CONTINUOUS NONINVASIVE HEMOGLOBIN MONITORING: THE STANDARD OF CARE AND FUTURE IMPACT

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EDITORIAL

Frasca et al. (1) report that continuous noninvasive hemoglobin monitoring (CNHM) “…has absolute accuracy and trending accuracy similar to widely used, invasive methods of hemoglobin measurement at bedside”. While the population was small (N=62), the prospective observational study was conducted in a surgical ICU and representative of the performance of Rainbow® adult “resposable” (reusable) sensors (R2-25, Revision E) connected to a Radical-7 Pulse CO-Oximeter (software version 7.6.0.1, Masimo®, Irvine, CA, USA) used with critically ill (SAPS II 46±23, SOFA 6±3) medical and emergency-elective surgery patients. However, “…none of the included patients had active major bleeding”.

While the authors present analysis of trends, observations reflect more static, than dynamic hematological conditions, and they suggest that CNHM “…may be a feasible alternative to invasive hemoglobin monitoring”. However, they do not present decision-making or outcomes results, per se, and wisely, stop short of implying CNHM should replace discrete in vitro diagnostic hemoglobin testing when the article ends with the somewhat circuitous caveat, “A laboratory hemoglobin determination could be limited to situations where a blood transfusion is considered”.

Oxygen saturation measured noninvasively by traditional pulse oximetry using red (~660 nm) and infrared (~905 nm) light emitting diodes (LEDs) differentiates oxy- versus deoxyhemoglobin, respectively (2). The ratio of red versus infrared light is correlated with a calibration curve empirically derived from clinical studies to calculate oxygen saturation over a limited range (2, 3), while pulse rate is determined from the plethysmogram. Newer devices incorporate robust treatment of the red/infrared ratio, multiple wavelengths, advanced algorithms, and proprietary sensor calibrations integrated (3). These principles extend to pulse co-oximetry, where up to twelve wavelengths and sophisticated signal reduction enable measurement of carboxyhemoglobin, methemoglobin, total hemoglobin,
and total oxygen content (4) with real-time tracking. Table 1 (4–11) presents CNHM systems, characteristics, and intended uses.

Devices may be limited to adults and children weighing more than 30 kilograms (7)—pediatric intensivists should proceed with caution. Notable is the limited range of hemoglobin measurements. Lower bounds of 7 to 8 g/dL could compromise transfusion decisions in critically ill trauma, emergency, and burn surgery patients (12), for whom it would be wise to use CNHM strictly according to FDA-approved intended uses and only as trend monitors. In fact, Frasca et al. (1) present convincing analysis of trend data that serves to validate this purpose for patients who are not actively bleeding.

Other investigators have mixed recent findings. In an ED study, Gayat et al. (13) concluded, “Results from this widely available noninvasive point-of-care hemoglobin monitoring device were systematically biased and too unreliable to guide transfusion decisions.” and “…use of the Masimo Radical-7 Pulse CO-Oximeter would lead to 13% error in terms of transfusion decisions.” Miller et al. (14) found, “…SpHb [CNHM] may not be as accurate as clinically necessary in some patients.” and “When perfusion diminishes, SpHb underestimates true Hb, so it should not be used to determine the need for blood transfusions without validation using a direct measurement methodology.” Causey et al. (15) observed a correlation of the Masimo Radical-7 SpHb Station versus laboratory hemoglobin measurements of 0.77 (P < 0.001) with a mean difference of 0.29 g/dL (95% CI, 0.08–0.49) and reasoned “…the device SpHb to have clinically acceptable accuracy during most types of surgery including those with significant blood loss—….44% of patients in the study sustained significant intraoperative blood loss, the patient population for which the device would prove to be most useful.”

Frasca et al. (1) recommend additional study to evaluate the merits of CNHM in hemorrhaging patients, early detection of bleeding, and monitoring of blood management. We recommend also validation of performance in patients with anemia, hemodilution, severe hypotension, low tissue perfusion, and restrictive blood transfusion thresholds (hemoglobin ≤ 7 g/dL). Noting limitations, the authors (1) state, “…less than 10% of measures were performed in patients with hemoglobin concentration below 8 g/dL.” In fact, data sets presented to the FDA typically lack these low range observations (6–8).

The litany of confounders plaguing pulse (co-)oximetry is extensive [e.g., ambient light, bilirubin, hemoglobin variants, intravascular dyes, patient motion, pressure necrosis, sensor malpositioning and type, skin temperature readings (see recall: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfres/res.cfm?id=97029), and venous congestion]. Investigators point to potential technical issues with hemoglobin monitoring, such as edema and multiple physiological changes that render optical spectroscopic tissue parameters inaccurate or impossible to track (16), inconsistent inter-individual path length and high tissue lipid content that challenge calibration assumptions (17), and blood volume depletion that alters optical scattering and absorption characteristics (18).

Clearly, the use of CNHM in critically ill patients shows strong merit. Trend monitoring may be a useful alternative to serial in vitro testing, especially when reducing iatrogenic blood loss, conserving patient blood volume, enhancing the timeliness of decision-making, and improving the cost-effectiveness of transfusions. Thus, Frasca et al. (1) imply a disruptive shift toward continuous measurement at the point of need (19) and a subtle, but interesting drift in the standard of care for hemoglobin determinations.

The concept of standard of care is based on Vaughn v. Menlove (1837), wherein the judge instructed the jury to reason whether the defendant “proceed[ed] with such reasonable caution as a prudent man would have exercised under such circumstances.” Before declaring
that CNHM has changed the standard of critical care, reasonable caution dictates a) the technology be improved and validated better in the low range (< 8 g/dL); b) continuous validation occurs during dynamic, rather than static, hematological conditions; and c) multicenter investigators provide evidence of improved decision-making and outcomes related to early detection of bleeding episodes and transfusion practices.

Whether or not these challenges are fully met, CNHM has the potential to reduce the medical-financial burden of repeated or unnecessary in vitro laboratory hemoglobin measurements, help conserve patient blood volume by reducing iatrogenic losses, avoid the risks of anemia, optimize intraoperative transfusions, and even enhance care in low-resource settings, such as epidemic Dengue hemorrhagic fever outbreaks where erythrocyte repletion based on hourly spun hematocrits can be partially or completely supplanted by following trends in hemoglobin. Therefore, future impact is high.

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References


### Table 1
Clinical Utility of Non-Invasive Continuous Hemoglobin Monitoring Technology in Critically Ill Patients

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Device Name (Format)</th>
<th>Continuous Measurements</th>
<th>Methodology</th>
<th>Hb Analytical Measurement Range</th>
<th>Manufacturer’s Product Claims</th>
<th>FDA Approved</th>
<th>Intended Use</th>
</tr>
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<tbody>
<tr>
<td>Biosense</td>
<td>TouchHb&lt;sup&gt;a&lt;/sup&gt; (Portable)</td>
<td>THb</td>
<td>In development</td>
<td>In development</td>
<td>In development</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>Hutchinson Technologies</td>
<td>InSpectra Model 325</td>
<td>Tissue Hb&lt;sup&gt;a&lt;/sup&gt;, StO2</td>
<td>3 wavelengths spectrophotometry (5)</td>
<td>Tissue Hb sensor In development</td>
<td>THb spot checking</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>Masimo</td>
<td>Pronto&lt;sup&gt;b&lt;/sup&gt; (Handheld)</td>
<td>THb, SpO2, pulse</td>
<td>8-wavelength spectrophotometry</td>
<td>8 – 17 g/dL ±1 g/dL&lt;sup&gt;c,d&lt;/sup&gt; (adults and pediatrics) (6)</td>
<td>THb spot checking</td>
<td>THb spot checking in clinical and non-clinical settings (6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pronto-7&lt;sup&gt;b&lt;/sup&gt; (Handheld)</td>
<td>THb, SpO2, pulse, Pi&lt;sup&gt;f&lt;/sup&gt;</td>
<td>&quot;</td>
<td>6 – 18 g/dL ±1 g/dL&lt;sup&gt;c,d&lt;/sup&gt; (adults and pediatrics &gt;30 kg) (7)</td>
<td>&quot;</td>
<td>THb spot checking in clinical and non-clinical settings (7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rad-57 (Portable)</td>
<td>THb, SpO2, COHb, MetHb, pulse, PVF&lt;sup&gt;e,g&lt;/sup&gt;</td>
<td>≤8 wavelengths spectrophotometry (4)</td>
<td>7 – 17 g/dL ±1 g/dL&lt;sup&gt;c,d&lt;/sup&gt; (adults and pediatrics) (8)</td>
<td>Continuous monitoring of THb</td>
<td>Continuous monitoring of THb monitoring (8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rad-87 (Handheld)</td>
<td>THb, SpO2, COHb, MetHb, pulse, PVF&lt;sup&gt;e,g&lt;/sup&gt;, RR</td>
<td>&quot;</td>
<td>&quot;</td>
<td>Continuous THb monitoring with wireless connectivity</td>
<td>&quot;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Radical-7 (Portable)</td>
<td>THb, SpO2, COHb, MetHb, Pi&lt;sup&gt;f&lt;/sup&gt;, PVF&lt;sup&gt;e,g&lt;/sup&gt;, total O2</td>
<td>≤12 wavelengths spectrophotometry</td>
<td>&quot;</td>
<td>Continuous and trend monitoring of THb</td>
<td>&quot;</td>
<td></td>
</tr>
<tr>
<td>MBR Optical Systems</td>
<td>Mediscan 2000 (portable)</td>
<td>THb</td>
<td>Wavelength ranging from 350 – 1020 nm&lt;sup&gt;h,i&lt;/sup&gt; (9,10)</td>
<td>In development</td>
<td>In development</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>OrSense</td>
<td>NBM-200MP&lt;sup&gt;a&lt;/sup&gt; (Portable)</td>
<td>THb, SpO2, pulse, pleth.</td>
<td>4-wavelength spectrophotometry</td>
<td>THb sensor in development</td>
<td>In development</td>
<td>Not applicable</td>
<td></td>
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<tr>
<td>Sysmex</td>
<td>Astrin&lt;sup&gt;d&lt;/sup&gt; (Portable)</td>
<td>THb</td>
<td>In development</td>
<td>Evaluated with Hb from 6.7 – 18.4 g/dL (11)</td>
<td>In development</td>
<td>Not applicable</td>
<td></td>
</tr>
</tbody>
</table>

Footnote:

<sup>a</sup> Not FDA-approved;

<sup>b</sup> CLIA-waived;

<sup>c</sup> accuracy claim from 510k FDA-approval;
d determined during conditions of non-motion and good perfusion;

e calculated parameter,

f PI = (constant amount of absorbed light/variable amount of absorbed light) × 100%;

PVI = [(PI_{max} - PI_{min})/(PI_{max})] × 100%;

h infants; and

i neonates.

Abbreviations: COHb, carboxyhemoglobin; Hb, hemoglobin; MetHb, methemoglobin; PI, perfusion index; pleth, plethymographic waveform; PVI, plethymographic waveform variability index; RR, respiratory rate; SpO2, oxygen saturation; StO2, tissue oxygen saturation and THb, total hemoglobin.