Pulse Oximetry: Beyond S_{pO_2}

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Newer pulse oximetry technology is available that uses multiple wavelengths of light and is thereby able to measure more than 2 forms of hemoglobin, including carboxyhemoglobin (SpCO), methemoglobin (SpMet), and total hemoglobin (SpHb). Several studies have shown relatively low bias, but poor precision, for SpCO compared with HbCO. Evaluations of SpMet have been conducted primarily in normal subjects. Clinical evaluations of SpHb suggest that it might not yet be accurate enough to make transfusion decisions. Respiratory waveform variability of the pulse oximeter plethysmogram might be useful to assess pulsus paradoxus in patients with airway obstruction; it might also be used to measure the breathing frequency. The change in pulse pressure over the respiratory cycle has been used to assess fluid responsiveness in mechanically ventilated patients, and similarly, the pulse oximetry plethysmogram waveform amplitude variability might be used to assess fluid responsiveness. However, there are limitations to this approach, and it remains to be determined how well it can be applied clinically using existing pulse oximetry technology. The pulse oximeter signal is probably useful for applications beyond S_{pO_2}. However, the current technology is not mature, and improvements are necessary. With technology improvements, the use of pulse oximetry to detect SpCO, SpMet, SpHb, pulsus paradoxus, breathing frequency, and fluid responsiveness is likely to improve in the future. *Key words: breathing frequency; carboxyhemoglobin; fluid responsiveness; methemoglobin; oxygen saturation; pulse oximetry; pulsus paradoxus*. [Respir Care 2016;61(12):1671–1680. © 2016 Daedalus Enterprises]

Introduction

Pulse oximetry is commonly used to assess S_{pO_2} and heart rate. Conventional pulse oximetry uses 2 wavelengths of light (red and infrared) transmitted through a pulsating vascular bed, such as the distal phalanx of the finger. Pulse oximeters use the red/infrared signal ratio and proprietary calibration tables to calculate S_{pO_2}.[1,2] Manufacturers claim

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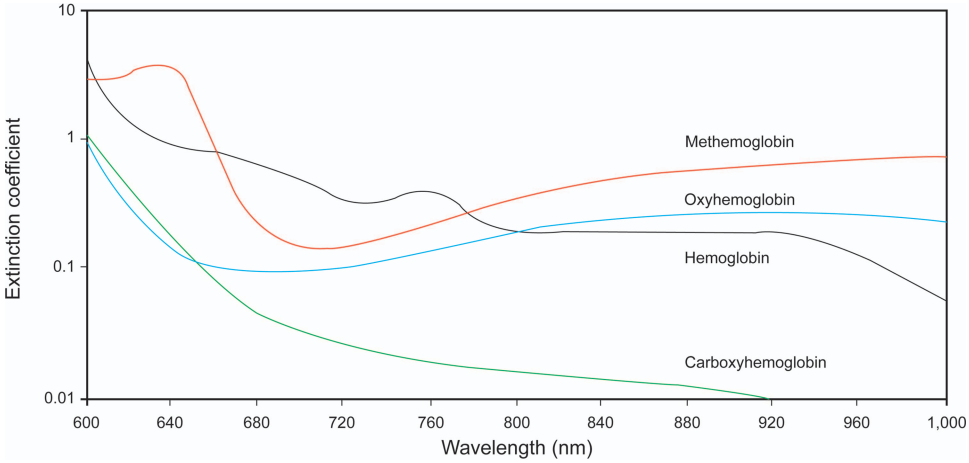

Fig. 1. Light absorption characteristics of hemoglobin, oxyhemoglobin, carboxyhemoglobin, and methemoglobin. At 660 nm, the absorptions for oxyhemoglobin and for carboxyhemoglobin are nearly identical. From Reference 5, with permission.

an accuracy of 2%, evaluated by the SD of the differences between S_{pO_2} and oxyhemoglobin (HbO_2) by co-oximetry, measured simultaneously in healthy subjects. An SD of 2% reflects an expected error of 4% (2 SD), which agrees with an error of 3–4% reported in clinical studies.[3] The performance of the current generation of pulse oximeters has improved in the setting of poor signal/noise ratio, such as motion artifact and poor perfusion. Recently, pulse oximeter technology has expanded beyond measurement of S_{pO_2} to other applications, such as measurement of carboxyhemoglobin (HbCO), methemoglobin (HbMet), and total hemoglobin (SpHb). Pulse oximetry has also be used for the assessment of pulsus paradoxus, fluid responsiveness, and breathing frequency. The purpose of this paper is to review these recent advances in pulse oximetry.

Carboxyhemoglobin, Methemoglobin, Total Hemoglobin

Carboxyhemoglobin

Inaccuracy of traditional 2-wavelength S_{pO_2} in the presence of HbCO has been appreciated for nearly as long as pulse oximetry has been commercially available.[4] This relates to the light absorption characteristics of HbCO versus those of HbO_2 (Fig. 1).[5] An elevated HbCO falsely elevates S_{pO_2}, usually by an amount less than the HbCO but which can result in an extreme overestimation of HbO_2.[6] The difference between S_{pO_2} and HbO_2 due to HbCO has been called the pulse oximetry gap.[7] Pulse oximetry technology that uses 7+ wavelengths of light is now available, instead of the usual 2, and is thereby able to measure >2 species of human hemoglobin, including carboxyhemoglobin (SpCO).

In the first published study of this technology, 10 volunteers breathed 500 ppm CO until their HbCO reached 15%.[8] SpCO had a bias (mean error) of −1% (SpCO − HbCO) and a precision (SD of the error) of 2%. Thus, the limits of agreement were −5 to 3%. In another normal volunteer study, Feiner et al[9] determined whether hypoxemia interferes with the accurate detection of HbCO. F_{IO_2} was decreased to HbO_2 of 80%, and inhaled CO was increased to HbCO of 12%. Pulse oximetry accurately detected hypoxemia with both normal and elevated levels of HbCO (bias 0.44% ± 1.69% at HbCO <4% and −0.29% ± 1.64% at HbCO ≥4%). HbCO was accurately detected during normoxia and moderate hypoxia (bias −0.98 ± 2.6 at HbO_2 ≥95% and −0.7 ± 4.0 at HbO_2 <95%). However, when HbO_2 decreased below 85%, the pulse oximeter always gave low signal quality errors and did not report SpCO. The authors concluded that, in healthy volunteers, the pulse oximeter accurately detected hypoxemia with both low and elevated HbCO, and SpCO accurately detects HbCO only when HbO_2 is >85%.

Abnormal Hb and HbCO levels affect the diffusing capacity for carbon monoxide (D_{LCO}). Ruppel et al[10] compared SpHb and SpCO with measured Hb and HbCO for adjusting D_{LCO}. SpCO did not differ significantly from HbCO (2.1 ± 4.0 vs 2.5 ± 2.3), but there was wide variability. There were small, but significant, differences in the adjusted D_{LCO}, depending on whether blood or pulse oximetry values were used. Predicted D_{LCO} adjusted for Hb and HbCO was 22.5 ± 4.8 mL/min/mm Hg measured with the pulse oximeter and 23.5 ± 4.5 mL/min/mm Hg

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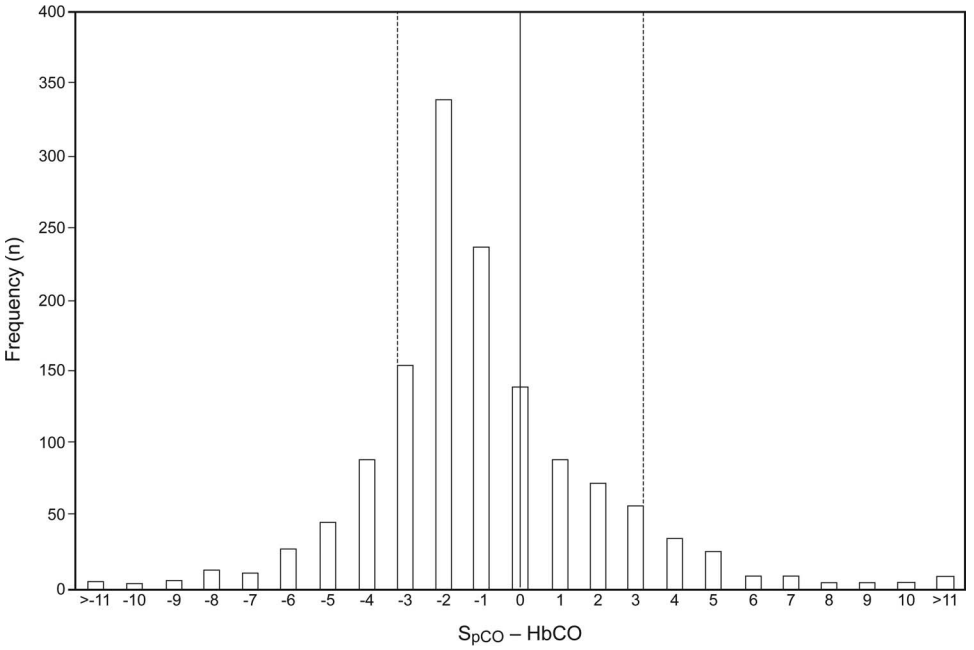

Fig. 2. Distribution of the differences between carboxyhemoglobin measured noninvasively (SpCO) versus via blood (HbCO), rounded to the nearest full percentage point. The dashed lines around zero represent the accuracy range of ±3 percentage points, reported by the manufacturer to be ±1 SD. There are 3 individuals with SpCO − HbCO ≤ 11% and 8 individuals with SpCO − HbCO ≥ 11%. The data suggest that these monitors more frequently underestimated HbCO. From Reference 15.

by measured values from arterial blood gas analysis. The limits of agreement for pulse oximetry adjusted D_{LCO} exceeded the clinical threshold of 3 mL/min/mm Hg for Hb adjustments and for combined Hb + HbCO adjustments. Predicted D_{LCO} values differed by >3 mL/min/mm Hg in 17% of subjects. The authors concluded that pulse oximetry is of limited usefulness for adjusting either predicted or measured D_{LCO} values. However, they suggest that it might be useful to screen patients for invasive testing, particularly if the D_{LCO} is close to the lower limit of normal.

Touger et al[11] assessed agreement between SpCO and HbCO in a sample of emergency department subjects with suspected CO poisoning. HbCO levels ranged from 0 to 38%. They found a bias of 1.4% and limits of agreement of −11.6 to 14.4%. SpCO correctly identified 11 of 23 subjects with HbCO >15%, and there was one case of HbCO <15% in which SpCO was >15%. In one case, the HbCO exceeded 30%, whereas SpCO was <5%, and in another case, the SpCO value exceeded 20% and was >4 times the HbCO. In an editorial accompanying publication of this study, Maisel and Lewis[12] suggest that, because of its potential because of its potential inaccuracies, SpCO should not be used as a substitute for laboratory measurement of HbCO.

Roth et al[13] compared SpCO and HbCO in 1,578 subjects in an emergency department setting. Bland-Altman analysis revealed a bias between SpCO and HbCO of 2.3% (95% CI 2.1–2.5%) for all subjects, 1.4% (95% CI 1.0–1.8%) for smokers, and 2.8% (95% CI 2.5–3.1%) for nonsmokers and a precision of 4.0% (4.4% for smokers, 4.3% for nonsmokers), resulting in limits of agreement from −5.7 to 10.4% (−7.4 to 10.2% for smokers, −5.8 to 11.4% for nonsmokers). Because the relationship between SpCO and HbCO was not normally distributed, they also performed Bland-Altman analysis using log-transformed values. This resulted in a bias of 3.0% higher SpCO compared with HbCO (1.5% for smokers, 4.3% for nonsmokers) and a precision of 3.3% (2.9% for smokers, 2.98% for nonsmokers), with limits of agreement from −3.55 to 9.53% (−4.3 to 7.3% for smokers, −1.6 to 10.3% for nonsmokers).

Caboot et al[14] evaluated the accuracy of SpCO in 50 children with sickle cell disease. Compared with HbCO, the SpCO bias was 0.1% with a precision of ±2.1%. There was greater variability in the SpCO measurements (0–10%) compared with the invasive HbCO measurements (0.4–4.4%). Of note, the HbCO levels in this study were low (<5%), bringing into question the clinical relevance of these findings.

In a convenience sample presenting to an emergency department, Weaver et al[15] measured SpCO and simultaneously assayed HbCO. False positive or false negative values were defined as SpCO at least 3% greater or less than the HbCO level, reported by the manufacturer to be ±1 SD in performance. Of 1,363 subjects, 122 (9%) met the criteria for a false positive value (range 3–19%), whereas 247 (18%) met the criteria for a false negative value (−13 to −3%) (Fig. 2). Risks for a false positive

SpCO reading included being female and having a lower perfusion index. HbMet, body temperature, and blood pressure also appeared to influence the SpCO accuracy. The authors also reported variability among monitors. The authors concluded that, although the pulse oximeter functioned within the manufacturer's specifications, using this device should cause the clinician to expect some SpCO readings to be significantly higher or lower than HbCO measurements. Moreover, the authors recommend against using SpCO to direct triage or patient management. Although an elevated SpCO could possibly broaden the diagnosis of CO poisoning in patients with nonspecific symptoms, a negative SpCO level in patients suspected of having CO poisoning should never rule out CO poisoning and should not be used without confirmation with measured HbCO.

Sebbane et al[16] compared SpCO with direct measurement of HbCO in subjects with suspected CO poisoning in an emergency department. SpCO ranged from 1 to 30%, and HbCO ranged from 0 to 34%. The mean differences between HbCO and SpCO were −0.2 ± 3.3% (95% limits of agreement of −6.7 and 6.3%) for the whole cohort, −0.7% (limits of agreement −7.7 and 6.2%) for non-smokers, and 0.6% (limits of agreement −5.0 and 6.2%) for smokers (Fig. 3). The optimal thresholds for detecting CO poisoning were SpCO of 9 and 6% for smokers and non-smokers, respectively. The authors concluded that SpCO was not a substitute for blood HbCO measurement. They suggest, however, that SpCO could be useful as a first-line screening test in the emergency department.

Common to these studies is a finding of relatively low bias, but poor precision, for SpCO compared with HbCO. It may be that bias is low because of erroneous results occurring equally above and below the true value, which effectively cancel each other.[17] Several editorials have been published on the accuracy of SpCO. Maisel and Lewis[12] acknowledge that accurate and reliable SpCO would be an important clinical advance, providing the potential for faster diagnosis and earlier treatment of HbCO. Because of its inaccuracies, however, SpCO should not be viewed as a substitute for HbCO. They suggest that efforts to develop a more accurate measurement of SpCO should be undertaken. Wilcox and Richards[18] suggest that broad reliance on SpCO is premature. Clinicians must be aware of the limitations of SpCO, and patients considered to be at risk for carboxyhemoglobinemia must have confirmatory blood levels checked. In a review by Shamir et al[17] published in 2012, the authors suggested that currently there is too much bias in SpCO to warrant a recommendation for clinical decision making.

An important issue to be appreciated is that pulse oximeters that measure SpCO use the conventional 2-wavelength algorithm to determine S_{pO_2}. When there are significant levels of HbCO, the displayed S_{pO_2} values include the same errors as conventional pulse oximetry.[19]

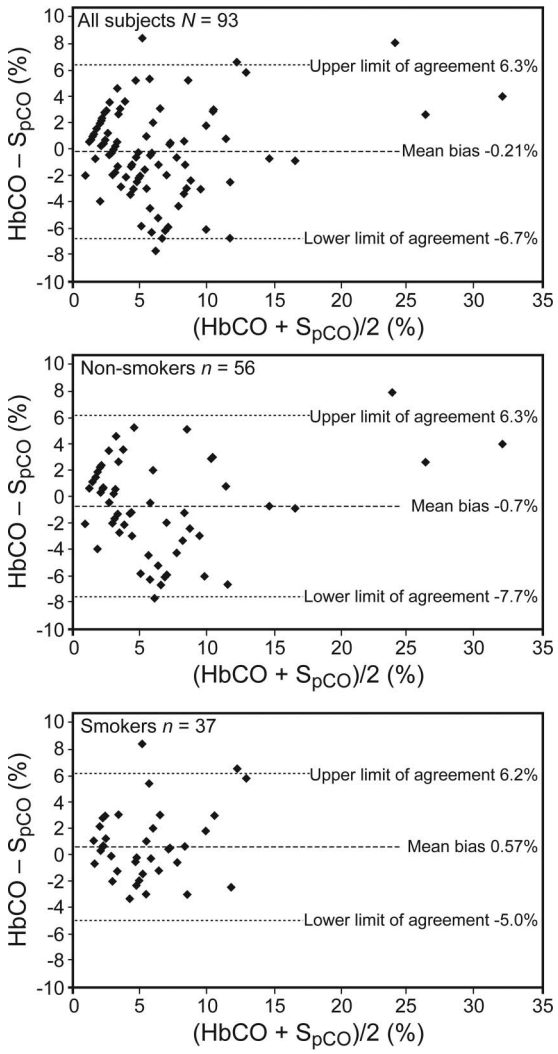

Fig. 3. Bland-Altman plots of the difference between carboxyhemoglobin (HbCO) measured with a pulse oximeter (SpCO) and measured via laboratory blood gas analysis against the average of measurements. From Reference 16.

Methemoglobin

HbMet is produced when the iron in hemoglobin is oxidized from the ferrous state (Fe^{2+}) to the ferric state (Fe^{3+}), rendering it incapable of oxygen transport and shifting the HbO_2 dissociation curve to the left.[20] HbMet forms normally in response to oxidative stress, which is counteracted by protective mechanisms that keep HbMet levels below 1%. HbMet can be hereditary or acquired. Patients with hereditary HbMet tolerate high levels without symptoms. HbMet is more commonly acquired after exposure to an exogenous oxidizing agent. These include nitrates, chlorates, aniline compounds, dapsone, benzocaine, and inhaled nitric oxide.

S_{pO_2} values of conventional 2-wavelength pulse oximeters are forced toward 85% in the presence of high HbMet

levels.[19] Pulse oximetry technology is now available to measure methemoglobin (SpMet). Barker et al[8] induced HbMet in 10 normal subjects by intravenous infusion of sodium nitrite, resulting in levels as high as 12%. The SpMet − HbMet bias was 0, and the precision was 0.45. Feiner and Bickler[21] induced methemoglobinemia in 12 normal subjects by administration of sodium nitrite to produce a target HbMet of 0.4–14.4%. The accuracy of SpMet was assessed both at normoxemia and with induced hypoxemia with a target HbO_2 as low as 74%. SpMet bias was 0.16% with a precision of 0.83% and was similar across the range of HbO_2.

Aside from normal subjects, there have been few assessments of the accuracy of SpMet. In children with sickle cell disease, Caboot and colleagues[14] reported a bias of −0.22% and a precision of ±0.33% within a HbMet range of 0.1–1.1%. Given that HbMet was normal in this study, the clinical relevance of these results is unclear. Annabi and Barker[22] described the case of a patient who developed HbMet secondary to topical benzocaine spray to the oropharynx in preparation for intubation. SpMet was monitored during diagnosis and treatment with methylene blue, and the values it provided (as high as 33%) were very close to measured HbMet.

As with pulse oximetry to assess SpCO, the displayed S_{pO_2} uses the conventional 2-wavelength algorithm. There is also crosstalk between the SpMet and SpCO measurement channels such that, in the presence of significant HbMet, the instrument displays a falsely elevated SpCO when it displays a correct SpMet.[19]

Hemoglobin

Measurement of Hb is necessary in the care of patients during surgery, following trauma, and in the ICU. Continuous and noninvasive measurement of Hb can be performed by pulse oximetry (SpHb). There have been several systematic reviews of this technology published, and those will be reviewed here.

Kim et al[23] conducted a comprehensive search of the literature (from 2005 to August 2013) to identify studies assessing the accuracy of SpHb against laboratory Hb measurements. They included 32 studies (4,425 subjects, median sample size of 44, range from 10 to 569 subjects/study) in the meta-analysis. The bias (mean difference between noninvasive and laboratory) was 0.10 g/dL, and limits of agreement were −2.59 to 2.80 g/dL. The bias was 0.39 (limits of agreement −2.21 to 2.98 g/dL) in 13 studies conducted in the perioperative setting, −0.51 g/dL (limits of agreement −3.63 to 2.62 g/dL) in 5 studies performed in the ICU setting, and −0.39 g/dL (limits of agreement −3.78 to 2.99 g/dL) in the emergency department setting. The bias and limits of agreement were similar among the 3 devices included in the meta-analysis. The authors concluded that, although the bias between noninvasive Hb and laboratory measurements was small, the wide limits of agreement suggest that clinicians should be cautious when making clinical decisions based on SpHb.

Hiscock et al[24] identified 18 studies (1,516 subjects) since 2011 that compared SpHb with laboratory measurement of hemoglobin. The bias (SpHb − laboratory) was −0.11, and the limits of agreement were −3.3 to 3.0. The authors concluded that clinicians should carefully consider the limits of agreement before basing clinical decisions on SpHb.

The Bland-Altman approach[25] is commonly used when comparing the performance of one device with that of another. The mean of the reference and tested device is plotted on the x axis versus the difference between the values on the y axis. Bias is the mean difference between values, precision is the SD of the differences, and the limits of agreement are calculated as the bias ± 1.96 × SD. Approximately 95% of all values are between the positive and negative limits of agreement. The Bland-Altman analysis assumes 1 sample/subject, a measured parameter that does not change over the course of repeated observations in each subject, a relatively large number of observations, equal variance within subjects, and normal distributions of data. Rice et al[26] argue that these assumptions are often violated when assessing the accuracy of SpHb. They argue that is more important to consider how the device will affect clinical decision making. The important question to be answered for SpHb is: Does the patient need to be transfused? They describe a hemoglobin error grid that can be used to evaluate the clinical accuracy of SpHb to determine whether to transfuse an individual patient. The decision to transfuse a patient requires both an accurate hemoglobin measurement and a physiologic reason to elect transfusion. Rice et al[26] conclude that the published accuracy data for SpHb are not sufficient to make the transfusion decision. SpHb, at best, can suggest to the clinician that a confirmatory blood sample should be obtained.

Pulsus Paradoxus

Negative pressure in the thorax increases venous return, resulting in increased flow in the right side of the heart. However, the decrease in intra-thoracic pressure also expands the compliant pulmonary vasculature, which causes blood to pool in the lungs, effectively decreasing flow to the left side of the heart. Right heart filling also causes septal shift, which compromises left heart filling. The result is a reduced stroke volume during spontaneous inspiration, causing in a decrease in systolic blood pressure. Pulsus paradoxus is an abnormally large decrease in systolic blood pressure and pulse wave amplitude during spontaneous inspiration. The opposite effect occurs during positive-pressure breathing, which is called reverse pulsus

paradoxus. Pulsus paradoxus >10 mm Hg is indicative of cardiac tamponade, upper-airway obstruction, and obstructive lung diseases, such as asthma and COPD. The systolic blood pressure changes can be detected by changes of the amplitude of the plethysmogram measured by the pulse oximeter.

Frey and Butt[27] evaluated the relationship between intra-arterial measured pulsus paradoxus and changes in the pulse oximeter plethysmogram. Their study included 62 non-intubated subjects with an indwelling arterial line. In 57 children, the variability in the plethysmogram correlated with pulsus paradoxus measured from the arterial blood pressure ($r = 0.85$). The sensitivity to detect pulsus paradoxus >10 mm Hg with a change in plethysmogram >8 mm was 89%, and the specificity was 90%. The authors concluded that the pulse oximetry plethysmogram is a rapid and easily performed noninvasive method for objective estimation of pulsus paradoxus.

Clark et al[28] compared pulsus paradoxus determined from the pulse oximeter plethysmogram with that determined manually by sphygmomanometer in 36 children. To determine pulsus paradoxus using the pulse oximeter, a blood pressure cuff was inflated until the plethysmogram disappeared. The cuff pressure was released at 2 mm Hg/s, and the first appearance of an intermittent plethysmogram was taken as systolic pressure during exhalation. Cuff pressure was further decreased until the appearance of a complete plethysmogram, which was taken as systolic pressure during inhalation. The difference between these 2 pressures was pulsus paradoxus. The mean difference between the pulsus paradoxus measured by sphygmomanometer and the pulse oximeter was −0.1 mm Hg, with limits of agreement from −3.9 to 3.8 mm Hg.

Pulsus paradoxus was estimated by Arnold et al[29] by use of the dynamic change in area under the pulse oximeter plethysmogram. In 219 children with acute asthma, they found that pulsus paradoxus estimated from the pulse oximeter correlated with measure of pulmonary function and accessory muscle use. The authors suggest that this use of the pulse oximeter to assess pulsus paradoxus might allow for earlier recognition and improved management of disorders causing elevated pulsus paradoxus.

In 26 subjects admitted to the ICU with either asthma or COPD, Hartert et al[30] assessed the severity of air flow with pulsus paradoxus. They defined the altered pulse oximetry baseline plethysmogram as respiratory waveform variation, measured as the change (in mm) from baseline (Fig. 4). Pulsus paradoxus correlated with the respiratory waveform variability of the pulse oximetry tracing. They also found that analysis of the respiratory variation in the pulse oximetry waveform in subjects with obstructive lung disease reflects the presence and degree of auto-PEEP. The authors concluded that, since pulse oximetry is available universally in ICUs and emergency departments, it might be a useful noninvasive means of continually assessing pulsus paradoxus and air trapping severity in patients with obstructive lung disease.

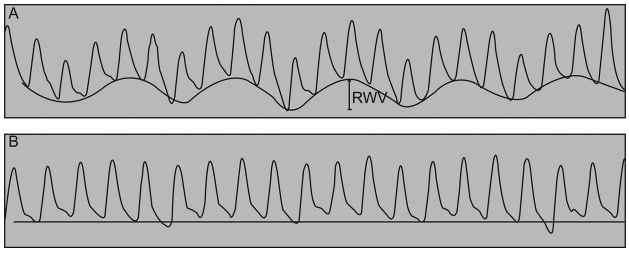

Fig. 4. Pulse oximetry tracings from a 60-y-old woman with a COPD exacerbation who was admitted to the ICU in ventilatory failure. A: The patient's pulse oximetry tracing at the time of admission, revealing the respiratory variability in the pulse oximeter plethysmogram. Her measured pulsus paradoxus at this time was 16 mm Hg. B: The patient's pulse oximetry plethysmogram after 12 h of aggressive therapy. Her pulsus paradoxus at this time was 8 mm Hg. Note the absence of respiratory waveform variation (RWV) in the baseline of the oximeter tracing after the clinical improvement in airflow and the resolution of elevated pulsus paradoxus. From Reference 30, with permission.

Perel[31] reported clinical waveform variability in the pulse oximeter plethysmogram associated with significant upper-airway obstruction. The perfusion index is calculated as the ratio of the pulsatile to the non-pulsatile infrared signal, reflecting the amplitude of the pulse oximeter waveform. The pulse oximeter plethysmogram index is calculated from the maximal and minimal perfusion index measured by the pulse oximeter: Plethysmogram index $= [(PI_{max} - PI_{min})/PI_{max}] \times 100$, where PI_{max} and PI_{min} represent the maximal and the minimal values of the perfusion index, respectively. In 4 cases of upper-airway obstruction, the plethysmogram index was 25–39%. This illustrates an approach to assessment of pulsus paradoxus due to upper-airway obstruction.

Fluid Responsiveness

Positive-pressure ventilation causes a lower left-ventricular stroke volume during exhalation. The primary mechanism is the decrease in left-ventricular filling during exhalation, after a delay caused by the long pulmonary transit time of blood, due to the decrease in right-ventricular stroke volume during inhalation. The decrease in right-ventricular stroke volume during inhalation is due to the decrease in right-ventricular preload and the increase in right-ventricular afterload. The result is an increase in pulse pressure during inhalation (PP_{max}) and a decrease in pulse pressure during exhalation (PP_{min}). The change in pulse pressure over the respiratory cycle is calculated as: $\Delta PP\ (\%) = \{[PP_{max} - PP_{min}]/[(PP_{max} + PP_{min})/2]\} \times 100$. Michard et al[32] reported that an increase in PEEP was associated with a decrease in cardiac output and an in-

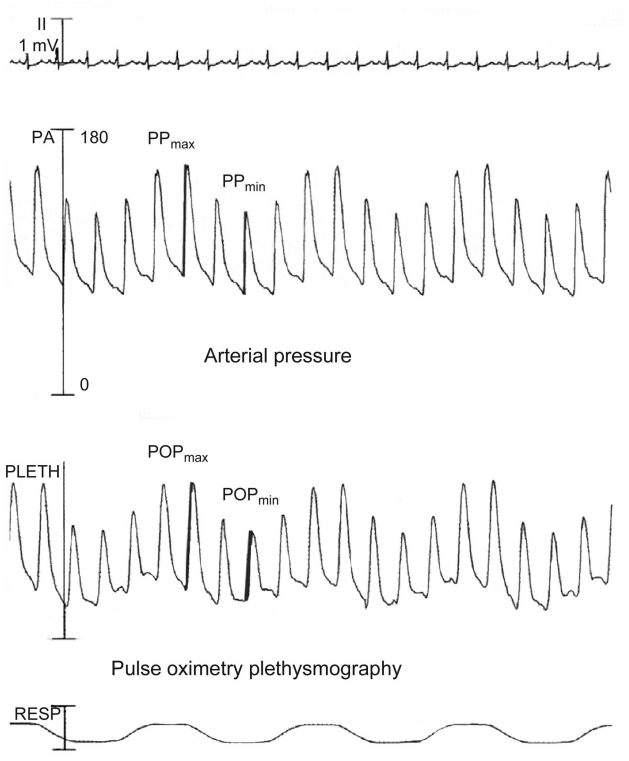

Fig. 5. Comparison between invasive arterial pressure and pulse oximetry plethysmogram recordings. Simultaneous recording of electrocardiographic lead (II), systemic arterial pressure (PA), pulse oximetry plethysmogram (pleth), and respiratory signal (resp) in one illustrative patient. POP = pulse oximetry plethysmogram; PP = pulse pressure. From Reference 34, with permission.

crease in ΔPP from 9 ± 7 to 16 ± 13%. With fluid administration, there was an increase in cardiac output, and ΔPP decreased from 27 ± 13 to 14 ± 9%. In a follow-up study by Michard et al,[33] ΔPP of 13% allowed discrimination between fluid responders and non-responders with a sensitivity of 94% and a specificity of 96%. There are 2 important limitations of the ΔPP approach. First, it was described before the era of lung-protective ventilation, using a tidal volume of 8–12 mL/kg. Second, it is valid only if spontaneous breathing efforts are absent, and it might require paralysis for correct assessment.

Recently, there has been an interest in using changes in the pulse oximeter plethysmogram to assess ΔPP. The plethysmogram is characterized by a fast waveform synchronous with the heart rate and a slow waveform synchronous with the breathing frequency. Cannesson et al[34] compared the pulse oximetry plethysmogram amplitude (ΔPOP) and ΔPP in mechanically ventilated critically ill patients. ΔPOP was calculated using a formula similar to that for ΔPP: $\Delta POP = 100 \times \{[POP_{max} - POP_{min}]/[(POP_{max} + POP_{min})/2]\}$. There was good agreement (bias = 0.8, precision ±3.5%) between ΔPOP and ΔPP (Fig. 5). They found that ΔPOP >15% allowed discrimination between patients with respiratory variation in ΔPP >13% (positive predictive value 100%). The plethysmogram index measures changes in perfusion index over a time interval that includes one or more respiratory cycles. Cannesson et al[35] reported that a plethysmogram index threshold value of 11.5% was able to discriminate between ΔPOP >13% and ΔPOP <13%, with a sensitivity of 93% and a specificity of 97%.

ΔPOP could have value during PEEP titration.[32] An increase in ΔPOP when PEEP is increased might suggest alveolar overdistention and adverse hemodynamic effects of PEEP. This concept is utilized in the Intellivent closed-loop management of oxygenation (Hamilton Medical, Reno, Nevada). The manufacturer calls this the heart-lung interaction index, but it is functionally equivalent to ΔPOP. If the heart-lung interaction index is >15%, Intellivent limits the maximum level of PEEP and favors an increase in F_{IO_2} to manage hypoxemia.

Sandroni et al[36] conducted a systematic review and meta-analysis of the accuracy of ΔPOP and the plethysmogram index as predictors of fluid responsiveness in mechanically ventilated adults. Their review included 10 studies enrolling 233 subjects. Volume control ventilation was used in each study, and most used a tidal volume of 8–10 mL/kg. The pooled area under the receiver operating characteristic curve for identification of fluid responders was 0.85 (95% CI 0.79–0.92). The pooled sensitivity was 0.80 (95% CI 0.74–0.85), and the pooled specificity was 0.76 (0.68–0.82). The area under the curve, sensitivity, and specificity were greater in studies with a large bolus amount than in those with a small bolus. The authors concluded that ΔPOP and the plethysmogram index were equally effective for predicting fluid responsiveness, but the prediction was more accurate when a large fluid bolus was administered.

Commonly used pulse oximeter sites (finger, ear, and forehead) were evaluated by Shelley et al[37] to determine which allows for the best extraction of the respiratory signal during positive pressure and spontaneous ventilation. They used spectral analysis to isolate the respiratory signal from the plethysmogram. The effect of ventilation was 18 times stronger in the ear plethysmogram compared with the finger plethysmogram during positive-pressure ventilation and 12 times stronger with spontaneous ventilation. The respiratory signal in the pulse oximeter waveform was >10 times stronger in the head region when compared with the finger during both positive-pressure ventilation and spontaneous breathing. The authors attribute this finding to the shorter distance between the head and chest, compared with the distance between the finger and chest, and to the fact that the vasculature of the head is relatively insensitive to local sympathetically mediated vasoconstriction. It might also be secondary to the fact that the veins from the head do not have valves and thus there

Table 1. Desirable Characteristics for a Pulse Oximeter Used for Plethysmogram Analysis

Waveform display: Ability to change time scales, switch between scroll and erase bar display modes, wavelength selectable (infrared signal vs red signal vs other)
Ability to turn off auto-gain function and auto-center function
Ability to set the amplitude gain
Numeric display of amplitude and direct current signal
Ability to use a wide range of probes (finger, ear, and reflective)
Digital and analog outputs for capture by data collection equipment

Data from Reference 39.

is more venous backflow during positive-pressure ventilation.

Alian et al[38] assessed the frequency-analyzed plethysmogram and arterial pressure waveform variables to detect early bleeding in children during surgery. They found that the plethysmogram and arterial waveform parameters could track changes in blood volume during the bleeding phase, suggesting the potential for use of the plethysmogram as a noninvasive monitor for tracking changes in blood volume in pediatric patients.

Shelley[39] suggests a number of desirable characteristics for pulse oximeter plethysmogram analysis (Table 1). It is important to appreciate that a large pulse amplitude on the plethysmogram is not necessarily associated with a high arterial blood pressure, and vice versa. The plethysmogram amplitude will decrease during significant increases in arterial blood pressure that are due to increased sympathetic tone. With vasodilatation, the plethysmogram amplitude is increased.[39]

Addison[40] wrote a critical assessment of the use of the pulse oximetry plethysmogram waveform to assess fluid responsiveness. He provides a detailed overview of the signal processing methods used in individual studies, such as the details of exclusion criteria, manual filtering and preprocessing, gain change issues, acquisition details, selection of registration periods, averaging methods, and physiological influences on the plethysmogram. Issues identified include the number of respiratory cycles over which ΔPOP and the plethysmogram index are evaluated, clinician manual filtering to determine which waveforms to use, and probe position. The plethysmogram index is a proprietary algorithm, and there is very little information available concerning its signal processing. The plethysmogram available to clinicians at the bedside is a highly processed signal, which varies among manufacturers. Most pulse oximeters use an auto-gain function designed to maximize the size of the waveform displayed.[39] Without the option to turn off this automatic resizing function, it is impossible to analyze the amplitude changes of the plethysmogram. Addison[40] suggests that more rigorous signal processing is required for a robust, fully automated ΔPOP algorithm for use in the clinical environment.

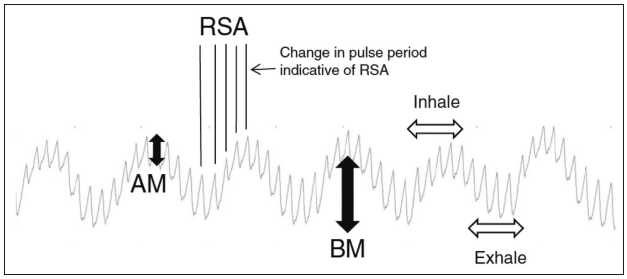

Fig. 6. A segment of plethysmogram exhibiting the 3 modulations. BM = baseline modulation (cardiac pulses riding on top of baseline modulation); AM = amplitude modulation (cardiac pulse amplitudes varying over respiratory cycle); RSA = respiratory sinus arrhythmia (pulse period varying over respiratory cycle). Regions of inhalation and exhalation are shown schematically on one respiratory cycle. From Reference 45, with permission.

Use of the pulse oximeter plethysmogram to assess fluid responsiveness is attractive. However, it remains to be determined how well it can be applied clinically using existing pulse oximetry technology. Moreover, its application is limited because its physiologic application depends on full ventilator support (positive-pressure ventilation) and might be less useful with lung-protective low-tidal volume ventilation. Finally, differences in the plethysmogram due to sensor site of application bring into question the generalizability of this approach.

Breathing Frequency

The pulse oximeter plethysmogram depends on changes in arterial and venous blood volume under the pulse oximeter probe. The alternating current signal corresponds to the pulse oximeter plethysmogram amplitude modulation, which corresponds to ΔPOP. The direct current signal corresponds to baseline modulation of the plethysmogram at the breathing frequency, related to the movement of nonpulsatile venous blood under the probe. The plethysmogram thus has both heart rate and breathing frequency synchronous components, wherein the direct current part reflects breathing frequency and the alternating current part reflects arterial pulsations. The amplitude of respiratory-induced intensity variations varies with changes in intrathoracic pressure due to tidal breathing. The amplitude of the direct current signal is also affected by breathing frequency, with an amplitude decrease with increased breathing frequency.[41]

Algorithms have been developed to allow extraction of the breathing frequency from the pulse oximeter plethysmogram.[42-48] Addison and colleagues[45] describe a method that determines breathing frequency from 3 aspects of the plethysmogram (Fig. 6): (1) baseline (direct current) mod-

ulation, (2) pulse amplitude modulation (POP), and (3) respiratory sinus arrhythmia due to the variation in heart rate that occurs throughout the respiratory cycle (sinus arrhythmia). In 63 hospitalized subjects with a variety of diagnoses, there was good agreement between breathing frequency determined by this algorithm and capnography (bias −0.48 breaths/min with a precision of 1.77 breaths/min).

Summary

The pulse oximeter signal is probably useful for applications beyond S_{pO_2}. However, the current technology is not mature, and improvements are necessary. With technology improvements, the use of pulse oximetry to detect SpCO, SpMet, SpHb, pulsus paradoxus, breathing frequency, and fluid responsiveness is likely to improve in the future.

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