Accuracy of non-invasive measurement of haemoglobin concentration by pulse co-oximetry during steady-state and dynamic conditions in liver surgery

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Editor’s key points
- Continuous monitoring of blood haemoglobin (Hb) concentration by multi-wavelength spectrophotometry might provide a non-invasive method to guide erythrocyte transfusion.
- The Masimo Radical 7 device was compared with point-of-care blood gas analysis for tracking Hb concentration during major liver surgery.
- Measurements of Hb by pulse co-oximetry correlated with direct measurements but underestimated values, particularly at higher Hb values and with colloid infusion.

Background. The Masimo Radical 7 (Masimo Corp., Irvine, CA, USA) pulse co-oximeter calculates haemoglobin concentration (SpHb) non-invasively using transcutaneous spectrophotometry. We compared SpHb with invasive satellite-lab haemoglobin monitoring (Hb\(_{\text{satlab}}\)) during major hepatic resections both under steady-state conditions and in a dynamic phase with fluid administration of crystalloid and colloid solutions.

Methods. Thirty patients undergoing major hepatic resection were included and randomized to receive a fluid bolus of 15 ml kg\(^{-1}\) colloid (n=15) or crystalloid (n=15) solution over 30 min. SpHb was continuously measured on the index finger, and venous blood samples were analysed in both the steady-state phase (from induction until completion of parenchymal transection) and the dynamic phase (during fluid bolus).

Results. Correlation was significant between SpHb and Hb\(_{\text{satlab}}\) (\(R^2=0.50, n=543\)). The modified Bland–Altman analysis for repeated measurements showed a bias (precision) of \(-0.27 (1.06)\) and \(-0.02 (1.07)\) g dl\(^{-1}\) for the steady-state and dynamic phases, respectively. SpHb accuracy increased when Hb\(_{\text{satlab}}\) was <10 g dl\(^{-1}\), with a bias (precision) of 0.41 (0.47) vs -0.26 (1.12) g dl\(^{-1}\) for values >10 g dl\(^{-1}\), but accuracy decreased after colloid administration (\(R^2=0.25\)).

Conclusions. SpHb correlated moderately with Hb\(_{\text{satlab}}\) with a slight underestimation in both phases in patients undergoing major hepatic resection. Accuracy increased for lower Hb\(_{\text{satlab}}\) values but decreased in the presence of colloid solution. Further improvements are necessary to improve device accuracy under these conditions, so that SpHb might become a sensitive screening device for clinically significant anaemia.

Keywords: haemoglobin; i.v. fluids; method comparison; transcutaneous oximetry

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factors influencing the accuracy of SpHb monitoring. We studied the accuracy of SpHb monitoring under steady-state conditions during hepatic parenchymal transection with a continuous standardized fluid administration. In addition, we studied SpHb accuracy under dynamic conditions by administration of bolus fluid administration after completion of parenchymal transection. Subjects were randomized to receive either crystalloid or colloid solutions in this phase to investigate their influence on SpHb accuracy.

Methods

This observational prospective randomized controlled trial was approved by the local ethics committee (Ref: 2009/174, University Medical Center Groningen, The Netherlands) and was registered at clinicaltrials.gov (NCT01060683). Inclusion of patients was performed using the CONSORT group statement (Fig. 1). All eligible ASA I–III patients undergoing major hepatic resection between June 2010 and May 2011 were approached and screened. Patients with an intraoperatively diagnosed unresectable tumour or patients who required extra i.v. fluids in order to maintain haemodynamic stability and thereby violated the study protocol (see further) were excluded.

After signing written informed consent, all included subjects were randomized shortly before the start of the dynamic phase (see below) using opaque envelopes allocating subjects to either the crystalloid or the colloid group.

Anaesthetic management

A thoracic epidural catheter was inserted at T7 or T8 before the induction of general anaesthesia. Anaesthesia was induced with propofol 2 mg kg\(^{-1}\) and sufentanil 0.3 \(\mu\)g kg\(^{-1}\). Tracheal intubation was facilitated with rocuronium 0.6 mg kg\(^{-1}\) and additional rocuronium administration was guided by neuromuscular monitoring during the procedure. Anaesthesia was maintained with isoflurane, target bispectral index (Aspect Medical Systems, Norwood, MA, USA) around 50 (range 40–60). Sufentanil was administered continuously at 20 \(\mu\)g h\(^{-1}\) i.v. A central venous line (7 Fr triple lumen) was inserted in the right internal jugular vein for continuous monitoring of central venous pressure (CVP), blood sampling, and drug infusion. A radial artery was cannulated (20 G catheter) for continuous monitoring of arterial blood pressure and blood gas analysis.

If necessary, norepinephrine infusion was titrated to obtain a mean arterial pressure above 60 mm Hg. Subjects were ventilated using volume-controlled mechanical ventilation (tidal volume: 6–8 ml kg\(^{-1}\)) with a mixture of \(O_2/air\) (inspired oxygen fraction, \(F_{IO_2}\), 0.30–0.35) and isoflurane. Respiratory rate was adjusted to maintain normocapnia.

Fluid administration

The steady-state phase was defined as the time between the induction of anaesthesia and the completion of hepatic parenchymal transection. During this phase, fluid administration was restricted to 6 ml kg\(^{-1}\) h\(^{-1}\) crystalloid solution (NaCl 0.9%, Baxter, Deerfield, IL, USA) to create a low CVP in order to minimize blood loss.9 10

The dynamic phase was defined as the time between the start of the standardized fluid bolus administration and 30 min thereafter. Patients were randomly assigned to receive a bolus of either 15 ml kg\(^{-1}\) crystalloid (NaCl 0.9%) or 15 ml kg\(^{-1}\) colloid (Voluven 6%, Fresenius, Bad Homburg, Germany) in 30 min.

Continuous non-invasive SpHb measurement

SpHb was measured non-invasively and continuously using a Masimo Radical 7 device running Masimo SET V7.6.0.1 using a finger sensor (R2-25, Rev E). Perfusion index (PI)—the ratio of pulsatile blood to non-pulsatile blood—can influence SpHb accuracy and is additionally calculated by this device continuously.3

Before the induction of anaesthesia, the sensor was attached to the index finger, contralateral to the arterial line, and connected to the device according to the manufacturer’s instructions.

Invasive Hb concentration measurement

\(Hb_{satlab}\) was measured using the ABL 800 (Radiometer GmbH, Copenhagen, Denmark) point-of-care satellite-lab blood gas analyser, which was located in a room next to the operating theatre. This device measures Hb concentration by spectrophotometric analysis, is well correlated to central laboratory Hb analysis, and has a repeatability error below 2% over a test range between 2.5 and 23 g dl\(^{-1}\).1 The device is linked to the central laboratory; maintenance, calibration, and quality control are performed on a daily basis. After the induction of anaesthesia but before incision, a baseline blood sample was drawn from the cannulated jugular vein for \(Hb_{satlab}\) analysis, and subsequently every 30 min during the steady-state phase. In the dynamic phase, \(Hb_{satlab}\) was measured every 5 min. Blood samples were drawn into standard 2 ml heparinized collection syringes, after 2 ml blood was extracted and removed in separate collection syringes to ensure valid blood gas analysis. Blood samples were analysed immediately after collection.

Data registration

All continuous data, including SpHb, PI, and \(F_{IO_2}\), were recorded by a medical grade Windows XP-based personal computer running RugLoop II software (Demed Engineering, Temse, Belgium). Data were stored every second, and data extraction was performed using Labgrab software (Demed Engineering) and subsequently exported to Microsoft Excel 2010 (Microsoft, Redmond, WA, USA).

Statistical analysis

Statistical analysis was performed using Microsoft Excel 2010 and SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). Continuous data were tested for normal distribution using the
Kolmogorov–Smirnov test and were expressed as mean (SD) for normally distributed variables and as median (range) for non-normally distributed variables. Patient and surgical characteristics were tested using the Mann–Whitney test or Fisher’s exact test, when appropriate.

Correlation between simultaneous \( \text{Hb}_{\text{satlab}} \) and SpHb measurement pairs was depicted in a scatter plot, and coefficients of determination (\( R^2 \) values) were calculated. To assess SpHb accuracy in time, consecutive \( R^2 \) values were calculated for all measured intervals in the steady-state and dynamic phases.

SpHb accuracy was assessed using a modified Bland–Altman analysis corrected for multiple measurements for comparison of all SpHb and \( \text{Hb}_{\text{satlab}} \) values in the steady-state and dynamic phases.\(^{11, 12} \) The bias (mean absolute difference, calculated as SpHb–\( \text{Hb}_{\text{satlab}} \)) [precision (1 SD of the bias)] and limits of agreement [LOA (1.96 SD of the bias)] were calculated and corrected for repeated measurements. For the measurement pairs at specific time points (baseline, start, and end of dynamic phase), a conventional Bland–Altman analysis was performed.

Differences of SpHb and \( \text{Hb}_{\text{satlab}} \) values (delta values) between consecutive time points were depicted in a scatter plot, aimed to assess whether a directional change of \( \text{Hb}_{\text{satlab}} \) corresponds with a comparable directional change of SpHb. A threshold of 1.0 g dl\(^{-1} \) for a delta value was used to compensate for intrinsic SpHb bias.\(^{13} \) Correlation analysis was performed to assess the influence of \( \text{Hb}_{\text{satlab}} \) concentration, PI, and \( F_1O_2 \) on SpHb accuracy.

All tests were two-sided and a \( P \)-value of <0.05 was considered statistically significant.

**Results**

A total of 30 subjects were randomized (Fig. 1). Except for height, there were no significant differences in subject characteristics between the groups (Table 1). More men were randomized to the colloid group and more women were randomized to the crystalloid group, but this was not statistically significant.

In total, 543 simultaneous SpHb and \( \text{Hb}_{\text{satlab}} \) data samples were obtained during the investigation. The mean SpHb was 11.5 (1.6) g dl\(^{-1} \) (range 7.3–15.3 g dl\(^{-1} \)). The mean \( \text{Hb}_{\text{satlab}} \) was 11.7 (1.6) g dl\(^{-1} \) (range 7.4–15.3 g dl\(^{-1} \)). The \( R^2 \) value between all SpHb and \( \text{Hb}_{\text{satlab}} \) data points (Fig. 2) was 0.50 [95% confidence interval (CI) 0.45–0.55]. In the steady-state phase (\( n=335 \)), \( R^2 \) was 0.45 (CI 0.37–0.53), and was 0.42 (CI 0.31–0.52) in the dynamic phase (\( n=208 \)).

A modified Bland–Altman analysis for repeated measurements was performed for all data points (not shown) and for data points during the steady-state and dynamic phase (Fig. 3A and B, respectively). The bias (precision) was –0.17 (CI −0.21 to −0.13) (1.0), −0.27 (CI −0.32 to −0.21) (1.06), and −0.02 (CI −0.09 to 0.05) (1.07) g dl\(^{-1} \), respectively, with concomitant LOA of −2.16/2.12 g dl\(^{-1} \). A conventional Bland–Altman analysis for the measurement intervals at baseline and at the start and end of the...
dynamic phase showed a bias (precision) of $-0.55$ (CI $-0.75$ to $-0.35$) (1.13), $-0.47$ (CI $-0.21$ to $-0.72$) (1.44), and $0.18$ (CI $0.02$ to $0.33$) (0.89), respectively, with LOA of $-2.81/1.70$, $-3.35/2.41$, and $-1.60/1.95$ g dl$^{-1}$ (data not shown).

### Trend analysis of SpHb accuracy

Consecutive directional Hb concentration changes of $>1.0$ g dl$^{-1}$ for both SpHb and Hb$\text{satlab}$ values were calculated and plotted (Fig. 4). Of these points ($n=60$), 72% ($n=43$) are from Hb$\text{satlab}$ values $>10$ g dl$^{-1}$ (blue filled circles), whereas 28% ($n=17$) are from Hb$\text{satlab}$ values $<10$ g dl$^{-1}$ (green empty circles), while 66% of all measurement points are from an Hb$\text{satlab}$ value $>10$ g dl$^{-1}$, and 34% from an Hb$\text{satlab}$ value $<10$ g dl$^{-1}$.

### Influence of the dynamic phase and type of fluid on SpHb accuracy

$R^2$ values ranged from 0.36 to 0.56 with a mean of 0.45 (CI $0.37–0.53$) at the measurement intervals in the steady-state phase (data not shown). At the last measurement interval in the steady-state phase, $R^2$ was 0.56 (CI $0.34–0.78$) for all subjects and 0.71 (CI $0.49–0.93$) and 0.55 (CI $0.25–0.85$) for those subjects later allocated to receive crystalloids or colloids, respectively (Fig. 5).

Repetitive $R^2$ values and the corresponding Hb$\text{satlab}$ values at all measurement points in the dynamic phase are shown for the crystalloid and colloid groups in Figure 5.

At the start of the dynamic phase, Hb$\text{satlab}$ was significantly lower in the crystalloid group compared with the colloid group [11.4 (1.1) g dl$^{-1}$ compared with 12.5 (1.4) g dl$^{-1}$, ...
The $R^2$ value dropped upon start of the dynamic phase from 0.72 (CI 0.51–0.93) to 0.56 (CI 0.27–0.85) for crystalloid subjects ($n=15$) and from 0.41 (CI 0.08–0.74) to 0.13 (CI –0.14 to 0.41) for colloid subjects ($n=15$). In the crystalloid group, $R^2$ gradually increased to 0.81 (CI 0.66–0.96) at the end of the dynamic phase, whereas for colloid subjects, $R^2$ decreased to 0.11 (CI –0.15 to 0.37) 15 min after the start of the dynamic phase, but eventually recovered to 0.45 (CI 0.12–0.78) at the end of this phase. The $R^2$ values of all data points in the dynamic phase for the crystalloid ($n=104$) and colloid ($n=104$) groups were 0.72 (CI 0.63–0.81) and 0.25 (CI 0.11–0.39), respectively.

**Other influencing factors on SpHb accuracy**

Correlation was significant between the bias (SpHb–$H_{b\text{satlab}}$) and the $H_{b\text{satlab}}$ concentration ($P<0.001$), and corresponded with an $R^2$ value of 0.14.

For $H_{b\text{satlab}}$ values <10 g dl$^{-1}$, the corrected Bland–Altman analysis showed a mean bias (precision) of 0.41 (0.47) g dl$^{-1}$ with LOA between –0.55 and 1.36 g dl$^{-1}$.

For $H_{b\text{satlab}}$ values >10 g dl$^{-1}$, the mean bias (precision) was –0.26 (1.12) g dl$^{-1}$ with wider LOA: –2.50 to 1.84 g dl$^{-1}$. The bias between SpHb and $H_{b\text{satlab}}$ correlated significantly with the PI ($P<0.001$ with a corresponding $R^2$ value of 0.14), which was not true for $F_{I/O_2}$ (corresponding $R^2=0.01$).

**Discussion**

In this randomized prospective study, we evaluated the accuracy of transcutaneous SpHb measurement by the Masimo Radical 7 monitor during both steady-state and dynamic phases in patients undergoing major hepatic resection. We found the SpHb to be moderately correlated with $H_{b\text{satlab}}$ in both phases. The overall correlation between SpHb and $H_{b\text{satlab}}$ remained stable in the dynamic phase, although much lower SpHb accuracy was observed after bolus administration of colloid solution. In addition, we found superior accuracy of SpHb for $H_{b\text{satlab}}$ values <10 g dl$^{-1}$.

In the steady-state phase between the induction of anesthesia and the completion of hepatic parenchymal transection, SpHb accuracy was relatively stable while fluid was administered in a continuous matter at 6 ml kg$^{-1}$ h$^{-1}$ NaCl 0.9%. SpHb accuracy was also relatively stable in the dynamic phase with repetitive $R^2$ values ranging from 0.28 to 0.56 in the dynamic phase when subjects receiving crystalloid and colloids are analysed together.

Bias, precision, and LOA were generally comparable in the two phases and showed SpHb to slightly underestimate $H_{b\text{satlab}}$.

The accuracy of the SpHb measurement has been previously assessed under several clinical circumstances,
SpHb accuracy under steady-state and dynamic conditions

including patients undergoing surgery. One study in a mixed population of surgical patients \(n=44\) found a mean SpHb bias of \(-0.02\) with a precision of \(1.39\) g dl\(^{-1}\), LOA of \(-2.75/2.70\) g dl\(^{-1}\), and \(R\) of 0.77 compared with laboratory Hb measurements. Another study comparing SpHb with laboratory Hb measurements found a mean bias of \(0.26\) g dl\(^{-1}\) with the corresponding LOA of \(-3.24\) and \(3.77\) g dl\(^{-1}\) in patients undergoing spine surgery \(n=20\).

Our results are in accordance with these studies, as we found an overall \(R^2\) of 0.50 and a mean bias and precision of \(-0.17\) and \(1.0\) g dl\(^{-1}\) for all data points, but our LOA was generally more narrow.

An important finding in this study is the dependence of SpHb accuracy on the Hb concentration: for \(Hb_{satlab}\) values <10 g dl\(^{-1}\), SpHb accuracy improved dramatically with more precision and narrow LOA compared with values >10 g dl\(^{-1}\). Interestingly, SpHb tended to overestimate \(Hb_{satlab}\) in the lower range, while it tended to underestimate it in the higher \(Hb_{satlab}\) range. In a previous study investigating SpHb accuracy in healthy volunteers \(n=20\) undergoing haemodilution by infusion of crystalloid infusion, a weaker relationship was found between SpHb accuracy and Hb concentration. The dependence we observed of SpHb accuracy on actual Hb concentration is of major clinical importance since decisions on whether or not blood transfusion should be administered require accurate SpHb measurement in lower Hb concentration ranges. Patients receiving colloids showed a decrease in SpHb correlation that remained throughout the dynamic phase, although it seemed to recover at the end of the dynamic phase.

There were more women than men randomized in the crystalloid group, whereas in the colloid group, the converse was true. The observed imbalance was not statistically significant, so the selection procedure appears unbiased. Men and women did not have different preoperative Hb concentrations [14.1 (1.4) g dl\(^{-1}\) compared with 13.2 (1.8) g dl\(^{-1}\), respectively; \(P=0.24\)], but at the start of the dynamic phase, a small difference was observed [12.5 (1.0) or 11.5 (1.5) g dl\(^{-1}\), for men or women; \(P=0.047\)]. The slightly higher Hb concentration in men (about 1.0 g dl\(^{-1}\)) combined with the greater number of men in the colloid group could explain the higher Hb concentrations observed in this group compared with the crystalloid group. This imbalance could also to some extent underlie the decreased accuracy of SpHb in subjects receiving colloids since we found SpHb is less accurate for the higher \(Hb_{satlab}\) values. We did not stratify for sampling between men and women (ensuring equal numbers in each group), but this would probably have, in retrospect, made the results easier to interpret.

The difference between \(R^2\) values for the crystalloid and colloid groups in the dynamic phase suggests that the colloid solution influences non-invasive spectrophotometric analysis of total Hb concentration. We speculate that accuracy is decreased immediately after colloid administration; however, the temporal resolution of the current study is insufficient to demonstrate this conclusively. There are some reports on the influence of colloid solution on in vitro Hb measurement, but we found no reports on possible effects of colloid solutions on the accuracy of in vivo transcutaneous spectrophotometry. Our data suggest that the accuracy of SpHb is decreased after rapid colloid administration. Colloids are often administered for volume expansion, especially during massive and rapid blood loss. The measured Hb is important for the decision to administer red blood cells. Therefore, the accuracy of the SpHb measurement while rapidly administering colloid solution requires further elucidation to avoid unnecessary blood transfusion or, on the other hand, omission of necessary blood transfusion, as both situations are potentially harmful.

We found the accuracy of SpHb to be slightly influenced by the local index of perfusion (PI) of the finger bearing the measurement probe with an overall \(R^2\) of the absolute bias and PI of 0.14. This finding is not surprising as diminished tissue perfusion is expected to disrupt spectrophotometric SpHb measurement as reported before.

A recent pilot study found that SpHb values changed significantly during preoxygenation with a high \(FIO_2\), suggesting that SpHb accuracy is influenced by high concentrations of oxygen. In our study, subjects were ventilated with a constant \(FIO_2\) between 0.30 and 0.35, so we cannot speculate on the influence of \(FIO_2\) on SpHb.

According to the manufacturer, SpHb measurement should be accurate within 1.0 g dl\(^{-1}\). If this threshold for accuracy is applied to our data, 61% of all data points and 58% and 66% of data points obtained during the static and dynamic phases, respectively, are within this range. For the steady-state and dynamic data points in our study, precision was slightly above 1.0 g dl\(^{-1}\) and thus slightly above this accuracy limit.

**Study limitations**

There are multiple technologies and devices available to measure blood Hb concentration. Every device has an intrinsic variability, and between devices there is also intra-device variability. No gold standard exists for the determination of Hb concentration. In this study, SpHb measurements correlated with Hb measurements by point-of-care satellite laboratory (\(Hb_{satlab}\)) analysis. \(Hb_{satlab}\) blood gas measurement was used because it is regarded as the clinical standard in the operating theatre in our hospital and in many other Western European hospitals for decisions regarding blood transfusion. In addition, the satellite laboratory device we used has a very small bias compared with central laboratory analysis with a repeatability error below 2% and is superior to two other frequently used satellite laboratory devices. The baseline \(Hb_{satlab}\) value of the studied subjects correlated highly with preoperative Hb concentration as measured by the central laboratory Sysmex XE-2100 (Sysmex, Kobe, Japan) analyser of our hospital (\(R^2=0.90\)). Nevertheless, one must take into account the inter- and intra-device variation in Hb measurement devices, especially when repeated measurement analyses are performed.
The lowest observed Hb_satlab value was 7.4 g dl\(^{-1}\) and the lowest observed SpHb value was 7.3 g dl\(^{-1}\). Although we observed increased SpHb accuracy for Hb_satlab values <10 g dl\(^{-1}\), we cannot speculate about SpHb accuracy for Hb values lower than we observed in our subjects. Further studies should elucidate SpHb accuracy in patients with low Hb concentrations.

Finally, spectrophotometric analysis can be influenced by the concentration of serum bilirubin.\(^9\) However, none of our patients had a preoperatively elevated serum bilirubin; the mean (sd) serum bilirubin was 8 (3) \(\mu\)mol litre\(^{-1}\).

In conclusion, in patients undergoing major hepatic resection, non-invasive SpHb measurement by a Masimo Radical 7 pulse co-oximeter correlated moderately with Hb_satlab and showed increased accuracy for lower Hb concentrations. On the other hand, rapid colloid administration might decrease the accuracy of SpHb monitoring. Further technical improvements of the sensor and software are necessary to improve the accuracy of SpHb spectrophotometry in order to be less influenced by Hb concentration and possibly by the use of colloid solutions. Non-invasive SpHb monitoring might become a sensitive screening device for clinically significant anaemia.

**Declaration of interest**

M.M.R.F.S. is an editor for the *British Journal of Anaesthesia*, but had no role in the handling of this manuscript. He has also served three times as a panel member of the Masimo advisory board.

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