Comparison of the Accuracy of Noninvasive Hemoglobin Monitoring by Spectrophotometry (SpHb) and HemoCue® with Automated Laboratory Hemoglobin Measurement

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ABSTRACT

Background: The reference method for hemoglobin concentration measurement remains automated analysis in the laboratory. Although point-of-care devices such as the HemoCue® 201+ (HemoCue, Angelholm, Sweden) provide immediate hemoglobin values, a noninvasive, spectrophotometry-based technology (Radical-7®; Masimo Corp., Irvine, CA) that provides continuous online hemoglobin (SpHb) measurements has been introduced. This clinical study aimed to test the hypothesis that SpHb monitoring was equivalent to that of HemoCue® (the automated hemoglobin measurement in the laboratory taken as a reference method) during acute surgical hemorrhage.

Methods: Blood for laboratory analysis was sampled after induction of anesthesia, during surgery according to the requirements of the anesthesiologist, and finally after the transfer of the patient to the recovery room. When each blood sample was taken, capillary samples were obtained for analysis with HemoCue®. SpHb monitoring was performed continuously during surgery. Using the automated hemoglobin measurement in the laboratory as a reference method, the authors tested the hypothesis that SpHb monitoring was equivalent to that of HemoCue®. The agreement between two methods was evaluated by linear regression and Bland and Altman analysis.

Results: Eighty-five simultaneous measurements from SpHb, HemoCue®, and the laboratory were obtained from 44 patients. Bland and Altman comparison of SpHb and HemoCue® with the laboratory measurement showed, respectively, bias of $-0.02 \pm 1.39$ g·dl$^{-1}$ and $-0.17 \pm 1.05$ g·dl$^{-1}$, and a precision of $1.11 \pm 0.83$ g·dl$^{-1}$ and $0.67 \pm 0.83$ g·dl$^{-1}$. Considering an acceptable difference of $\pm 1.0$ g·dl$^{-1}$ with the laboratory measurement, the percentage of outliers was significantly higher for SpHb than for HemoCue® (46% vs. 16%, P < 0.05).

Conclusions: Taking automated laboratory hemoglobin measurement as a reference, the study shows that SpHb monitoring with Radical-7® gives lower readings than does the HemoCue® for assessment of hemoglobin concentration during hemorrhagic surgery.

What We Already Know about This Topic

• Point-of-care devices may help to get intraoperative immediate information on hemoglobin values. In the clinical setting the accuracy of the devices is a matter of controversy.

What This Article Tells Us That Is New

• During hemorrhagic events, the accuracy of different point-of-care hemoglobin measurements may differ. In this study in acute hemorrhagic patients, the spectrophotometry-based technique used in the Radical-7® Pulse CO-Oximeter (noninvasive and continuous measurements) showed lower readings than did the HemoCue®.

DURING surgery, anesthesiologists frequently are required to manage hemorrhagic events. However, the precise quantification of hemorrhage may be clinically imprecise because of blood lost in the surgical dressings and dilution by other liquids from the surgical field in the aspiration system. Consequently, intraoperative measurement of hemoglobin concentration is essential to decide if transfusions of erythrocyte concentrates should be performed.

Hemoglobin measurement with an automated analyzer in the clinical laboratory is the gold standard for the measurement of the hemoglobin concentration, as recommended by the International Committee for Standardization in Hematology. 

Currently, the photometric cyanmethemoglobin method is the most widely used for this assay. In addition to...
its reliability, laboratory analysis provides supplemental diagnostic information, such as platelet counts, which are essential during surgery associated with major blood loss. However, this method has several limitations, one of the more important of which is the time needed for the anesthesiologist to obtain the result. The delay in obtaining the result is attributable to the time required for blood sampling, transport to the laboratory, analysis of the sample, validation of the measurement, and return of the result to the physician, and all of which can delay the acquisition of the critical data from minutes to hours. In addition, repeated measurements may induce significant blood spoliation, which could be of extreme importance in the intensive care unit and neonatology.

Immediate hemoglobin measurements are available with portable point-of-care devices such as the HemoCue® (HemoCue, Ängelholm, Sweden), which uses the azide-methemoglobin reaction and photometry absorbance. A small volume of blood (10 µl) must be deposited into a single-use cuvette for analysis, after which the HemoCue® device displays the hemoglobin concentration in less than 1 min. The precision of this method is reported to be ± 1.5% compared with the laboratory analysis, with a correlation coefficient of 0.89.

Recently, a new noninvasive, spectrophotometry-based monitoring technology has been introduced (Radical-7® Pulse CO-Oximeter; Masimo Corp., Irvine, CA) that provides immediate and continuous hemoglobin (SpHb) measurement. Similar to conventional pulse oximetry, the method is based on the measurement of the differential optical density of different wavelengths of light passed through the finger. Transmitted light is captured by photodiode receptor and analyzed to create an analog signal that in turn is converted to a digital signal, using proprietary algorithms. The first validation study of this device was presented as an abstract in 2007 by Macknet et al. and recently published. The authors compared SpHb measurements to measured hemoglobin concentrations in both surgical patients and volunteers, and reported a correlation coefficient of 0.88 compared with laboratory CO-oximetry, for hemoglobin values ranging from 4.4 to 15.8 g·dl⁻¹. However the accuracy of SpHb monitoring during acute surgical hemorrhage has not been evaluated.

In the current study, we tested the hypothesis that SpHb monitoring was equivalent to that of HemoCue® (the automated hemoglobin measurement in the laboratory taken as a reference method) during acute hemorrhage in patients scheduled for elective urologic surgical procedures.

**Materials and Methods**

**Patients**

Approval for this study was obtained from an ethical committee (Comité de Protection des Personnes Île-de-France IV, Hôpital Saint-Louis, Paris, France). According to French law, because blood samples for hemoglobin measurement in the laboratory and with the HemoCue® were performed as routine care, and because SpHb monitoring is a noninvasive method, the ethical committee determined that consent of patients was waived for participation in this study. Between December 2008 and April 2009, we consecutively included adult patients scheduled for potentially hemorrhagic major urologic surgery (i.e., nephrectomy, renal transplantation, prostatic adenomectomy, radical prostatectomy, or total cystectomy with replacement cystoplasty).

**Anesthesia and Monitoring**

A standardized total intravenous anesthesia protocol was performed in all patients, based on continuous infusion of propofol (target induction concentration: 6 mcg·ml⁻¹) and remifentanil (target induction concentration: 4 ng·ml⁻¹), further adapted during surgery to maintain a bispectral index (BIS-XP®; Aspect Medical Systems, Norwood, MA) of approximately 40. The standard hemodynamic monitoring used was electrocardiogram, pulse oximetry, and noninvasive or invasive arterial pressure, as needed. Central body temperature was also monitored. A single device for measurement of hemoglobin concentration, a Radical-7® Pulse CO-Oximeter, software version 7409, with disposable adhesive SpHb finger sensor (Rev C) was added to the standard monitoring. To eliminate light interference, this sensor was placed on a hand without a pulse oximeter probe and covered with an opaque shield to protect it from bright ambient light, as recommended by the manufacturer.

**Hemoglobin Measurements**

Hemoglobin measurements with the automated analyzer in the laboratory (hemoglobinLaboratory) and with the HemoCue® (hemoglobinHemoCue) were performed in accordance with our standard clinical practice for potentially hemorrhagic surgery. Briefly, blood for analysis in the laboratory was sampled immediately after induction of anesthesia while the second venous line was being inserted into the patient; again during surgery, according to the requirement of the anesthesiologist; and after the transfer of the patient to the recovery room. Hemoglobin measurements in the laboratory were performed using a hematology analyzer (SP 1000®; Sysmex Corp., Kobe, Japan). Capillary blood for hemoglobin measurements with the HemoCue® 201+ (HemoCue, Ängelholm, Sweden) was obtained only from finger or ear punctures, which were performed at the same time as blood samples taken for laboratory analysis. Because analysis of a single drop of blood may result in imprecise measurements, even when samples are collected by experienced personnel, duplicate blood samples were collected by only one person from only one finger or ear puncture site in the patient, and the mean value of the two analyses was retained, as described previously, and as is the standard practice for our institution. Finally, to guarantee HemoCue® cuvette function, all cuvettes used in this study were recently (within 1 month) obtained from the manufacturer.

Monitoring with the Radical-7® Pulse CO-Oximeter was performed continuously from the induction of anesthesia.
until the transfer of the patient to the recovery room. The variables recorded from the Radical-7® Pulse CO-Oximeter were SpHb values (hemoglobinSpHb) and the perfusion index. Because SpHb is continuous monitoring, the value that was considered for comparison with invasive measurements was averaged over the time interval of blood sampling, which was usually less than 1 min. Data were stored by the Radical-7® Pulse CO-Oximeter and later transferred to a computer for off-line analysis.

**Erythrocyte Concentrate Transfusion during Surgery**

Hemoglobin thresholds for erythrocyte concentrate transfusion were those currently recommended by the French Health Authorities: 7 g · dl⁻¹ for patients without disease, 8–9 g · dl⁻¹ for patients with cardiovascular diseases, and 10 g · dl⁻¹ for patients with cardiac and/or coronary insufficiency. Therefore, according to our usual clinical practice, because most of our patients scheduled for urologic surgery have preexisting cardiovascular disease, the relevant threshold for erythrocyte concentrate transfusion during surgery often was 8 g · dl⁻¹. Erythrocyte concentrate transfusion usually was decided either from a hemoglobin value obtained from HemoCue® and/or from laboratory analysis, and/or according to the clinical judgment of the anesthesiologist in charge of the patient. Conversely, during this study, SpHb values obtained from the Radical-7® monitor were never used for any decision concerning erythrocyte concentrate transfusion.

**Statistical Analysis**

We conducted an equivalence trial comparing HemoCue® and SpHb. Assuming an α risk of 0.05 and a β risk of 0.10, a proportion of outliers in the HemoCue® group of 20%, and a maximum tolerable proportion of outliers in the SpHb group of 35% with a proportion of discordant measurements of 20%, we calculated that 77 measurements were required to test equivalence between HemoCue® and SpHb, taking automated laboratory analysis as a reference method (NQuery Advisor 6.0; Statistical Solutions Ltd., Cork, Ireland). Assuming a proportion of drop-out measurements of 10%, we decided to include at least 85 measurements.

Statistical analysis was performed using NCSS 2001© (Statistical Solutions Ltd.). Data are expressed as mean ± SD or median and its 25–75 interquartile interval for nonnormally distributed variables, or number and percentages. The concordance between two methods was evaluated by linear regression (correlation coefficients) and Bland and Altman analysis, which determined bias, precision, and agreement of SpHb monitoring and HemoCue®, taking the automated analysis in the laboratory as the reference. Because our design included clustering of measurements within individuals over time performed in the same patient, we used appropriate correction for calculating the limits of agreement.

Lastly, we calculated the percentage of outliers for both SpHb monitoring and HemoCue®, which were defined as difference values with the reference method of the interval ± 1 g · dl⁻¹, as described previously. This variable was considered as the main endpoint. All P values were two-tailed, and a P value <0.05 was considered significant.

**Results**

The characteristics of the patients in the study and the surgical procedures performed are presented in table 1. Hemoglobin measurements were performed in 44 patients, which provided 141 values for hemoglobinSpHb, 126 values for hemoglobinHemoCue, and 102 values for hemoglobinLaboratory. However, only 85 hemoglobin measurements simultaneously performed with SpHb, HemoCue®, and analyzer in the laboratory were retained for final analysis. Hemoglobin measurements are presented in table 2. With the hemoglobin measurement performed in the laboratory considered as the reference value, 27 (32%) hemoglobin values were lower than 10 g · dl⁻¹, and 10 (12%) were lower than 8 g · dl⁻¹.

SpHb monitoring was uneventful in all patients. The Radical-7® Pulse CO-Oximeter displayed a continuous online trend of SpHb variations during surgery. Figure 1 represents typical tracing of SpHb monitoring during nephrectomy and cavectomy in a 50-yr-old patient. Variables of comparison of hemoglobin measurements by the Radical-7® Pulse CO-Oximeter, the HemoCue®, and the automated analyzer are presented in table 2. Linear regression showed a good correlation between hemoglobinHemoCue and hemoglobinLaboratory (coefficient of correlation: 0.85 [95% CI 0.78–0.90]) and between hemoglobinSpHb and hemoglobinLaboratory (coefficient of correlation: 0.77 [95% CI 0.67–0.84]) (fig. 2). Bland and Altman analysis showed a better agreement of hemoglobinHemoCue with he-

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### Table 1. Characteristics of Patients and Surgical Procedures

<table>
<thead>
<tr>
<th>Patients</th>
<th>n = 44</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>58 ± 13</td>
</tr>
<tr>
<td>Sex ratio M/F</td>
<td>31/13</td>
</tr>
<tr>
<td>Surgical procedures</td>
<td></td>
</tr>
<tr>
<td>Nephrectomy (of which 2 with cavectomy)</td>
<td>15</td>
</tr>
<tr>
<td>Renal transplantation</td>
<td>15</td>
</tr>
<tr>
<td>Prostatic adenomectomy</td>
<td>4</td>
</tr>
<tr>
<td>Radical prostatectomy</td>
<td>9</td>
</tr>
<tr>
<td>Total cystectomy with replacement cystoplasty</td>
<td>1</td>
</tr>
</tbody>
</table>

Hemoglobin values are reference measurements performed by automated laboratory analysis. Data are expressed as mean ± SD, or median [interquartile range].

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moglobin_{Laboratory} than the agreement of hemoglobin_{SpHb} with hemoglobin_{Laboratory} (fig. 3). The bias was not significantly different from 0 with both methods. The precision of hemoglobin_{HemoCue} was significantly better than that of hemoglobin_{SpHb} (table 2). Consecutively, the percentage of outliers for SpHb monitoring was significantly higher than for the HemoCue® (46% vs. 16%, P < 0.05), which leads to rejection of the hypothesis of the equivalence between SpHb monitoring and HemoCue®. Finally, linear regression analysis showed no significant correlation between the difference (hemoglobin_{SpHb} − hemoglobin_{Laboratory}) and perfusion index (R = 0.09, NS) or temperature (R = 0.05, NS).

### Discussion

In this study, we have shown that hemoglobin monitoring with the Radical-7 Pulse CO-Oximeter gives lower readings than the HemoCue® compared with the automated hemoglobin measurement in the laboratory. Considering an acceptable difference to be less than ±1 g · dl⁻¹ with the laboratory measurement, the percentage of outliers for SpHb monitoring was significantly higher than for the HemoCue® (46% vs. 16%, P < 0.05), so the hypothesis of equivalence between SpHb and HemoCue® must be rejected.

Traditionally, clinical measurement of hemoglobin values requires analysis of a blood sample with an automated laboratory device, such as a CO-oximeter, usually performed in the hematology department.²,³ However, whereas CO-oximeters represent the reference method for hemoglobin measurement, their accuracy range in the clinical setting is often wider than the official specification. For example, comparing two identical devices of five different manufacturers, Gehring et al. reported significant intradevice and interdevice variations in hemoglobin measurements.¹⁸ It is also important to note that there is no standard procedure for checking the measurement error of CO-oximeters, and both the reference device and test device may have inherent errors. In addition, from the Bland and Altman comparison, we must bear in mind that both reference device and test device could be responsible for inherent errors.¹⁸ Finally, the expected percentage difference between several instruments measuring hemoglobin in a laboratory is estimated to be ±7% of the target value, as suggested by the Clinical Laboratories Improvement Act of 1988.¹⁹

The HemoCue® portable hemoglobinometer has been available for several years and has been found to give precise and accurate results when used on venous blood in laboratory conditions.⁴ Indeed, when blood samples are obtained under ideal conditions (i.e., from a venous site rather than a capillary stick), the coefficient of variation of HemoCue® ranges between 1.4% and 2.2%, which is only slightly higher than the precision of current hematology analyzers.¹⁰,²⁰–²² In this study, for capillary blood samples obtained from finger and ear punctures, we showed a significant correlation (R = 0.85, P < 0.001) between HemoCue® and automated hemoglobin analysis in the laboratory, with a nonsignificant bias of −0.17 ± 1.05 g · dl⁻¹ (fig. 2 and 3). This result is in agreement with previous studies, which reported that finger stick samples may overestimate in hemoglobin measurements from −0.1 to +0.4 g · dl⁻¹ and that ear stick samples may differ from the hemoglobin concentration in a range of −0.7 to +2.8 g · dl⁻¹.¹⁷,²²–²⁵ Using capillary blood samples to
compare HemoCue® and automated hemoglobin analysis, Van de Louw et al. reported discrepancies of more than 1 g/dL in 21% of cases and more than 2 g/dL in 4% of cases.26 In critically ill patients, Seguin et al.27 recently showed a poor agreement between laboratory hemoglobin measurement and HemoCue®, especially with capillary blood samples and to a much greater extent for patients with edema. Nevertheless, whereas skin punctures do not represent the ideal sample for HemoCue® measurement, we decided to use this method in the study for the following reasons: it is the one currently performed in our daily practice, hemoglobin measurements have to be repeated during surgery, and most of our patients were not equipped with invasive arterial pressure monitoring that enabled repeated samples. Elsewhere, to limit the measurement variability, the hemoglobin value that we retained for analysis was the mean value of a duplicate blood sample obtained after the finger or ear puncture, as described previously.10 The method of blood collection from a skin puncture may effectively interfere with hemoglobin measurement by HemoCue®. For example, Reeves et al. reported a difference of 0.5 g/dL between duplicate skin puncture samples, with 10% of paired values differing by ≥1 g/dL.28 To limit such variations, Mills and Meadows suggested that HemoCue® cuvettes should be filled from bottle capillary samples, rather than a single blood drop taken directly from the finger.29 On the other hand, the manufacturer recommends the analysis of a single drop of blood, of which the most representative should be the fourth one forming at the puncture site. Finally, because environmental storage conditions such as high humidity may affect HemoCue® cuvette function, we used only cuvettes that had been recently (within 1 month) supplied by the manufacturer.11 The cuvette itself may explain as much as 68% of the variability between the HemoCue® and CO-oximeter hemoglobin measurements.30

Fig. 2. Representation of linear regression between hemoglobinSpHb and hemoglobinLaboratory (A), and between hemoglobinHemoCue and hemoglobinLaboratory (B). Regression line (continuous line) and 95% CI lines (dashed lines) are represented on the graphs. The interception lines do not occur at 0 because of the respective bias of SpHb and HemoCue®, with the automated laboratory hemoglobin measurement considered as the reference method. HemoglobinHemoCue = hemoglobin measurement by HemoCue® 201+ (HemoCue, Ängelholm, Sweden); hemoglobinLaboratory = automated laboratory hemoglobin measurement (n = 85); hemoglobinSpHb = SpHb monitoring by the Radical-7® Pulse CO-Oximeter monitor (Masimo Corp., Irvine, CA).

Fig. 3. Bland and Altman representation of comparison analysis between hemoglobinSpHb and hemoglobinLaboratory (A) and between hemoglobinHemoCue and hemoglobinLaboratory (B). Bias (continuous line), limits of agreement (bias ± 1.96·SD, dashed lines) and outlier limits (bias ± 1 g/dL, dotted lines) are represented on the graphs (n = 85). HemoglobinHemoCue = hemoglobin measurement by HemoCue® 201+ (HemoCue, Ängelholm, Sweden); hemoglobinLaboratory = automated laboratory hemoglobin measurement; HemoglobinSpHb = SpHb monitoring by the Radical-7® Pulse CO-Oximeter monitor (Masimo Corp., Irvine, CA).
Considering SpHb monitoring, we showed a significant correlation (R = 0.77, P < 0.001) and a nonsignificant bias in hemoglobin measurement of −0.02 ± 1.39 g · dl⁻¹ compared with automated analysis in the laboratory (figs. 2 and 3). This is in close agreement with the preliminary study of Macknet et al., published as an abstract, who reported a bias of 0.03 ± 1.12 g · dl⁻¹. However, 18 of the 48 subjects investigated by these authors were not surgical patients but healthy volunteers who underwent an hemodilution protocol. To the best of our knowledge, our study is the first to evaluate the accuracy of SpHb monitoring during hemorrhagic surgery, and we note that approximately one third of our hemoglobin measurements were less than 10 g · dl⁻¹. We showed no correlation between the difference (hemoglobinSpHb − hemoglobinLaboratory) and perfusion index (R = 0.09, NS) or temperature (R = 0.05, NS), which means that the accuracy of SpHb monitoring in our study was not linked to local circulation conditions.

We reported in this study a lower correlation between SpHb and laboratory hemoglobin measurement than that between HemoCue® and laboratory measurement. Similarly, the precision of SpHb was significantly less and the number of outliers significantly higher than that of HemoCue®. To the best of our knowledge, our study is the first to evaluate the equivalence between SpHb monitoring and HemoCue®. From our findings, we conclude that these two devices are not equivalent for hemoglobin measurement during acute surgical hemorrhage, taking as reference the hemoglobin measurements made in the laboratory.

However, we must keep in mind that automated hemoglobin analysis in the laboratory, the HemoCue® point-of-care device, and SpHb monitoring may not be considered only as competing, but also complementary, methods for hemoglobin measurement. First, automated analysis performed in the hematology laboratory represents the reference method for the hemoglobin measurement, recommended for several decades by the International Committee for Standardization in Hematology.²,3 The major limitations of this method are the need for a blood sample, the time needed for the physician to obtain the result, and the blood spoilation induced by repeated measurements.⁴ Second, the HemoCue® is a portable point-of-care device, which displays the hemoglobin concentration in less than 1 min after analysis of a very small volume of blood sampled either from a venous or skin puncture.⁶,⁷ However, the accuracy of the HemoCue® device is lower than that of CO-oximeters in the laboratory, and the variability is much more significant for capillary samples.¹⁷,²²–²⁷ In addition to these two invasive methods, SpHb monitoring is a new continuous noninvasive method of hemoglobin measurement based on spectrophotometry technology, still under improvement, for which the first validation studies were presented in 2007 by Macknet et al. Although results from these authors and our studies seem to show good correlation between SpHb and hemoglobin laboratory measurement, our study clearly shows that SpHb is not equivalent to HemoCue® for hemoglobin measurement, taking as reference the automated hemoglobin measurement in the laboratory (figs. 2 and 3). However, the main benefits of SpHb monitoring are the noninvasiveness (no blood sample is required) and the continuous online assessment of hemoglobin concentration (fig. 1). Indeed, continuous online monitoring of SpHb enables the instantaneous detection of a hemoglobin drop, whereas the physician had not yet scheduled an invasive hemoglobin measurement, either by a point of care device (result in 1 min) or by analysis in the hematology laboratory (delayed result). In this situation, by the time the result arrived from an invasive measurement, acute anemia might be responsible for coronary ischemia, especially in patients with preexisting cardiovascular diseases. Thus, continuity and noninvasiveness of online SpHb monitoring undoubtedly represent an improvement for transfusion management during perioperative patient care. Finally, more than the absolute and instantaneous hemoglobin value displayed by the Radical-7® Pulse CO-Oximeter, continuous measurement allows the physician to focus on the hemoglobin trend and detect either a slow decrease or a significant rapid drop in hemoglobin, and therefore decide the appropriate time to perform an invasive measurement of hemoglobin.

We note several limitations of our study. First, this innovative technology is still developing, and the study was conducted using a sensor version (Rev C) that is now obsolete. Indeed, research continues on this new technology to develop new and more reliable finger probes, to improve performance during hypothermia, vasoconstriction, and hypoperfusion. Second, considering that both the site and method used for blood sampling could affect hemoglobin measurement, we have to bear in mind that SpHb values from the Radical-7® Pulse CO-Oximeter, values from capillary blood samples, and values from venous blood samples represent different endpoints. Third, in our study, whereas approximately one third of hemoglobin values were less than 10 g · dl⁻¹, only 12% were less than our current erythrocyte concentration transfusion threshold of 8.0 g · dl⁻¹, which could limit its relevancy for evaluating SpHb monitoring during hemorrhage. Nevertheless, because most of our urologic surgical procedures were performed on patients with preexisting cardiovascular diseases, we obviously could not tolerate prolonged decreased hemoglobin values in this population. Finally, as suggested previously by Radtke et al., we chose an acceptable difference of less than ± 1 g · dl⁻¹ between SpHb or HemoCue® versus the reference hemoglobin measurement in the laboratory.¹⁷ The relevancy of this limit should be interpreted with caution because a 1 g · dl⁻¹ error obviously does not have similar consequences for a hemoglobin measurement of 14 or 8 g · dl⁻¹.

In conclusion, taking an automated laboratory hemoglobin measurement as reference, our study shows that SpHb monitoring with Radical-7® Pulse CO-Oximeter gives lower readings than the HemoCue® for assessment of hemoglobin concentration during hemorrhagic surgery. However, this
should be weighed against the advantage of continuity and the noninvasiveness of online assessment of hemoglobin concentration.

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