period of ECG signals (leads I, II, II and V) as well as the IP waveform (Resp). The spikes at the very end of the IP tracing are upward and downward flags added to the IP waveform to show inspiration and expiration.



B. The left side of the figure shows IP RR parameter alarms during this patient monitoring period. The highlighted IP alarm (RESP 41 > 30) was for a high parameter RR alarm. The panel to the right of the alarm shows a one-minute period of ECG signals (leads I, II, II and V) as well as the IP waveform (Resp). The IP waveform has motion artifact throughout the tracing with upward and downward flags in some parts of the tracing.



Figures 4.2. (2A, 2B, and 2C) Scatterplots (left) and Bland-Altman plots (right) for normal, low and high respiratory rate (RR) comparing 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 there is more than one value at this measure. For example, a three-armed sunflower plot indicates that there are three individual values at this one location.

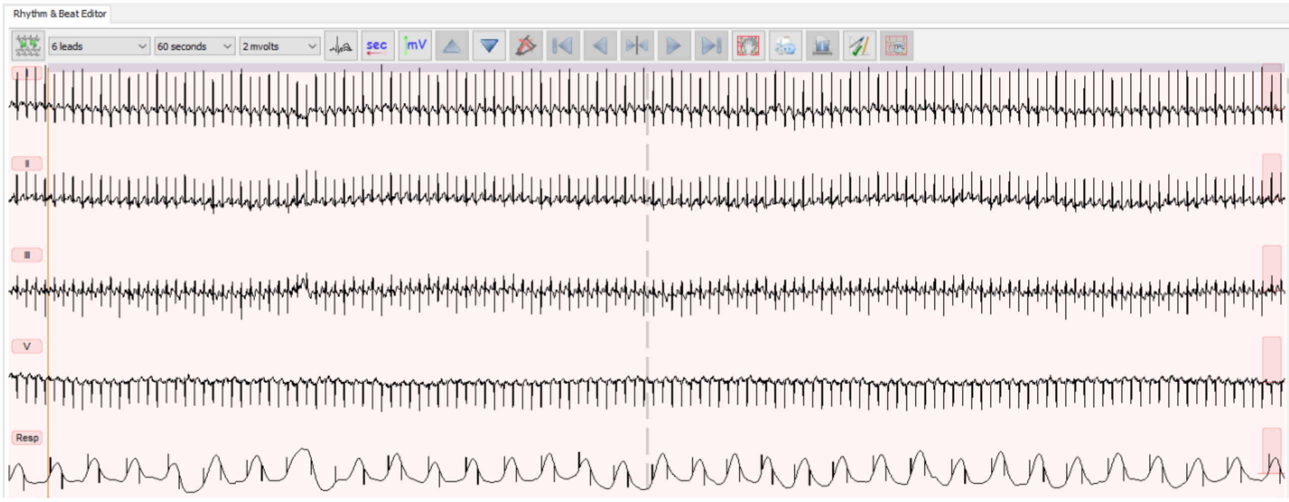
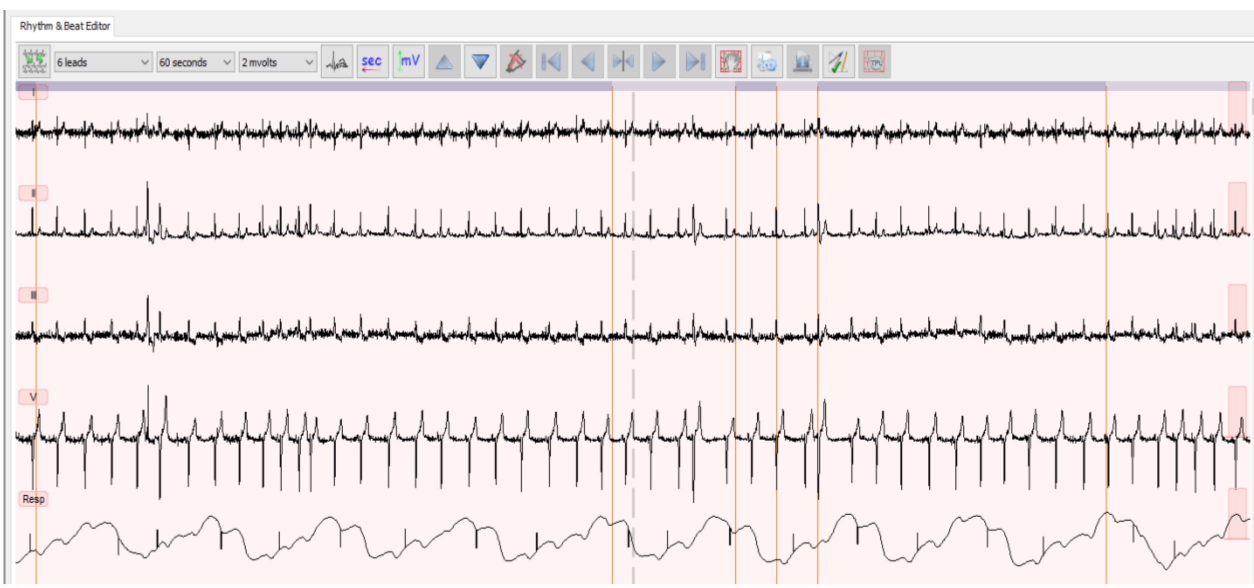


Figure 4.3 Illustrates the respiratory rate (RR) measured using impedance pneumography (IP) in two different intensive care unit patients during tachypnea (A) and bradypnea (B). Shown are one minute time periods with electrocardiographic (ECG) leads I, II, II, and V (V1) and the IP waveform. The IP waveform has an upward flag during inspiration and a downward flag during expiration.

A. Patient with an IP RR of 33 breath per minute (bpm). The combined-EDR method RR was 33 bpm. This patient has a heart rate of 150 beats/minute, which when combined with the tachypnea suggests this that patient is in acute distress.



B. Patient with an IP RR of 9 bpm. The combined-EDR method RR was 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/minute, with pre-mature atrial complexes and a short run of supra-ventricular tachycardia.

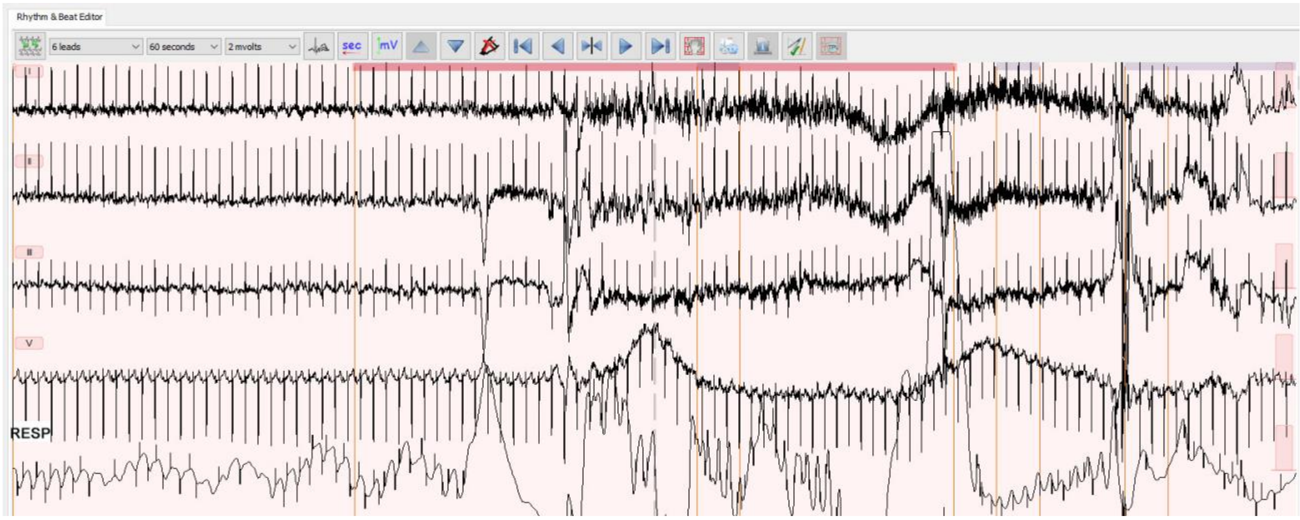


Figure 4.4 Illustrates a high respiratory rate (RR) measured using impedance pneumography (IP) in an intensive care unit patient. The IP RR was 69 breath per minute (bpm), the combined-electrocardiographic RR was 15 bpm. Shown is a one-minute time period with ECG leads I, II, II, and V (V1) and the IP waveform (RESP). The IP waveform has upward flags and downward flags calculated using the IP waveform, which in this case is contaminated with both cardiac and motion artifact.

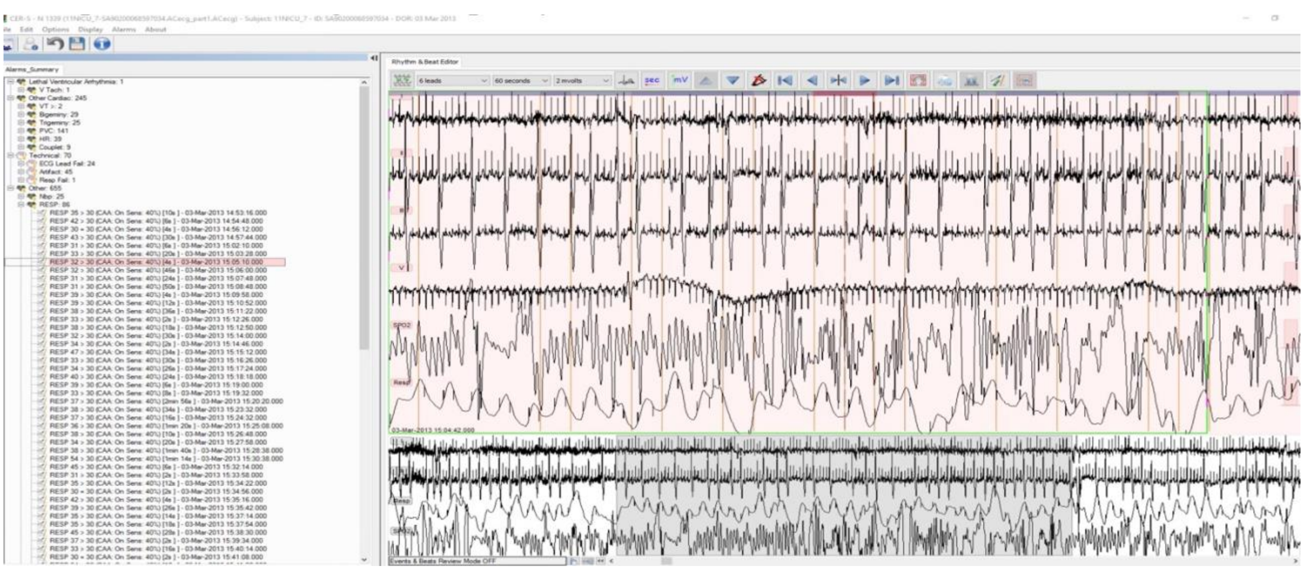


Figure 4.5 Illustrates a high respiratory rate (RR) measured using impedance pneumography (IP) in an intensive care unit patient. The IP RR was 32 breath per minute (bpm), the combined-electrocardiographic RR was 50 bpm. Shown is a one-minute time period with ECG leads I, II, II, and V (V1) and the IP waveform (RESP). The IP waveform shows the outlier patient with high RR (50 bpm) compared to the low IP RR (32 bpm), which in this case is contaminated with both cardiac and motion artifact.

Table 4.1 Demographic and clinical characteristics of 100 intensive care patients.

Characteristics	**Normal RR** n = 50	**Low RR** (≤5 bpm) n = 50	**High RR** (≥30 bpm) n = 50
Demographic characteristics			
Age (mean ± SD, in years)	60.14 ± (18.01)	61.80 ± 16.89	60.86 ±16.13
BMI (mean ± SD, kg/m^2)	26.72 ± 4.73	26.84 ± 4.83	29.50 ± 9.79
	n (%)	**n (%)**	**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			
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)
Median monitoring time in hours (IQR)	1.11 (0.23 – 29.13)	1.52 (0.33 – 10.67)	0.99 (0.18 – 29.1)

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

Table 4.2 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.

CHAPTER 5

CONCLUSION

Conclusion

In hospitalized patients, respiratory rate (RR) assessment is an essential indicator of respiratory instability and/or compromise and is often the first indication of impending respiratory arrest.[1, 2] While visual assessment (VA) is the non-invasive standard of care used to assess the RR and breathing characteristics (i.e., depth, effort, skin color), studies show that this method is plagued with inaccuracies because clinicians often omit, repeat, or even guess a patient's RR.[3-7] In addition, VA of RR is performed intermittently (e.g., every 30 minutes with vital signs), which means that acute changes can be missed. Therefore, accurate and frequent assessment of RR is important for identifying high risk patients. Impedance pneumography (IP) is the current device-driven method used to measure RR in hospitalized patients. However, RR alarms are common using this method and contribute to alarm fatigue in clinical staff. Newer RR algorithms that use electrocardiographic features (i.e., QRS, heart rate and myogram) hold promise, but to date have not been compared to the IP method. Alternative methods using non-invasive device-driven techniques, such as impedance pneumography (IP) and Electrocardiographic (ECG) - Derived Respiration (EDR) + myogram, have been examined.[8,9,10] However, only the IP method is currently available in hospital settings that use ECG monitoring. Importantly, the IP method is riddled with frequent alarms, which can lead to alarm fatigue in nurses.[8, 9] Therefore, this dissertation research was designed to addresses the gaps in knowledge regarding IP generated alarms and test a new algorithm that combines several physiologic waveforms to measure RR namely: IP; ECG waveforms (i.e., R-R-interval, QRS area) and the myogram. Of note, the combined-EDR method uses physiologic signals that are currently available in bedside physiologic monitors; hence, no new equipment or devices are needed to measure RR with our algorithm.

The first aim of this dissertation research was to systematically review the literature regarding respiratory rate (RR) measurement methods in hospitalized patients by comparing the accuracy, strength, and limitations of VA to two methods that use physiologic data namely: IP and EDR. Of the 78 studies identified, full manuscripts for 23 studies were reviewed. While designed to be a systematic review that compared the accuracy, strengths, and limitations of VA, IP, and EDR methods to measure RR, only four studies were identified.[11-14] Of note, none of these studies compared all three methods in the same sample of patients. In terms of accuracy, when Bland-Altman analyses were performed, the upper and lower levels of agreement were extremely poor for both the VA and IP and VA and EDR comparisons. Several study limitations contribute to these significant discrepancies including relatively small sample sizes, lack of inter-rater reliability assessments, cross-sectional designs, and heterogeneity in patient samples. Given the clinical need to have accurate counts of RR in critical care settings,[15,16,17] additional research is warranted on the use of both the IP and EDR methods. Future studies need to develop rigorous research protocols that include: training and evaluation of the inter-rater reliability of the research staff who perform the VA of RR; power calculations to determine appropriate sample sizes; pre-specified criteria for acceptable LOA; conducting experiments to determine acceptable and clinically meaningful LOA for various clinical conditions (e.g., tachypnea, bradypnea, normal RR); and a critical evaluation of outliers (e.g., changes in patient's position during data collection). Given the paucity of research and the fact that no studies have compared all three methods in the same patients, no definitive conclusions can be drawn about the accuracy of these three methods.

The second aim was a secondary data analysis from the University of California San Francisco (UCSF) Alarm Study.[18] The objectives of this study were to examine RR alarms by type (i.e., parameter high/low and apnea), duration and for associations with patients' demographics and clinical characteristics. One strength of our study in 461 ICU patients was that three adult intensive care units (ICU) were included (i.e., cardiac, medical-surgical, and neurological). We examined nearly 160,000 IP RR alarms during more than 48,000 hours of ECG monitoring. The vast majority (88.2%) of all types of RR alarms were parameter alarms. Of the RR parameter alarms, over 80% were high parameter alarms. Using multivariate analysis, after controlling for the length of ICU monitoring, alarm occurrence rates were associated with: type of ICU unit; the use of mechanical ventilation; and the lack of a ventricular assist device or pacemaker. Male gender was associated with low parameter and apnea alarms. Patients treated in the cardiac and neurological ICU were more likely to have a higher median number of all types of RR alarms. This study shows that there are a very high number of RR IP alarms, specifically 67 RR alarms/bed/day and illustrates that RR alarms, especially high parameter RR alarms, make a significant contribution to overall alarm fatigue. In addition, it provides new information on characteristics that are associated with higher alarm rates.

In the final aim of this dissertation research, we examined RR agreement between the IP and the combined-EDR method for normal RR; low RR ($\leq$5 bpm); and high RR ($\geq$30 bpm). Data used in this study also came from the UCSF Alarm Study.[8. 9,10] This study is the first to evaluate the level of agreement between two algorithm-based methods to measure RR, the IP method and a novel combined-EDR algorithm that combines signals from the IP, myogram, and ECG waveforms in a group of ICU patients. Good agreement was found between the two methods for the normal RR. An inverse agreement was found between the two methods for both the low and high RR comparisons. For low RR, the combined-EDR algorithm was consistently higher than the IP method. For high RR, the combined-EDR algorithm was consistently lower as than the IP method in all but one patient. Our data suggest that the combined-EDR method is comparable to the IP method with regards to normal RR, was consistently higher than low IP RR, and almost always lower than the higher IP RR. This latter finding is of significant interest, since we found that tachypnea was common in our ICU sample.

Implication for Clinical Practice

Based on a systematic review, whether visual assessment of respiratory rate was better or worse than impedance pneumography or electrocardiographic-derived respiration for adult patients in the intensive care unit was inconclusive.

High and low respiratory parameter alarms were more common than apnea alarms during impedance pneumography for adult patients in the intensive care unit, particularly for patients with high respiratory rates. In addition, focused consideration should be given to male patients who tended to have a higher number of occurrences of low respiratory parameter and apnea alarms as compared to female patients.

Depending on the respiratory rate (normal, low or high) of adult patients in the intensive care unit, the combined electrocardiographic derived method varied in agreement with the impedance pneumography method for respiratory rate measurement. Evaluating patient scenarios or alarm adjustments made by clinicians would add important context to the study findings. For example, Low frequency signals may influence respiratory rate using the impedance pneumography method. Cardiac artifact may be a major contributor to high respiratory rate using the impedance pneumography method RRs often exceeded the upper limit of normal (i.e., <20 bpm) in the ICU – may suggest tachypnea is common.

The high occurrence rates for RR parameter and apnea alarms suggests that these alarms make a significant contribution to overall alarm fatigue. The prevalence of high parameter alarms in the ICU setting and the impact of demographic (being male) and clinical (being on mechanical ventilation, not having a ventricular assist device or pacemaker, length of ICU monitoring time, being in a cardiac or neurological ICU) characteristics that are associated with higher alarm rates must be noted by clinicians. To decrease the number of RR alarms, clinicians need to evaluate the most appropriate alarm settings, as well as the demographic and clinical characteristics identified. In addition, clinicians should aim to reduce the patients' length of ICU stay through vigorous and adequate management of their condition(s).

Low RR using the IP method may be influenced by low frequency signals, which can cause inaccurate low RR. However, low RR can occur with shallow breathing, which would be of clinical significance in hospitalized patients at risk for respiratory compromise. High RR, using the IP method, can be caused by cardiac artifact. However, we found RRs often exceeded the upper limit of normal (i.e., $\geq$20 bpm) in the ICU sample we examined, which may suggest tachypnea is common.

Recommendation for Future Research

The systematic literature review was inconclusive with regards to the accuracy of the visual assessment, impedance pneumography and electrocardiographic derived methods for measuring respiration. Given the importance of accurate and frequent RR assessment in the fast-paced critical care environment, methods that take advantage of available physiologic data that can detect respiratory signals are warranted. Given the promise, but limitations of both the IP and EDR methods, future research needs to focus on making refinements to these algorithms and/or developing new algorithms that are easily integrated into existing physiologic devices used in the critical care environment. The use of a combined approach that utilizes the strengths of both IP and EDR may provide more precise and accurate results. However, the optimal approach to combining these methods warrants additional investigation. Future studies need to include diverse patient populations with a variety of clinical conditions and employ the most robust analytic methods and evaluate different device monitoring vendors. This line of scientific inquiry will result in a clinically useful method to detect dynamic and acute changes to RR in critically ill patients who may require interventions to avert untoward outcomes.

Finally, examining whether daily skin electrode changes would reduce RR alarms by ensuring optimal IP signal quality should be explored. The study in chapter four revealed that the combined-EDR method was in good agreement with the IP method for normal breathing. However, for low RR compared to the IP method the combined-EDR was consistently higher. The study should be replicated for confirmation of the findings with VA method and other monitoring devices since only one vendor was used in this study and the gold standard was not compared due to the secondary data utilized for this research study.

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