(Acta Anaesth. Belg., 2020, 71, 123-130)

Reliability of a spot check non-invasive hemoglobin monitoring (SpHb) of the Masimo RAD-67™ and the HemoCue® for anemia screening

W. Baulig (*), U. Eichenberger (**), O.M. Theusinger (***)

Abstract : *Background :* To test the reliability of the spot check Masimo Rad-67 (Masimo Corp., Irvine, CA, USA) as part of a preoperative anemia screening, hemoglobin measurements were compared to those of the HemoCue® Hb 201+ System (HemoCue AB, Ängelholm, Sweden) and the standard laboratory measurement.

Methods : During preoperative evaluation of patients scheduled for elective orthopedic surgery hemoglobin concentration was simultaneously determined by standard laboratory analysis (Hb_{Lab}), the HemoCue® Hb 201+ System ($Hb_{Hemocue}$) and by Pulse Co-Oximetry using the Masimo Rad-67 (SpHb) with the rainbow® DCI®-mini Sensor (Masimo Corp., Irvine, CA, USA). Linear correlation, agreement (Bland-Altman analysis), sensitivity/specificity and positive/negative prediction values (PPV/NPV) for anemic hemoglobin values were determined. P-values less than 0.05 were considered statistically significant.

Results : 303 patients were analyzed. Twenty-one patients (12 male and 9 female) had mild or moderate anemia, detected by Hb_{Lab}. In 20 patients, the $Hb_{Hemocue}$, and in 34 patients, the SpHb detected anemia. Linear correlation and mean bias (limits of agreement, LOA) for $Hb_{Hemocue}$ and Hb_{Lab} were r = 0.969 and -1.08 (+6.44/-8.60) g/L, and for SpHb and Hb_{Lab} r = 0.61 and +1.76 (+26.92/-23.4) g/L. Sensitivity/specificity of the $Hb_{Hemocue}$ to detect anemia in all, male and female patients were 85.0/99.3%, 75.0/100/% and 88.9/98.9/% with a PPV/NPV of 89.5/98.9%, 100/98.0% and 80.0/99.3%, respectively. Sensitivity/specificity of SpHb to detect anemia for all, male and female patients were 71.4%, 93.3%, 75.0/95.2/% and 66.7/91.1%, with a PPV/NPV for all, male and female patients of 44.1/97.8%, 56.3/97.9% and 33.3/97.7%, respectively.

Conclusions : $Hb_{Hemocue}$ and Hb_{Lab} show a strong linear correlation and a good agreement, while linear correlation of SpHb and Hb_{Lab} is moderate and agreement poor. For both devices, anemia detection is moderate, but the positive prediction value for anemia is much better with the $Hb_{Hemocue}$. Both devices reliably detected non-anemic patients.

Glossary : CO = carbon monoxide ; PPV = positive predicted value ; NPV = negative predicted value ; Hb_{Lab} = hemoglobin determined by the laboratory ; $Hb_{Hemocue}$ = hemoglobin determined by the HemoCue device ; SpHb = hemoglobin determined by the Masimo-RAD67 device ; LOA = limits of agreement ; LOS = length of stay ; POC = point of care ; SpO_2 = arterial hemoglobin ; PR = pulse rate ; PI = perfusion index ; PVI = plethysmography variability index ; SpCO = carboxyhemoglobin ; SpMet = methemoglobin ; LED = Light Emitting Diodes ; HiCN = hemiglobincyanide ; SLS = Sodium Lauryl Sulphate ; BMI = body mass index ; BT = body temperature ; WHO = World Health Organization ; IQR = interquartile range ; MAP = mean arterial pressure ; HF = heart frequency ; SD = standard deviation

Key point Summary :

– *Question :* Is Hb measurement of the Masimo Rad-67 and of the HemoCue reliable?

– *Findings :* Non-anemic patients are reliably detected with the Masimo Rad-67. Of the 303 patients examined, Hb_{Lab} detected twenty-one patients (12 male and 9 female) with mild or moderate anemia. The Hbh_{emocue} showed anemia in 20 patients, while the SpHb identified 34 patients as anemic. $Hb_{Hemocue}$ and Hb_{Lab} showed a strong linear correlation and a good agreement, while linear correlation of SpHb and Hb_{Lab} was moderate and agreement poor. For both devices, anemia detection is moderate, but the positive prediction value for anemia is much better with the $Hb_{Hemocue}$. Both devices reliably detected non-anemic patients.

Werner Baulig, MD ; Urs Eichenberger, MD ; Oliver M. Theusinger, MD

(*) Department of Anesthesiology and Intensive Care Medicine, Klinik Im Park, Zurich, Switzerland

(**) Department of Anesthesiology, University Hospital Balgrist and University of Zurich, Zurich, Switzerland

(***) During the Study Department of Anesthesiology, University Hospital Balgrist and University of Zurich, Zurich, Switzerland, actually University of Zurich, Zurich, Switzerland

Corresponding author : Oliver M. Theusinger, MD, University of Zurich, CH – 8001 Zurich, Switzerland - Phone : + 41 79 659 50 05

Email : Oliver@theusinger.de

Paper submitted on May 15, 2020 and accepted on August 25, 2020

Conflict of interest : Oliver M. Theusinger has received honoraria or travel support for consulting or lecturing from the following companies : CSL Behring Schweiz, Zurich, Switzerland, Vifor SA, Villars-sur-Glâne, Switzerland, Roche Pharma (Schweiz) AG, Reinach, Switzerland, Pentapharm AG, München, Germany, TEM International GmbH, München, Germany, Octapharma AG Lachen, Switzerland, Instrumentation Laboratory, Bedford, MA, USA. Urs Eichenberger has no conflict of interest. Werner Baulig has no conflict of interest.

– *Meaning :* With both devices, non-anemic patients are reliably recognized, while anemia detection is moderate. However, the prediction for the presence of anemia is much better with the $Hb_{hemocue}$.

Key words : Anemia ; orthopedic surgery ; non-invasive hemoglobin measurement ; Masimo ; RAD-67™ ; HemoCue®.

Introduction

Preoperative evaluation and optimization of the patients' red blood cells have been shown to be beneficial for outcomes after major surgery (1). In patients undergoing elective orthopedic surgery, preoperative anemia, most commonly attributed to iron deficiency, is present in about 19.4 to 35% and associated with increased hospital length of stay (LOS), morbidity and mortality (2,3). Recently, Froessler et al. showed that perioperative administration of ferric carboxymaltose in preoperative anemia resulted in a significant reduction of patient-related hospital costs, mainly based on reduced blood transfusions and LOS (4).

Screening for anemia in elective orthopedic surgery during a first preoperative evaluation is important to create the best possible entry conditions for the patient. In our center, preoperative evaluation is usually done 4 to 6 weeks prior to surgery with hemoglobin concentration being measured using a Point of care (POC) device HemoCue® Hb 201$^+$ Analyzer (HemoCue AB, Ängelholm, Sweden). In case of preoperative anemia, the general practitioner is encouraged to carry out further diagnostics and initiate preoperative anemia therapy. Most recently, the Rad-67™ Pulse CO-Oximeter® (Masimo Corp., Irvine, CA, USA) with the rainbow® DCI®-mini Sensor (Masimo Corp., Irvine, CA, USA) has become available, providing hemoglobin concentration by non-invasive spot-check measurements using the multi-wavelength pulse CO-oximetry technology.

The aim of this study was to investigate the feasibility and reliability of the spot check Rad-67 ™ Pulse CO-Oximeter® (Rad-67) and the HemoCue® Hb 20$^+$ Analyzer in measuring hemoglobin concentrations during the early preoperative evaluation of elective orthopedic surgery patients. For this, we compared the obtained results of with those measured using a standard laboratory analyzer (XN 9000 Hematology analyzer, Sysmex (Sysmex Corporation, Kobe, Japan).

Materials and Methods

This study was performed after obtaining approval from the local ethics committee (Kantonale Ethikkommission, Kanton Zürich, Switzerland, BASEC-Nr :2017-01361/ cliniclatrials.gov NCT 03328780). After written informed consent had been obtained from the patient, demographic data were collected and measurements were performed. Data were collected in the University Hospital Balgrist in Zurich, Switzerland, from 11/2017 till 02/2018.

The spot check Rad-67™ Pulse CO-Oximeter® (Rad-67) is a non-invasive device monitoring the functional oxygen saturation of arterial hemoglobin (SpO_2), pulse rate (PR), perfusion index (PI), plethysmography variability index (PVI), and allowing a spot check monitoring of total hemoglobin (SpHb), carboxyhemoglobin (SpCO) and methemoglobin (SpMet). SpO_2 and PR measurements are possible even during motion and at phases of weak circulation. After the sensor is initialized, the signal stabilized and sufficient blood perfusion detected, the one-time SpHb value is displayed for 5 minutes or until the sensor is removed. With the Signal Extraction Technology® (SET®), the impact of motion of the arterial or venous blood during changes in the patient's position is removed by adaptive filters. The Rad-67 ™ uses the rainbow® DCI®-mini Sensor with different Light Emitting Diodes (LED) which guide light to a photodiode (photodetector). The signal data is determined by passing different visible light and infrared light of wavelengths between 500 and 1400nm through the capillary bed at the tip of the patient's finger and measuring the changes in light absorption during the pulsatile blood cycle. The photodetector receives the light, converts it to an electrical signal, and transmits the signal to the Rad-67 ™ device. SpHb measurement relies on a calibration equation of multiple wavelengths which quantifies the percentage of total blood hemoglobin.

The PI (range 0 to 20) is the ratio of pulsatile blood flow to non-pulsatile or static blood in the peripheral tissue. PI < 1 is associated with incorrect measurement results. The Rad-67 ™ displays the calculated data of methemoglobin as a percentage for SpMet and values > 1% in non-smoking adults are defined as pathological.

The HemoCue® Hb 201$^+$ analyzer (HemoCue) is a POC device providing quantitative determination of the total amount of hemoglobin ($Hb_{Hemocue}$) in whole blood. Capillary, venous or arterial whole blood may be used in specially designed microcuvettes. The system is factory

calibrated against the hemiglobincyanide (HiCN) method. Sodium deoxycholate hemolyzes the erythrocytes and hemoglobin is released. Using the modified Vanzetti's azide technique, sodium nitrite converts hemoglobin to methemoglobin, which, together with sodium azide, results in azide methemoglobin. The latter has almost the same absorbance spectrum as that of HiCN. Absorbance is measured at two wavelengths (570 and 880nm) in order to compensate for turbidity in the sample. The reliable measuring range of hemoglobin is 0 – 256 g/L (0 – 15.9mmol/L). Results above 256g/L (> 15.9mmol/L) are displayed as HHH. The analyzer is suited for both static and mobile use and stores test results, date and time for up to 600 measurements.

The XN 9000 Hematology Analyzer (XN 9000) for laboratories determines the total hemoglobin concentration (Hb_{Lab}) by the cyanide-free Sodium Lauryl Sulphate (SLS) method, the reliability of which has been demonstrated against the HiCN-Method in various investigations (5-8). SLS is a surfactant which both hemolyzes erythrocytes and rapidly forms a complex with the released hemoglobin. The product SLS-MetHb is stable for few hours and has a characteristic optical spectrum with maximum absorbance at 555 nm. Monochromatic light with a wavelength of 555 nm sent by the LED is absorbed by the SLS-MetHb complex. The extinction is measured by a photo sensor and is inversely proportional to the hemoglobin concentration of the sample, according to the Beer-Lambert's law. Turbidity of the sample caused by lipemia or leukocytosis is minimized due to the effect of the SLS reagent.

Upon arrival in the consulting room, the patient took place on a deckchair. According to the manufacturer's recommendation, the rainbow® DCI®-mini Sensor was attached to the finger as identified by the provided finger sizer of the dominant hand for transcutaneous measuring of SpHb and SpMet. The Rad-67 was calibrated for venous measurement of SpHb because blood samples for measuring Hb_{Lab} were taken from a venous vessel. After a five minutes waiting period, two blood samples were drawn from the cephalic vein of the opposite arm and the SpO_2, PR, PI, SpHb and SpMet values on the display of the Rad-67 were documented. The EDTA blood sample was sent to the central laboratory for analyzing Hb_{Lab}. One milliliter of venous blood was drawn in a blood gas analysis syringe (SafePICO aspirator, Radiometer Medical, Bronshoj, Denmark, containing 80 IU heparin) and $Hb_{Hemocue}$ was analyzed. In addition, gender (sex), age, body weight, height, body mass index (BMI), non-invasive blood pressure (systolic, diastolic, mean arterial pressure) and body temperature (BT) were registered. Anemia was defined as hemoglobin (Hb) levels < 120 g/L in women and < 130 g/L in men, according to the World Health Organization (WHO). Anemia was defined as mild, moderate or severe in women/men (15years of age and above) if Hb levels were 110-119/110-129g/L, 80-109/80-109 g/L and < 80/80 g/l, respectively (9).

Statistical Analyses :

Data were collected using Microsoft® Excel (Microsoft Office 2010, Microsoft Corporation Redmond, WA, US) and analyzed using IBM® SPSS® Statistics version 25 (IBM Corp, Armonk, NY, USA). The Kolmogorov-Smirnov-Test was used to test continuous variables on normality. Continuous variables of all patients were summarized as mean ± standard deviation (SD) or as median [IQR] according to the distribution of the data. Pearson Correlation Coefficient was used to test the linear relationship between Hb_{Lab} and $Hb_{Hemocue}$, and Hb_{Lab} and SpHb. For determination of the agreement between the different methods, Bland-Altman analysis was applied to assess mean bias and limits of agreement (LOA) of Hb_{Lab} with $Hb_{Hemocue}$ and SpHb (10). LOA is defined as (mean bias ± 2SD). To quantify the test performance, sensitivity / specificity and positive predictive value (PPV) / negative predictive value (NPV) of $Hb_{Hemocue}$ and SpHb were determined. Stepwise multiple regression analysis was used to estimate the impact of independent factors on the $Hb_{Hemocoue}$ and SpHb. P-values less than 0.05 were considered statistically significant.

Results

In total, 307 patients were investigated. Four patients had to be excluded from analysis because of a PI < 1. Demographic and physiologic data of the 303 remaining (157 male and 146 female) patients are presented in table 1. In 21 (7%) patients (12 male and 9 female), Hb_{Lab} detected anemia. Anemic patients were significantly older ($p = 0.021$) and the diastolic blood pressure was lower ($p = 0.021$) when compared to patients without anemia. Mild anemia was found in 11 male and 6 female patients. One male and three female patients had moderate anemia. In 64 (21%) patients (33 male and 31 female), MetHb > 1 was found. The median (IQR) PI of the Rad-67 was 5.3 (3.1; 8.1) with significant higher PI-values in males compared to females (Table 1).

Table I.

Demographic and physiologic data of all, female and male patients. Data are presented as mean ± SD or median [IQR] ; p-values less than 0.05 are considered statistically significant.

	All (n = 303)	Male (n = 157)	Female (n = 146)	p-value
Age, yr	53.3 [37.6; 67.6]	51.1 [38.6; 66.2]	55.8 [34.4; 69.0]	n.s.
Heigh, cm	170.1±10.4	176.3±8.4	163.3±7.9	< 0.001
Weight, kg	78.0 [67.5; 90.0]	84.0 [75.2; 98.5]	70.0 [60.4; 80.4]	< 0.001
BMI, kg/m^2	27.1 [23.7; 30.7]	27.5 [24.4; 31.2]	26.3 [22.5; 30.7]	n.s.
HF, bpm	75 [68; 84]	75 [67; 84]	76 [69; 83]	n.s.
BP_{syst}, mmHg	136.6±17.8	138.7±15.8	134.5±19.6	= 0.041
BP_{diast}, mmHg	82.5±11.9	84.8±11.8	79.9±11.4	< 0.001
MAP, mmHg	100.5±12.4	102.8±11.5	98.1±12.9	= 0.001
SpO_2, %	97 [96; 98]	97 [96; 98]	97 [96; 98]	n.s.
BT, °C	36.8 [36.5; 37.0]	36.6 [36.3; 36.9]	36.9 [36.6; 37.2]	n.s.
Hb_{Lab}, g/L	142.4±14.6	149.6±14.0	134.6±10.8	< 0.001
$Hb_{Hemocue}$, g/L	143.5±15.1	150.9±14.4	135.5±11.3	< 0.001
SpHb, g/L	140.6±13.7	145.4±12.5	135.5±13.1	< 0.001
PI	5.3 [3.1; 8.1]	6.3 [3.6; 8.8]	5.3 [2.4; 6.9]	> 0.001
MetHb	0.8 [0.5; 1.1]	0.8 [0.5; 1.1]	0.8 [0.5; 1.1]	n.s.

Abbreviations: BMI, body mass index; BP_{syst}, systolic arterial pressure; BP_{diast}, diastolic arterial blood pressure; MAP, mean arterial pressure; SpO_2, oxygen saturation measured by pulse oximetry; BT, body temperature; Hb_{Lab}, Hb measured by the XN 9000 Hematology Analyzer; $Hb_{Hemocue}$, Hb concentration measured by the Hemocue device; SpHb, Hb concentration measured by the RAD-67 device; PI, pulsation index measured by the Rad 67™ n.s., not significant.

Table II

Linear correlation and agreement of of Hb_{Lab} and $Hb_{Hemocue}$ in all, male and female patients, patients with and without anemia

	r	CI95	r^2	p-value	Bias (g/L)	SD (g/L)	LOA (g/L)
All	0.969	0.973; 1.031	0.938	< 0.001	-1.08	±3.76	(+6.44/-8.60)
Male	0.963	0.948; 1.037	0.927	< 0.001	-1.29	±3.90	(+6.52/-9.09)
Female	0.948	0.937; 1.046	0.899	< 0.001	-0.86	±3.60	(+6.35/-8.06)
$All_{no\ anemia}$	0.958	0.968; 1.038	0.918	< 0.001	-1.05	±3.78	(+6.51/-8.61)
$Male_{>130}$	0.936	0.923; 1.045	0.876	< 0.001	-1.25	±3.89	(+6.53/-9.03)
$Female_{>120}$	0.922	0.921; 1.063	0.850	< 0.001	-0.83	±3.66	(+6.49/8.15)
All_{anemia}	0.957	0.985; 1.319	0.917	< 0.001	-1.52	±3.53	(+5.54/-8.58)
$Male_{<130}$	0.953	0.958; 1.513	0.908	< 0.001	-1.75	±4.20	(+6.65/-10.15)
$Female_{<120}$	0.957	0.766; 1.333	0.916	< 0.001	-1.22	±2.59	(+3.95/-6.39)

Abbreviations: Hb_{Labs}, photometrically measured Hb; $Hb_{Hemocue}$, Hemoglobin concentration measurement by the Hemocue device; SpMet, Methemoglobin measured with the Rad 67; $All_{no\ anemia}$, all patients without anemia; $Male_{>130}$, Male with Hb_{Labs} > 130g/L; $Female_{>120}$, female with Hb_{Labs} > 120g/L; All_{anemia}, all patients with anemia; $Male_{<130}$, males with Hb_{Labs} < 130g/L; $Female_{<120}$, female with Hb_{Labs} < 120g/L; bias, mean of the differences between Hb_{Labs} and $Hb_{Hemocue}$; LOA, limits of agreement (mean bias ±2 SD).

Comparison between the Hb_{Lab} and $Hb_{Hemocue}$

In all patients, Hb_{Lab} and $Hb_{Hemocue}$ showed a strong linear correlation (r = 0.969) and a mean bias (LOA) of -1.08 (+6.44 / - 8.60) g/L (Table II, Fig. 1). No significant changes of the linear correlation and in the agreement were found in male and female patients or in patients with or without anemia (Table II, Fig 1). Stepwise multi-regression analysis showed a significant impact of HF (p = 0.036), MAP (p > 0.001), age (p < 0.001) and BT (p = 0.001) on the $Hb_{Hemocue}$. Sensitivity/specificity of the $Hb_{Hemocue}$ to detect anemia for all, male and female patients was 85.0/99.3%, 75.0/100% and 88.9/98.9% with a PPV/NPV for all, male and female patients of 89.5/98.9%, 100/98.0% and 80.0/99.3%, respectively (Table IV). $Hb_{Hemocue}$ detected anemic values in 20 patients (9 male and 11 female).

Comparison between the Hb_{Lab} and SpHb

In all patients, Hb_{Lab} and SpHb showed a moderate linear correlation (r = 0.607) and a mean bias (LOA) of +1.76 (+26.92 / - 23.40) g/L (Table III, Fig 2). In the subgroup of non-anemic males, the mean bias (LOA) of Hb_{Lab} and SpHb was +5.32 (+29.99/-19.35) g/L, while in anemic males and females a mean bias (LOA) of -8.83 (+9.86/27.52)

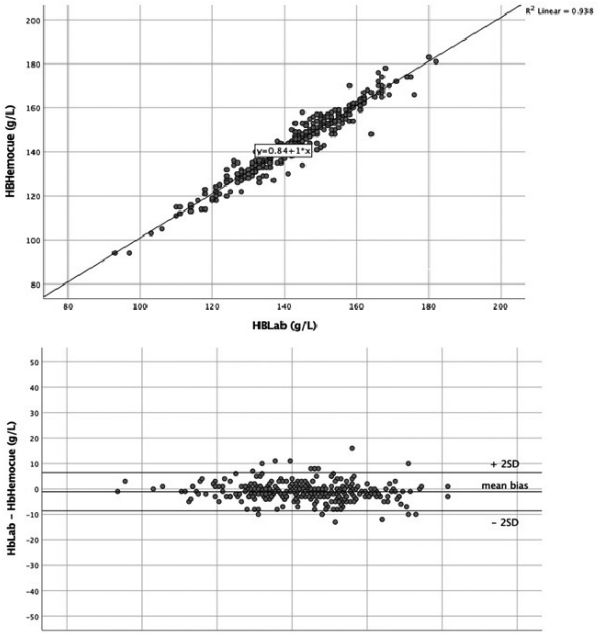

Fig.1. —A, Correlation of the Masimo-RAD67 hemoglobin measurements versus hemoglobin determination with HemoCue. B, Bland-Altmann plot for the hemoglobin determination with the Masimo-RAD67 and the determination with HemoCue.

surgery, we found anemic values in only 7% of the included patients, which might be explained by a high proportion of younger patients (< 65 years) (11). In the present study, $Hb_{Hemocue}$ showed a strong linear correlation and a good agreement with Hb_{Lab} in all patients, while linear correlation of SpHb with Hb_{Lab} was only moderate and the agreement poor. Our results are in accordance with those of comparative studies with other Pulse CO-Oximeter devices. In adult emergency department patients, Knutson et al. reported limits of agreement for laboratory hemoglobin and SpHb measured with the Radical-7 Pulse CO-Oximeter of -47/+38g/l which was beyond the clinically relevant standard of equivalency (12). Similar results were found by Gayat et al. who compared laboratory hemoglobin concentration values with non-invasive detected hemoglobin of the Pronto-7 and the Orsense NMB-200 device in emergency room patients (13). Interestingly, while mean bias and agreement of Hb_{Lab} and $Hb_{Hemocue}$ was not different in the subgroup analysis of our study, mean bias of Hb_{Lab} and SpHb

Table III

Linear correlation and agreement of Hb_{Lab} and SpHb in all, male and female patients, patients with and without anemia

	r	CI95	r^2	p-value	Bias (g/L)	SD (g/L)	LOA (g/L)
All	0.607	0.483; 0.652	0.368	< 0.001	+1.76	±12.58	(+26.92/-23.40)
Male	0.547	0.370; 0.607	0.300	< 0.001	+4.24	±12.68	(+29.59/-21.12)
Female	0.513	0.449; 0.791	0.263	< 0.001	-0.90	±11.96	(+23.01/-24.82)
$All_{no\ anemia}$	0.528	0.441; 0.648	0.278	< 0.001	+2.54	±12.45	(+27.45/-22.37)
$Male_{>130}$	0.369	0.232; 0.563	0.136	< 0.001	+5.32	±12.34	(+29.99/-19.35)
$Female_{>120}$	0.418	0.376; 0.818	0.174	< 0.001	-0.40	±11.93	(+23.46/-24.26)
All_{anemia}	0.491	0.071; 0.900	0.241	= 0.024	-8.71	±9.34	(+9.63 /-27.29)
$Male_{<130}$	0.469	-0.146; 1.041	0.220	= 0.146	-8.83	±9.23	(+9.86/-27.518)
$Female_{<120}$	0.240	-0.644; 1.137	0.058	= 0.534	-8.56	±10.05	(+11.54/-28.66)

Abbreviations: Hb_{Labs}, photometrically measured Hb; SpHb, Hemoglobin concentration measurement by the Rad 67; SpMet, Methemoglobin measured with the Rad 67; $All_{no\ anemia}$, all patients without anemia; $Male_{>130}$, Male with Hb_{Labs} > 130g/L; $Female_{>120}$, female with Hb_{Labs} > 120g/L; All_{anemia}, all patients with anemia; $Male_{<130}$, males with Hb_{Labs} < 130g/L; $Female_{<120}$, female with Hb_{Labs} < 120g/L; bias, mean of the differences between Hb_{Labs} and SpHb; LOA, limits of agreement (mean bias ±2 SD).

g/L and -8.56 (+11.54/-28.66) g/L was found, respectively (Table III). Stepwise multi-regression analysis showed a significant effect of HF ($p = 0.01$), MAP ($p < 0.001$), PI ($p < 0.001$), age ($p > 0.001$) and MetHb ($p = 0.001$) on SpHb. Sensitivity/specificity of SpHb to detect anemia for all, male and female patients was 71.4/93.3%, 75.0/95.2% and 66.7/91.1%, with a PPV/NPV for all, male and female patients of 44.1/97.8%, 56.3/97.8% and 33.3/97.7%, respectively (Table IV). SpHb detected anemic values in 34 patients (16 male and 18 females).

Discussion

The main results of this first investigation of the Rad-67 in comparison with the HemoCue are : i) $Hb_{Hemocue}$ showed a strong linear correlation and good agreement with Hb_{Lab}, while linear correlation of SpHb and Hb_{Lab} was moderate and agreement poor ; ii) for both devices, anemia detection was moderate, but the positive prediction value for anemia was much better with the $Hb_{Hemocue}$, iii) both devices reliably detected non-anemic patients.

In contrast to the expected prevalence of anemia in patients scheduled for elective orthopedic

Table IV

Sensitivity/specificity and PPV/NPV for $Hb_{Hemocue}$ and SpHb to detect anemia.
True normal was defined as Hb_{Lab} > 130g/L for men and Hb_{Lab} > 120g/l for female.

	all			Male			Female		
	Hb_{Lab}	$Hb_{Hemocue}$	SpHb	Hb_{Lab}	$Hb_{Hemocue}$	SpHb	Hb_{Lab}	$Hb_{Hemocue}$	SpHb
		n (%)	n (%)		n (%)	n (%)		n (%)	n (%)
All patients	n = 303			n = 157			n = 146		
True normal	282 (93.1)	281	263	145	145	138	137	135	125
True anemia	21 (6.9)	17	15	12	9	9	9	8	6
False normal		3	6		3	3		1	3
False anemia		2	19		0	7		2	12
Sensitivity		(85.0)	(71.4)		(75)	(75)		(88.9)	(66.7)
Specificity		(99.3)	(93.3)		(100)	(95.2)		(98.9)	(91.1)
PPV		(89.5)	(44.1)		(100)	(56.3)		(80.0)	(33.3)
NPV		(98.9)	(97.8)		(98.0)	(97.9)		(99.3)	(97.7)

Abbreviations: HbLab, photometrically measured Hemoglobin concentration; $Hb_{Hemocue}$, Hemoglobin concentration measured by the HemoCue device; SpHb, Hemoglobin concentration measured by the Rad 67; True normal, test detected patients without anemia; True anemia, test detected patients with anemia; False normal; Test did not detect anemia; False anemia, not anemic patients were detected as anemic patients by the test; PPV, positive predictive value; NPV, negative predictive value.

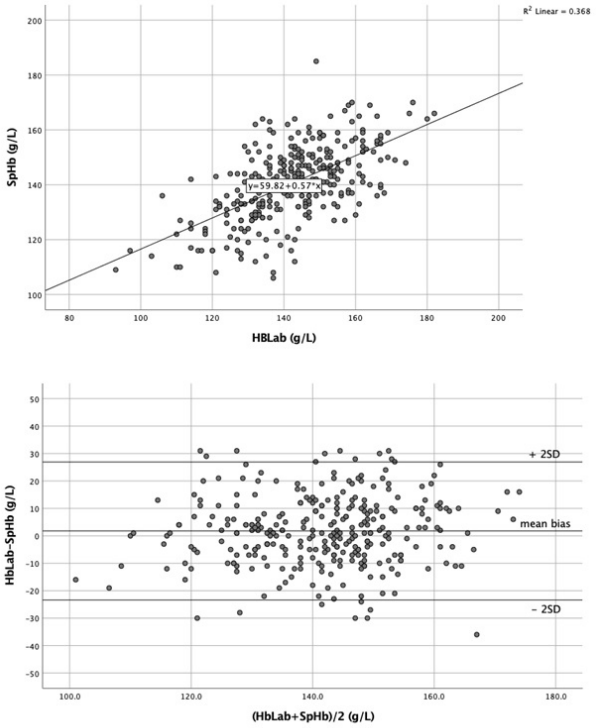

Fig. 2. — A, correlation of the Masimo-RAD67 hemoglobin measurements versus hemoglobin values measured in the laboratory. B, Bland-Altmann plot for the hemoglobin determination with the Masimo-RAD67 and the determination in the laboratory.

in non-anemic males and females was + 5.32 g/L and -0.40g/L, respectively. Additionally, in anemic males and females, a mean bias of Hb_{Lab} and SpHb of – 8.83g/L and – 8.56g/L was found. This finding suggests detection of falsely low hemoglobin values in non-anemic males and falsely high values in anemic patients by the SpHb. Detection of falsely low values in the high range and falsely high values in the low range Hb concentration by SpHb has also been reported during investigation of other Pulse CO-Oximeters (14-16). These findings could be explained by the site of venous blood sampling. Morris et al have shown in one individual a 6.3% difference between capillary blood samples drawn from the left and right hand (17). In our study, whole blood was drawn from the cephalic vein of the opposite arm, where the difference to the other side could possibly be considered much lower. Another reason might be the used rainbow® DCI®-mini Sensor of the Rad 67™ itself, in which the effect of ambient light cannot be completely ruled out. A black protective cover pulled over the sensor could prevent the effects of ambient light. However, this is not provided by the manufacturer for the rainbow® DCI®-mini sensor. Since the patients investigated in this study had all taken place on a deckchair, unforeseen patient movements as a further possible confounder could be most likely ruled out. Nail polish was removed before the sensor was attached. However, the event of an irregular heart rhythm would have had significant impact on the SpHb measurement, but was not explored in this investigation. Additionally, all measurement methodologies including so-called laboratory standard procedures have inherent variations and hemoglobin values will consistently differ within and between various invasive laboratory analyzers. In the same patient, Gehring et al reported a bias of

3g/L and SD of ± 2g/L between the hemoglobin-cyanide (HiCN) and a hematology analyzer (18). Additionally, a comparison between the HiCN method and a blood gas analyzer showed a bias of -2g/L an SD of ±3g/L. The impact of methemoglobin > 1% is questionable, as MetHb concentration was only determined with the Rad-67 and not in the laboratory. According to the recommendations of the manufacturer, SpHb values are considered to be no longer reliably measured if the detected MetHb content is > 2%.

With a cut off value of 130g/L for males and 120g/L for females, sensitivity/specificity of $Hb_{Hemocue}$ and SpHb to detect anemia were moderate with 75.0/100% and 75.0/95.2% for males and 88.9/98.9% and 66.7/91.1% for females, respectively. However, in males the PPV for anemia of the $Hb_{Hemocue}$ was excellent with 100% compared to 56.3% of the SpHb. In females, the PPV for anemia was only moderate with 80.0% for the $Hb_{Hemocue}$, but poor for the SpHb with 33.3.%. The finding of the less accurate identification of low hemoglobin levels by the SpHb especially in females confirms the results of investigations with other Pulse CO-oximeter devices. In 256 patients of a pre-anesthetic assessment clinic, Khalafallah et al. compared SpHb of the Masimo Pronto-7 device with Hb concentrations measured in the laboratory and reported a sensitivity to detect anemia of 57.1% for SpHb in females compared to 91.8% in males (19). Similar to our results they found significantly higher PI values in males compared to females, which might hint to a possible impact of the PI on the less precise anemia detection of the SpHb in females. The high rate of false positive anemia detection with the SpHb compared to the $Hb_{Hemocue}$ is remarkable. In total, false positive anemia detection was found with the $Hb_{Hemocue}$ in only two female patients compared to 19 patients (7 males and 12 females) using SpHb. While the false positive anemia detection of the $Hb_{Hemocue}$ was caused by a deviation of only 1g/L in each of the three patients, deviations of > 10g/L were found with the SpHb. Indeed, false positive anemia detection by SpHb was found in 4.5% of males and 8.9% of females, which is significantly lower than the results reported by Khalafallah et al, who found false positive anemia detection of SpHb using the Masimo Pronto-7 device in 19.1% of males and 15.6% of females (19).

However, both the $Hb_{Hemocue}$ and SpHb were useful for identification of preoperative non-anemic patients. Specificity and NPV were high in both devices.

Limitations of the study

The hemoglobin measurement of the HemoCue® using the modified Vanzetti's azide technique is from the methodological point of view largely similar to the cyanide-free Sodium Lauryl Sulphate (SLS) method of the laboratory analyzer XN 9000. For both, the HemoCue® and the XN 9000, the reliability against the HiCN-Method has been demonstrated (5-8). Methemoglobin concentration was not determined in the laboratory. Feiner et al. demonstrated an accuracy and precision of MetHb measured with the Radical 7 device of 1.9% ± 2.5% only in the 95-100% SaO_2 range (20). However, the Radical-7 readings become progressively more inaccurate as SaO_2 decreases < 95%, at times overestimating true values by 10 to 40%. In 22 patients (7.2%) in this study, SaO_2-values < 95% were measured. However, the impact of this proportion of patients is negligible. Irregular heart rhythm was not recorded in this investigation. Especially, in the elderly patients, atrial fibrillation is common and irregular heart rate causes a considerable variation of the pulse wave. In this study, 20.4% of the patients were older than 70 years and the prevalence of atrial fibrillation in this age group is nearly 11% for males and 5% for females. The exclusion for analysis of this population might have influenced the results for the SpHb measurement. The Rad-67 is not approved for patients with pre-existing renal failure. This population was not evaluated and therefore not excluded. Finally, all laboratory measurement methodologies have inherent variations and hemoglobin values will consistently differ within and between various invasive laboratory analyzers.

In conclusion, both devices reliably detected non-anemic patients. Linear correlation and agreement of Hb_{Lab} with $Hb_{Hemocue}$ were better than for SpHb. For both devices, anemia detection was moderate, but the positive prediction value for anemia was much better with the $Hb_{Hemocue}$. The current version of the Spot Check Rad-67™ Pulse CO-Oximeter® needs additional refinements to further improve its performance and reliability, before it can used as the sole basis for preoperative anemia screening.

References

1. Kehlet H. and Wilmore D.W. 2002. Multimodal strategies to improve surgical outcome. Am J Surg. 183(6):630-641.
2. Goodnough L.T., Maniatis A., Enshaw P., Benoni G., Beris P. and Bisbe E., et al. 2011. Detection, evaluation,

and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. Br J Anaesth.106(1):13-22.
3. Gruson K.I., Aharonoff G.B., Egol K.A., Zuckerman J.D. and Koval K.J. 2020. The relationship between admission hemoglobin level and outcome after hip fracture. J Orthop Trauma. 16(1):39-44.
4. Froessler B., Rueger A.M. and Connolly M.P. 2018. Assessing the costs and benefits of perioperative iron deficiency anemia management with ferric carboxymaltose in Germany. Risk Manag Healthc Policy. 11:77-82.
5. Lewis S.M., Garvey B., Manning R., Sharp S.A. and Wardle J. 1991. Lauryl sulphate haemoglobin: a non-hazardous substitute for HiCN in haemoglobinometry. Clin Lab Haematol. 13(3):279-290.
6. Karsan A., Maclaren I., Conn D. and Wadsworth L. 1993. An evaluation of hemoglobin determination using sodium lauryl sulfate. Am J Clin Pathol. 100(2):123-126.
7. Harris N., Jou J.M., Devoto G., Lotz J., Pappas J. and Wranovics D., et al. 2005. Performance evaluation of the ADVIA 2120 hematology analyzer: an international multicenter clinical trial. Lab Hematol. 11(1):62-70.
8. Kalyan Chakravarthy V., Naveen Chandra D., Santhoshi Prasanna B., Jaya Mastan Rao T. and Ranga Rao D. 2012. Haemoglobin Estimation by Non-cyanide Methods. Journal of Clinical and Diagnostic Research. 6:6. 955-958.
9. Organization WH. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. 2011; https://www.who.int/vmnis/indicators/haemoglobin/en/. Accessed 15.05.2020.
10. Bland J.M. and Altman D.G. 1986. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1(8476):307-310.
11. Munoz M., Gomez-Ramirez S., Campos A., Ruiz J. and Liumbruno G.M. 2015. Pre-operative anaemia: prevalence, consequences and approaches to management. Blood Transfus. 13(3):370-379.
12. Knutson T., Della-Giustina D., Tomich E., Wills B., Luerssen E. and Reynolds P. 2013. Evaluation of a new nonnvasive device in determining hemoglobin levels in emergency department patients. West J Emerg Med. 14(3):283-286.
13. Gayat E., Aulagnier J., Matthieu E., Boisson M. and Fischler M. 2012. Non-invasive measurement of hemoglobin: assessment of two different point-of-care technologies. PLoS One. 7(1):e30065.
14. Baulig W., Seifert B., Spahn D.R. and Theusinger O.M. 2017. Accuracy of non-invasive continuous total hemoglobin measurement by Pulse CO-Oximetry in severe traumatized and surgical bleeding patients. J Clin Monit Comput. 31(1):177-185.
15. Tsuei B.J., Hanseman D.J., Blakeman M.J., Blakeman T.C., Yang S.H. and Branson R.D., et al. 2014. Accuracy of noninvasive hemoglobin monitoring in patients at risk for hemorrhage. *J* Trauma Acute Care Surg. 77(3 Suppl 2):134-139.
16. Vos J.J., Kalmar A.F., Struys M.M., Porte R.J., Wietasch J.K. and Scheeren T.W. 2012. Accuracy of non-invasive measurement of haemoglobin concentration by pulse co-oximetry during steady-state and dynamic conditions in liver surgery. Br J Anaesth. 109(4):522-528.
17. Morris S.S., Ruel M.T., Cohen R.J., Dewey K.G., de la Briere B. and Hassan M.N. 1996. Precision, accuracy, and reliability of hemoglobin assessment with use of capillary blood. Am J Clin Nutr. 69(6):1243-1248.
18. Gehring H., Hornberger C., Dibbelt L., Rothsigkeit A., Gerlach K., Schumacher J. and Schmucker P. 2002. Accuracy of point-of-care-testing (POCT) for determining hemoglobin concentrations. Acta Anaesthesiol Scand. 46(8):980-986.
19. Khalafallah A.A., Chilvers C.R., Thomas M., Chilvers C.M., Sexton M., Vialle M. and Robertson I.K. 2015. Usefulness of non-invasive spectrophotometric haemoglobin estimation for detecting low haemoglobin levels when compared with a standard laboratory assay for preoperative assessment. Br J Anaesth. 114(4):669-676.
20. Feiner J.R., Bickler P.E. and Mannheimer P.D. 2010. Accuracy of methemoglobin detection by pulse CO-oximetry during hypoxia. Anesth Analg.111(1):143-148.