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PATIENT FACING SYSTEMS

Big Data for Clinical Trials: Automated Collection of SpO_2 for a Trial of Oxygen Targets during Mechanical Ventilation

Kevin G. Buell[1] · Jonathan D. Casey[2] · Li Wang[3] · Jonathan P. Wanderer[4,5] · Wesley H. Self[6] · Todd W. Rice[2] · Matthew W. Semler[2]

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Introduction

"Smoothing" is the phenomenon by which manually recorded vital signs are less likely to document values at the extremes compared to automated systems [1]. Intermittent manual recording of the peripheral oxygen saturation (SpO_2) has the potential to inaccurately reflect patients' true physiological states. Taenzer et al. observed that manually charted SpO_2 values were, on average, 6.5 percentage points greater than SpO_2 values collected by automated sampling [2]. Automated high-frequency SpO_2 monitoring may more reliably quantify the incidence and severity of hypoxemia and hyperoxemia.

Intensive Care Units (ICUs) have traditionally been more vigilant in preventing hypoxemia than hyperoxemia, and ICU patients frequently receive more supplemental oxygen than required to maintain normal values for SpO_2 [3]. Hyperoxemia has been associated with worse patient outcomes in observational studies [4, 5], but randomized trials evaluating oxygen saturation targets for mechanically ventilated adults have reported conflicting results [6–9]. These trials have used intermittent recording of SpO_2 by study personnel every 4 to 24 h to assess oxygenation. Automating data collection for SpO_2 has the potential to facilitate the design, conduct, and analysis of pragmatic clinical trials examining SpO_2 targets in mechanically ventilated ICU patients [10].

We developed a technique for automated extraction of large-volume data on SpO_2 values for use in a randomized clinical trial. We aimed to quantify the completeness and density of SpO_2 data among mechanically ventilated patients. We evaluated the reliability of automated extraction of SpO_2 data from pulse oximetry using physician manual review of photoplethysmographic waveforms.

Methods

Study design and oversight

We conducted an observational methodological study using data prospectively collected as a part of the Preliminary Investigation of optimaL Oxygen Targets (PILOT) trial. PILOT is an on-going, cluster-randomized cluster-crossover trial examining higher (96–100%), intermediate (92–96%) and lower (88–92%) SpO_2 targets among mechanically ventilated critically ill patients (Vanderbilt University IRB #171272).

Patient population

Deidentified data from patients receiving invasive mechanical ventilation at Vanderbilt University Medical Center in the medical ICU between July 1st 2018 and December 31st 2019 were included. Data from patients who were pregnant, prisoners, or admitted during 7-day washout periods specified in the design of the PILOT trial were excluded.

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✉ Kevin G. Buell
kevin.g.buell@vumc.org

[1] Department of Internal Medicine, Vanderbilt University Medical Center, 1161 21st Avenue South, D-3100 Medical Center North, Nashville, TN, USA

[2] Division of Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University Medical Center, Nashville, TN, USA

[3] Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN, USA

[4] Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, TN, USA

[5] Department of Biomedical Informatics, Vanderbilt University Medical Center, Nashville, TN, USA

[6] Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, TN, USA

Study outcomes

The primary outcome of interest for this methodological study of automated SpO_2 extraction was the number and frequency of SpO_2 values from the time of intubation until extubation among mechanically ventilated ICU patients. The secondary outcomes were adequacy of plethysmographic waveform on physician manual review and correlation between quality of plethysmographic waveform and values of SpO_2 in a subset of patients.

Electronically-extracted data

In the study ICU, SpO_2 is continuously monitored using Nellcor™ SpO_2 Adhesive Sensors, which report a non-normalized, real-time plethysmographic waveform and SpO_2 values. Plethysmography and SpO_2 are displayed on IntelliVue MP90 bedside patient monitors. SpO_2 values from the IntelliVue monitor are archived every 60 s and exported on a daily basis to our institution's enterprise data warehouse and electronically merged with the study dataset. Plethysmographic waveform from other sources, such as travel monitors, can be used to generate SpO_2 values, which are manually entered into the electronic health record by bedside clinical personnel. Manually entered SpO_2 values were also extracted from the electronic health record and merged with the study dataset, but were unable to be manually reviewed.

Manually-reviewed plethysmography

For a convenience sample of 49 mechanically ventilated patients located in the study ICU during the study period, 24 h of plethysmographic waveform was manually reviewed by a study physician, beginning at 00:00 and ending at 23:59 on that study day. Based on the study physician's clinical impression of the quality of the plethysmographic waveform, the waveform was segmented into intervals and each interval was categorized as: adequate quality; inadequate quality; or absent waveform. The shortest time interval per segment was set at 30 s. The physician was blinded to the values of SpO_2 associated with the plethysmographic waveforms being reviewed.

Statistical analysis

Categorical values were described using numbers and percentages, and continuous variables were described using medians and interquartile ranges. We sought to review more than 1000 h of plethysmographic waveforms, aiming for both a moderate number of patients and a moderate duration of plethysmography for each patient. No formal sample size calculation was performed. All analyses were performed using R version 3.2.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

Data from 1331 mechanically ventilated ICU patients were included in this analysis. Baseline characteristics are presented in Table 1. Median age was 58 years. Fifty-six percent were male, and 79% were white.

SpO_2 values by automated data extraction

Automated data extraction yielded a total of 3,589,705 SpO_2 values. The median number of SpO_2 values per patient during invasive mechanical ventilation was 1336 (IQR 486–3454). The median time from the initiation of invasive mechanical ventilation in the emergency department or ICU to the first recorded SpO_2 value was 8.31 min (IQR 0.97–160.00 min); 2.25 min (IQR 0.40–7.0 min) for patients administratively admitted to the ICU telemetry system prior to initiation of invasive mechanical ventilation and 237 min (IQR 162–312)

Table 1 Patient Demographic ($n = 1331$)

Characteristic	n = 1331
Age, median (IQR), years	58 (45–67)
Male sex, No. (%)	741 (56%)
Race, No. (%).	
White	1047 (79%)
Black or African American	199 (15%)
Asian	18 (1%)
Pacific Islander	2 (0%)
Declined or Unknown	65 (5%)
Location at Study Enrolment, No. (%)	
Emergency Department	442 (33%)
Medical Intensive Care Unit	889 (67%)
Indication for Intubation, No. (%)*	
Altered Mental Status	770 (58%)
Hypoxic Respiratory Failure	479 (36%)
Hypercarbic Hypoxic Respiratory Failure	209 (16%)
Hemodynamic Instability	180 (14%)
Comorbidities	
Coronary Artery Disease	245 (18%)
Chronic Obstructive Pulmonary Disease	241 (18%)
End-Stage Renal Disease	76 (6%)
Heart Failure with Reduced Ejection Fraction	59 (4%)

*Indication for intubation are not limited to one cause, accounting for 1638 indications from 1331 patients

for patients not administratively admitted to the ICU telemetry system before initiation of invasive mechanical ventilation (e.g., intubated in the emergency department). Thereafter, the median interval between SpO_2 measurements was 0.98 min (IQR 0.98–0.98 min), equivalent to 59 s. The median number of minutes between the final SpO_2 value during mechanical ventilation and tracheal extubation was 0.68 min (IQR 0.00–4.80 min), equivalent to 41 s.

Plethysmographic waveform analysis and correlation to $Sp0_2$ values

Twenty-four hours of plethysmographic waveform were reviewed for 49 (3.7%) patient admissions, totaling 1176 h of plethysmographic waveform. It was categorized into 1698 unique SpO_2 intervals: 1120 (95.2%) hours were adequate, 20 h (1.7%) were inadequate and 36 h (3.1%) were absent. The median total time spent per patient during the 24 h reviewed with adequate plethysmographic waveform was 23.5 h (IQR 22.9–23.8 h), 0.2 h (IQR 0.1–0.4 h) for inadequate plethysmographic waveform, and 0.0 h (IQR 0.0–0.6 h) for absent plethysmographic waveform.

Three patients for whom plethysmography waveforms were reviewed were admitted in a "washout period" between study blocks in PILOT and therefore did not have data on clinical characteristics or SpO_2 values for analysis in the PILOT dataset. For one patient, the 24 h period of plethysmographic waveform that was manually reviewed was a time period before the patient's transfer to the ICU for initiation of mechanical ventilation, and therefore did not overlap with SpO_2 values in the PILOT dataset. As a result, forty-five patient encounters had overlapping reviewed twenty-four hours plethysmographic waveforms and automated SpO_2 data extraction, yielding 33,092 SpO_2 values associated with reviewed waveform.

SpO_2 values associated with adequate plethysmographic waveform accounted for 31,754 of 33,092 SpO_2 values (96.0%). A total of 359 of 33,092 SpO_2 values (1.1%) were associated with inadequate plethysmographic waveform and 979 of 33,092 SpO_2 values (3.0%) were associated with periods where plethysmographic waveform was not available from bedside monitors in the study ICU. Six SpO_2 values from inadequate plethysmographic waveform and seven SpO_2 values from absent plethysmographic waveform were 85–88%. Five SpO_2 values from inadequate plethysmographic waveform and two SpO_2 values from absent plethysmographic waveform were less than 85%. In total, a maximum of 20 out of 33,092 SpO_2 values (0.06%) represented episodes of hypoxemia ($SpO_2 \leq 88\%$) associated with inadequate or absent plethysmographic waveform.

The 979 automatically abstracted SpO_2 values during periods when bedside monitors did not record any plethysmographic waveform corresponded to twenty-three separate intervals from 16 patients. Five intervals in four patients accounted for 922 (94.1%) of the SpO_2 values obtained during absent waveform. Of these, three intervals and 604 SpO_2 values originated, not from the ICU monitor for which the absent plethysmographic waveform had been reviewed, but from patient monitors in the operating room during a period in which the patient had been transported out of the ICU to undergo a procedure. The origin of 318 SpO_2 values during the two additional intervals of absent plethysmographic waveform could not be accounted for on manual chart review.

Discussion

This study found that automated extraction of SpO_2 data from bedside monitors and the electronic health record provided a median of 1336 individual SpO_2 values per patient during invasive mechanical ventilation in the emergency department and ICU, at a median frequency of one value per minute. SpO_2 values were available for extraction on average 8.3 min after intubation until 0.68 min (41 s) before extubation. A total of 96% of SpO_2 values were associated with an adequate plethysmographic waveform on physician review, and inadequate or missing plethysmographic waveform was an infrequent cause of spuriously low SpO_2 values.

The use of continuous pulse oximetry has previously been validated as a more reliable method of detecting hypoxemia compared to routine intermittent nursing checks [2]. In the operating room and post-anesthesia care unit, it decreases activation of rescue teams and patient transfer to the ICU for pulmonary reasons [11]. Automatic data collection also eliminates the smoothing effect and is more likely to demonstrate the wide swings in physiological parameters that occur in clinical practice. Smoothing has previously been demonstrated in intermittent recordings of SpO_2 values by ICU nurses compared to automatically archived data [12].

Methods to monitor oxygenation of mechanically ventilated patients in randomized clinical trials have differed [6–9]. Time-weighted averages and intermittent sampling every 4 to 24 h of the fraction of inspired oxygen, partial pressure of oxygen, SpO_2, and ventilator settings have all been employed. The largest study to date employed SpO_2 patient-hours and recorded approximately 170 values per patient [9]. As pragmatic trials recruit a larger number of patients, automated extraction of SpO_2 could allow collection of more granular data on oxygenation for conduct, monitoring, and analysis.

Our study has several strengths. Automated high frequency SpO_2 collection yielded nearly ten times as many SpO_2 values per patient as available in prior trials, potentially facilitating assessment of separation between groups and episodes of hypoxemia or hyperoxemia [9]. Despite concerns about poor signal quality from motion artifact [12, 13], in our study manual review of plethysmography waveform found 96% of SpO_2

values were associated with adequate plethysmography waveform and only 20 SpO_2 values out of 33,092 values (0.06%) were 88% or less due to inadequate or absent plethysmography.

Our study has limitations. Plethysmography waveform review was limited to 3.7% of patients due to its labor-intensive nature. Plethysmography waveform was reviewed by one physician only. No established criteria for adequacy exist against which waveform could be graded. During intervals in which the plethysmography is inadequate or absent, information are not available as to the true underlying SpO_2 values. High-frequency values for SpO_2 were archived for research starting at the time of administrative admission to the institutional telemetry system, which resulted in missing values immediately after tracheal intubation for a significant number of patients intubated in the ED. SpO_2 values may not always reflect partial pressure of oxygen [14].

Conclusions

Automated high-frequency extraction of SpO_2 values from bedside monitors in a clinical trial is feasible and allows measurement of SpO_2 as frequently as every minute. The vast majority of SpO_2 values from patient monitors are associated with plethysmographic waveforms of adequate quality.

Authors contributions Study concept and design: K.G.B, J.D.C, M.W.S; Acquisition of data: K.G.B, L.W; Analysis and interpretation of data: K.G.B, J.D.C, L.W, M.W.S; Drafting of the manuscript: K.G.B, M.W.S; Critical revision of the manuscript for important intellectual content: K.G.B, J.D.C, L.W, J.P.W, W.H.S, T.W.R, M.W.S; Guarantor of the paper: M.W.S.

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Data availability The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Code availability Not applicable.

Compliance with ethical standards

Conflict of interest All authors declare no conflicts of interest.

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