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SHORT COMMUNICATION

Evaluation of multiwave pulse total-hemoglobinometer during general anesthesia

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Abstract The purpose of this prospective study was to evaluate the accuracy and trending ability of a four-wavelength pulse-total hemoglobinometer that continuously and noninvasively measures hemoglobin in surgical patients. With IRB approval and informed consent, spectrophotometric hemoglobin (SpHb) was measured with a pulse-total hemoglobinometer manufactured by Nihon Kohden Corp (Tokyo, Japan) and compared to the CO-oximeter equipped with blood gas analyzer. Two hundred twenty-five samples from 56 subjects underwent analysis. Bland–Altman analysis revealed that the bias ± precision of the current technology was 0.0 ± 1.4 g/dl and -0.2 ± 1.3 g/dl for total samples and samples with $8 < \text{Hb} < 11$ g/dl, respectively. The percentages of samples with intermediate risk of therapeutic error in error grid analysis and the concordance rate of 4-quadrant trending assay was 17 % and 77 %, respectively. The Cohen kappa statistic for $\text{Hb} < 10$ g/dl was 0.38, suggesting that the agreement between SpHb and CO-oximeter-derived Hb was fair. Collectively, wide limits of agreement, especially at the critical level of hemoglobin, and less than moderate agreement against CO-oximeter-derived hemoglobin preclude the use of the pulse-total hemoglobinometer as a decision-making tool for transfusion.

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The determination of hemoglobin (Hb) concentration is an essential test to initiate or withhold blood transfusion during the perioperative period. Traditionally, it has been measured intermittently with a CO-oximeter in the operating room. Theoretically, Hb can be measured continuously and noninvasively by measuring pulsatile absorption of several wavelengths of visible and infrared light [1]. Accordingly, two types of spectrophotometry-based system have been commercially available (Masimo Radical-7; Masimo Corp, Irvine, CA, USA, referred as Masimo technology herein and NBM-200MPTM, OrSense, Nes Ziona, Israel) [2]. Additionally, a prototype four-wavelength pulse-oximeter has been developed by Nihon Kohden (Tokyo, Japan; referred to as 4W technology herein), and its performance was reported elsewhere [3]. However, intraoperative experience is limited, and the performance of 4W technology has not been fully elucidated. The purpose of this observational study was to evaluate the accuracy of 4W technology during surgery, especially its response to surgical blood loss and blood transfusion.

After IRB approval and informed consent, adult patients undergoing surgery with estimated blood loss exceeding 500 ml were enrolled in this prospective study. Each subject was monitored in accordance to the ASA standard, and a radial artery was cannulated for invasive blood pressure monitoring and blood sampling. Additionally, the reusable probe of the multi-wavelength pulse-oximeter was placed on the fingertip to continuously measure Hb concentration. 4W technology uses an additional two wavelengths (805 and 1,300 nm) compared to the standard pulse-oximeter to spectrophotometrically determine the absolute value of Hb

concentration (SpHb). Anesthetic management, the timing of blood sampling, and the decision to initiate blood transfusion were at the discretion of attending anesthesiologists. Hemoglobin concentration of the arterial blood sample [total Hb (tHb)] was determined when clinically indicated with a CO-oximeter (ABL725; Radiometer, Copenhagen, Denmark) and used as a clinical reference method [4]. Absorbance and AC/DC ratio of each wavelength (plethysmographic amplitude), calculated Hb concentration, pulse rate, and SpO_2 were stored in the device and later downloaded to a personal computer.

Data were expressed as mean ± SD. Accuracy of noninvasive hemoglobin concentration was analyzed with the following four methods: Bland and Altman analysis, four-quadrant trending analysis, error grid analysis, and Cohen's kappa statistic according to the published recommendation [5]. Measurements with low plethysmographic amplitude defined AC/DC less than 1 % were to be excluded from the analysis according to the previous report [6]. Prism (ver. 6; Graphpad Software, San Diego, CA, USA) and SPSS (ver. 20; IBM, Armonk, NY, USA) were used for statistical analysis.

Fifty-six subjects undergoing major gastrointestinal, vascular, gynecological, urological, and neurosurgical procedures were enrolled in this study. The mean ± SD of age, height, and weight of the subjects were 57 ± 17 years old, 162 ± 8 cm, and 59 ± 12 kg, respectively. Among them, 49 subjects underwent intraoperative erythrocyte transfusion. Arterial blood sampling and Hb measurement were performed 256 times, and 31 data pairs were excluded by low AC/DC ratio according to the protocol. Thus, 225 data pairs were included in the final analysis. The range of tHb was from 6.1 to 14.4 g/dl. The bias ± precision (1SD of difference) against the CO-oximeter was −0.0 ± 1.4, 1.2 ± 1.1, −0.2 ± 1.3, and −1.0 ± 1.1 g/dl for all the measurements, samples with tHb < 8 g/dl ($n = 21$), samples with 8 < tHb < 11 g/dl ($n = 155$), and samples with tHb > 11 g/dl ($n = 49$), respectively. No significant correlation was found between the AC/DC ratio and the measurement difference (Fig. 1). However, there was a larger difference at low AC/DC range compared to the higher AC/DC range. Trending ability was assessed with a four-quadrant plot and found a 77 % concordance rate between SpHb and tHb. The result of error grid analysis is presented in Fig. 2. There were no data with high risk of major therapeutic error. However, 17 % (39/225) of data points were assessed with intermediate risk of significant but less critical error. The result exceeded the suggested criteria that the number of data points in areas with intermediate risk of significant but less critical error should be less than 5 % of the total data points. The Cohen kappa statistic that assesses agreement of detecting Hb < 10 g/dl between two methods was 0.39. This result suggests that

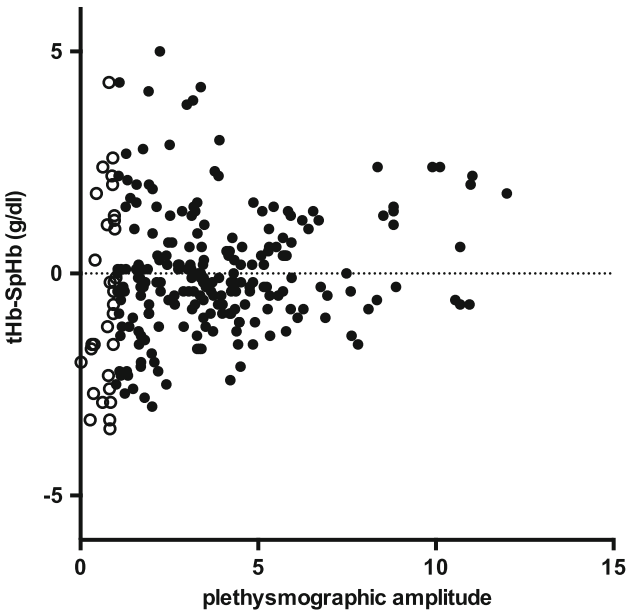

Fig. 1 Scattergram between plethysmographic amplitude versus measurement difference between spectrophotometric hemoglobin (SpHb) and CO-oximeter-derived total hemoglobin (tHb). Both the excluded data pairs (*open circles*) and included data pairs (*closed circles*) are demonstrated. There is no specific trend between the plethysmographic amplitude and measurement error

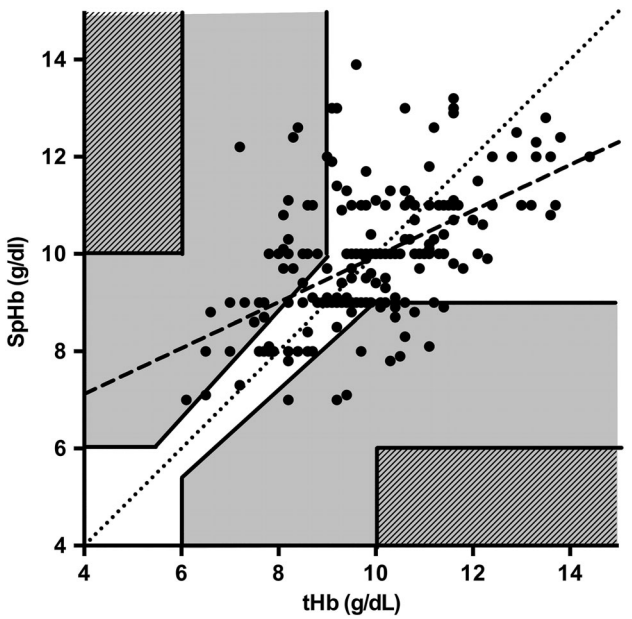

Fig. 2 Error grid analysis of spectrophotometric hemoglobin (SpHb) against CO-oximeter-derived total hemoglobin (tHb) measurement ($n = 225$). The *dotted line* and the *hatched line* represent regression line and line of unity, respectively. The *gray area* and the *hatched area* represent area with intermediate risk of significant but less critical error and area with high risk of major therapeutic error, respectively, according to Morey et al. [5]

the agreement between spectrophotometric measurement and CO-oximeter was less than moderate. Collectively, our result suggests that SpHb with the 4W technology cannot replace invasive determination of Hb.

In this study, we found that the systemic error of the 4W technology was small at the midrange of Hb compared to the lower and higher end of Hb level. However, the wide variation and suboptimal agreement against clinical standard measurement preclude the solo use of this device for decision making for blood transfusion.

It is intuitively advantageous if Hb level is continuously known in patients experiencing significant blood loss and transfusion. One solution to this clinical challenge is multiwavelength pulse oximetry, and the Masimo technology has been FDA approved and is commercially available. Masimo technology uses more than four wavelengths and is able to individually determine total hemoglobin, carboxyhemoglobin, and methemoglobin [2, 7]. In contrast, 4W technology uses four wavelength, and we examined the performance of 4W technology in surgical patients who underwent extensive surgical procedures and indirectly compared the results with Masimo technology.

In overall, this study demonstrated the almost comparable bias and precision of 4W technology to the Masimo technology [8–14]. However, several differences are noted. First, the bias is dependent on the Hb level, and there is a smaller bias when Hb is between 8 and 11 g/dl with this technology compared to Masimo technology. This finding is obviously advantageous because the Hb range between 8 and 10 g/dl has been repeatedly used as a transfusion trigger [15–17]. Second, there is a different relationship between plethysmographic amplitude and the difference between 4W technology and Masimo technology. As summarized in Fig. 1, low plethysmographic amplitude resulted in both overestimation and underestimation of Hb with 4W technology. In contrast, Nguyen et al. [9] reported that Masimo technology systematically underestimated the Hb value when perfusion index (an equivalent of plethysmographic waveform amplitude) decreased. Other studies also found that the bias decreased when perfusion index was more than 1.4 [14] or 2.0 [13]. Our data and these previous reports collectively suggest that care should be taken to interpret the data when plethysmographic amplitude is low because of either peripheral underperfusion or vasoconstriction.

Recently, a different approach such as modified error grid analysis and Cohen kappa analysis was proposed to evaluate Hb measurement [5]. Although these methods have not been applied to Masimo technology, another point-of-care Hb determination has been evaluated with these methods [18]. In that study, the authors concluded that the results should be cautiously interpreted because the percentage of data within the area with intermediate risk of significant but less critical error was more than 30 % in error grid analysis and Cohen kappa was below 0.4. Our results mostly correspond to these results and support the similar conclusion. Because the spectrophotometric method provides noninvasive and continuous measurement of Hb, the trending ability may be more important than the accuracy of a single measurement. The concordance rate of Masimo technology and 4W technology was 93 % [6] and 78 %, respectively, and these data suggest that the Masimo technology has better trending ability.

Obviously, there are several factors that are responsible for these discrepancies between spectrophotometric determination of Hb and CO-oximetry. It is beyond this study's scope to account for all the underlying mechanisms of the inaccuracies, but we suppose the effects of perfusion of the fingertip may play a significant role in the accuracy. Several studies demonstrated that there is a difference between peripheral hematocrit and central hematocrit in various conditions [19, 20]. If the increased bias in low-Hb samples can be attributed to the difference of hematocrit, our result that spectrophotometric Hb overestimated arterial Hb suggests increased peripheral hematocrit during hemorrhage. This possibility warrants further investigations.

This study has several limitations. First, the device investigated in this study still remains in the developmental phase, and this fact precludes its direct comparison against other commercially available technologies. Second, the effects of arterial oxygen saturation cannot be determined. A previous study demonstrated that accuracy of transcutaneous measurement of methemoglobin is dependent on arterial oxygen saturation [21]. Our study precludes exploring this possibility because all the measurements were made when SpO_2 was more than 97 %.

In conclusion, our study revealed that the systemic bias of noninvasive determination of hemoglobin by the prototypical four-wavelength pulse oximeter was minimal when total hemoglobin concentration was between 8 and 11 g/dl. However, our trend analysis, error grid analysis, and Cohen kappa statistic revealed that the current 4W technology is not suitable for decision making for transfusion. We believe that further development is obviously warranted to improve accuracy.

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