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REVIEW ARTICLE

Comparison of invasive and noninvasive blood hemoglobin measurement in the operating room: a systematic review and meta-analysis

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Abstract

Noninvasive hemoglobin (Hb)-monitoring devices are new inventions in pulse oximeter systems that show hemoglobin levels continuously. The aim of this systematic review and meta-analysis was to evaluate the accuracy and precision of noninvasive versus standard central laboratory Hb measurements in the operating room. We systematically searched multiple databases. Then, for the quality assessment of studies, we modified QUADAS-2 in the Revman 5.3 software. The GRADE approach was used to measure the quality of evidence (Grading of Recommendations Assessment, Development, and Evaluation). Data were analyzed using the meta-analysis method (random effect model) using STATA 11 software. A total of 28 studies on 2000 participants were included in the meta-analysis. Meta-analysis results of mean differences between noninvasive and the central laboratory Hb measurements in overall pooled random effects were −0.27 (95% LoA (0.44, −0.10); *P* value < 0.05). According to this meta-analysis, noninvasive hemoglobin measurement has acceptable accuracy in comparison with the standard invasive method.

Keywords Measurement · Pulse oximeter · Noninvasive · Hemoglobin · Monitoring

Introduction

Among the diagnostic parameters in patients undergoing surgery, measuring hemoglobin (Hb) concentration is vital [1]. It is necessary for the surgical team to manage the patient's

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clinical condition in bleeding and hemoglobin reduction [2]. As a precise and timely measurement of hemoglobin, as the first indication for blood transfusion can have a significant effect on reducing morbidity Treatment costs can be reduced by preventing blood transfusions and timely transfusion of blood to patients [3, 4] but it should be kept in mind that in case of an incorrect hemoglobin level diagnosis, blood transfusion can be associated with an allergic reaction and infectious diseases (viral and bacterial); this can lead to severe complications, such as hemolytic reactions, cardiac failure and even death [5, 6] Currently, the only para-clinical benchmark for measuring hemoglobin is the amount of laboratory hemoglobin [3]. Although the gold standard laboratory method is used to measure blood hemoglobin, it requires taking blood samples from the patient and transferring them to the laboratory, which is a time-consuming process. This can delay the timely decision for the patient [1, 7–9]. The new technology of noninvasive measurement of blood hemoglobin is the most advanced diagnostic technology for improving the health of patients under anesthesia [10]. Currently, noninvasive technology that measures blood hemoglobin includes multiwavelength co-oximetry (Radical-7™ and Pronto-7™; Masimo Corp., Irvine, CA, USA) and occlusion spectroscopy (NBM-200™, OrSense, Nes Ziona, Israel) [11]. The device displays the blood hemoglobin levels continuously through a finger probe connected to a digital monitor [12, 13]. The accuracy and precision of noninvasive hemoglobin measurements in various surgical procedures have been studied, but the results of these studies have been controversial and inconsistent. Hence, the aim of this systematic review was to evaluate between invasive and noninvasive methods in mean difference and 95% limits of agreement (LOA) using the meta-analysis method.

Methods

Data sources and literature searches

This meta-analysis was conducted to compare the invasive and noninvasive measurements of hemoglobin during surgery. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14]. We searched multiple databases including Scopus, PubMed, Center for Reviews and Dissemination (CRD), Cochrane library and web of science databases, published from their inception to the 15th of June 2018, using the following keywords: measure, oximeter, hemoglobin, noninvasive, SpHb, Hb, co-oximetry, Masimo, radical-7, and noninvasive. Reference lists of all accepted articles for studies that had not initially been identified were searched. The full articles of potentially eligible studies were reviewed, and articles published only in abstract form were excluded (literature searches, Online Resource1).

Inclusion and exclusion criteria

Study inclusion in our meta-analysis were the following: (i) published studies comparing the laboratory measurement of hemoglobin (Hb Lab) and noninvasive blood hemoglobin (Hb) measured, (ii) studies in children and adults in surgery, (iii) studies presenting mean difference and SD of the mean difference (or 95% LOA) between noninvasive Hb-monitoring systems and central laboratory Hb measurements, (iv) article was written in English, and (v) full-text publications. Exclusion criteria were the following: (i) studies that do not provide the mean difference (or 95% LOA) comparing Hb measured, (ii) studies in neonates, (iii) studies done in other healthcare departments, and (iv) full text of the article could not be retrieved.

Data extraction and quality assessment

The following data were recorded for each study transferred separately to a standard Excel spreadsheet: title, first author, journal name, sample size, study location, type of study, subjects, age, sex, height, weight, blood sample (venous or arterial) type of anesthesia (local or general), noninvasive device and sensor used, financial resources, and total number of measurement pairs, bias (mean difference) and standard deviation (SD) for bias. We evaluated the quality of the studies using Quality Assessment of Diagnostic Accuracy Studies guidelines (QUADAS-2) [15] in the Revman 5.3 software. We focused to evaluate the quality of the studies on four domains for the assessment of risk of bias patient selection, index selection, reference standard, and flow and timing, and three domains for the assessment of concerns related to applicability (patient selection, index test, and reference standard). Since most studies compared the two methods of observation, so we modified the checklist questions and four domains for the assessment of risk of bias (patient selection, index test, reference standard, as well as flow and timing) according to the type of study. We assessed the quality of evidence by means of Grading of Recommendations Assessment, Development and Evaluation (GRADE). So we assessed bias between the two measurement methods (evidence) in each subgroup risk of bias, inconsistency, indirectness, imprecision, and publication bias strength, dose response and confounding. Overall quality of the evidence was categorized at very low, low, moderate, and high.

Implementation of all the steps of the literature search, assessment for inclusion and data extraction, quality assessment and quality of evidence were carried out by two

independent reviewers, and any disagreements were resolved by consensus and a third author.

Outcome

The main outcome was measuring the accuracy of the index test compared to a reference standard, mean differences between noninvasive and the central laboratory Hb measurements from a single study.

Synthesis and analysis of data

To combine the results, the mean difference (defined as noninvasive–invasive measurement), SD, and 95% LOA (calculated by mean difference ± 1.96 SD of mean differences) from the studies were extracted. Heterogeneity was determined by the Chi square test with a significance level of 0.05 combined with an I^2 statistic for estimates of inconsistency within the meta-analyses. If the I^2 index is more than 75%, it indicated high heterogeneity, values between 75% and 50% indicated moderate heterogeneity and less than 50% showed low heterogeneity [16, 17]. Due to the elevated heterogeneity, a random effects model was used to calculate the pooled bias and corresponding 95% limit of agreements. We performed the subgroup analysis based on continent and sampling site for the central laboratory Hb measurement (arterial/venous), funding source, number of measurement per patient (multiple/single), country of study, age and also we conducted a meta-regression analysis on publication year, sample size, and age. The P value of $P < 0.1$ is considered to be the publication bias. Adjusted mean difference (bias) was calculated using trim and fill method. To investigate publication bias, the funnel plot and Egger's test were used. Statistical analysis was performed using Stata software version 11. P value < 0.05 was considered as a significant level.

Results

Characteristics of the included studies

In the systematic search of all databases, 3648 articles were extracted. 929 duplicate articles were excluded and

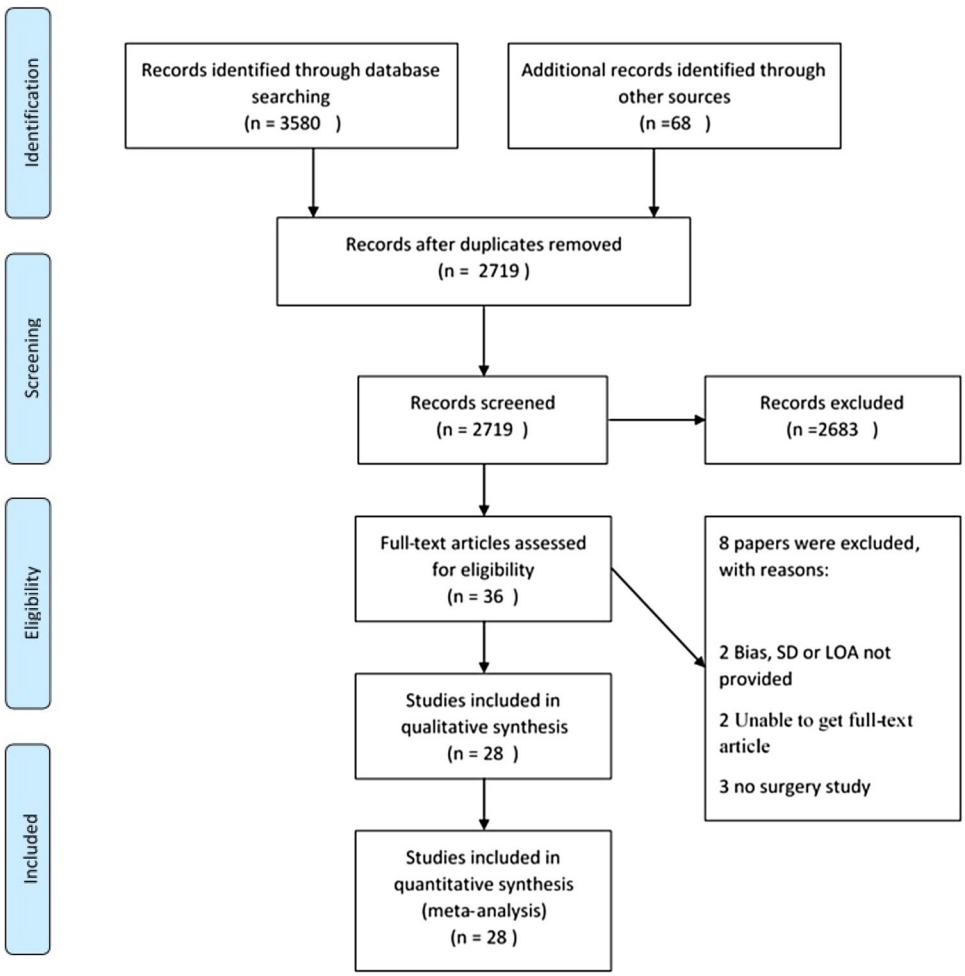

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for studies included in the review

2683 articles were excluded after reviewing their titles and abstracts. After reviewing the full text of the articles, 36 qualified articles were examined based on inclusion and exclusion criteria and 8 papers were excluded (Online Resource2). Finally, 28 articles entered the meta-analysis. The PRISMA flow diagram is shown in Fig. 1. In this study, 28 papers were ultimately included in the meta-analysis. In the selected studies, the total number of participants was 2000 and ultimately 4240 pairs of hemoglobin were measured in all studies, the accuracy of Radical7 was evaluated. The median (Min, Max) of the sample size of the study was 40 (19,155) and the age range of subjects studied in the studies was between 19 and 55 years. Based on 28 studies reporting age, the mean age was 45 years. From the total 28 studies in this meta-analysis, 25 studies were done on adults [1, 9, 13, 18–39], 3 studies performed on children [8, 40] and 1 study both on children and adults [41]. 20 studies were done in Asia [8, 9, 18, 27–29, 32, 34, 36, 37, 39, 40], 8 studies in the United States [9, 13, 21–24, 31, 41], and 8 studies were conducted in Europe [1, 20, 25, 26, 30, 33, 35, 38]. Venous blood samples were used in five studies [1, 13, 22, 35, 38], and a venous and arterial blood sample in one study [21] and arterial blood sample by the Hb laboratory were used in the rest of studies. Local anesthesia was used in two studies [23, 35] and general anesthesia was used in the 25 other studies [1, 8, 9, 13, 18–21, 23, 26–34, 39]. The primary characteristics of patients are briefly summarized in Table 1.

Risk of bias in included studies

Results of quality assessment using QUADAS-2 are shown in Figs. 2 and 3. It should be noted that only 12 studies were rated as low risk both in risk of bias and applicability concerns. 10 studies were deemed at high risk of bias and 6 study at unclear risk.

Quality of evidence

We assessed the quality of the evidence obtained from the meta-analysis results which was classified using the GRADE approach. The evidence was classified using into four grades: very low, low, moderate, and high. GRADE results are shown in Table 2.

Meta-analysis results

The mean difference in blood hemoglobin measured in both methods (bias = SpHb-Hblab) with a standard deviation of mean difference was extracted from the 28 articles entered into the meta-analysis. Then, these values were entered into the meta-analysis for combining the results. The study of heterogeneity of effect size between studies showed that heterogeneity was not significant between studies (I-squared = 0.0%, P value = 0.595). The random effects model was used to combine the results. Meta-analysis results showed the mean differences between noninvasive and the central laboratory Hb measurements with 95% of LoA −0.27 (95% LoA (−0.44, −0.10); P value < 0.05). Figure 4 shows the forest plot of the mean difference in hemoglobin measurement of the two methods.

Analysis of subgroups

The subgroup analysis for age variables was classified into four groups and the continental location was considered for studies. The results of the analysis of the subgroups showed that the mean difference between the two methods for the groups under age 20, 20–33, 34–45 and over 45 years old was 0.18, 0.27, −0.95 and −0.27, respectively. Subgroup analysis for the location of studies showed that the mean difference between the two methods for studies in the Asia, European, and American continents were −0.22, 0.03 and −0.26, respectively. Analysis of subgroups for blood sampling method in the venous and arterial was −0.26, −0.26 and −0.30, respectively. Subgroup analysis-based funding of studies showed that the mean difference between the two methods for funding and non-funding studies was 0.35 and −0.34, respectively; subgroup analysis-based measurement per studies showed that the mean difference between the two methods for studies single and multiple measurement was −0.291 and −0.122, respectively The results of the analysis of the subgroups are shown in Tables 3, 4, 5, 6 and 7. Forest plots related to the analysis of subgroups are shown in Online Resource 3–7 of analysis of subgroups.

Meta-regression analysis results

The meta-regression was conducted based on age and sample size. The results of meta-regression showed that for one unit increase in patients age and study sample size, the bias between two methods increase 0.008 and 0.0006, respectively, while, for one unit increase in year of publication, the bias decrease 0.06 and these values were not statistically significant ($P > 0.05$). Meta-regression results are shown in Online Resource 3.

Results of assessing publication bias

The results of Egger's regression test showed that the publication bias between the articles entered into the study was significant ($t = 1.78$, P value = 0.083). Therefore, the trim and fill analysis was performed and the results showed that after trim and fill, a study which did not affect the bias value

Table 1 Characteristics of studies included meta-analysis

Author	Year	Type of surgery	Test device (software version, sensor version)	Laboratory hemoglobin analyzer	Stage measurements	Sample size	Measurement pairs	Funding source
Vos, Jaap Jan	2012	Liver surgery	Masimo Radical7 (7.6.0.1,Rev E)	Hbsatlab ABL 800	Steady-state Dynamic phase Total	30	543	Masimo Radical 7device and sensors were kindly provided by Masimo Corp., IrvineCA, USA
Butwick et al.	2011	Cesarean	Radical7 (7.6.0.4,Rev E)	Hb hematology	Baseline Immediately post-cs 24 h post-cs	50	150	Masimo Corp. (Irvine, CA, USA) and by the Department of Anaesthesia
Park et al.	2012	Undergoing neurosurgery	Radical7 (7.6.1.1,Rev E)	Hb ABL820	After volume resuscitation After administration of colloid After administration of colloid Overall	40	119	No funding
Applegate et al.	2012	Abdominal or pelvic surgery	Radical7(rev E)	HB Radiometer ABL800	Total	91	360	Masimo
Lamhaut et al.	2011	Major urologic surgery	Radical7 (7409,Rev E)	HB SP 1000i	Total	44	85	Institutional and/or departmental sources
Dewhirst	2013	Congenital heart disease repair	Radical7 ((7.6.2.1) Rev E)	HB AVOXImeter	Total	40	50	No funding
Berkow et al.	2011	Complex spine surgery	Radical7 (7610,Rev E)	Hb ABL820	Total	29	186	Masimo
Miller et al.	2011	Spine surgery	Radical7(Rev E)	HB Bekman coulter	Total	20	78	Department of Anesthesia, and Masimo
Isosu et al.	2013	Laparostomy, thoracotomy, thoracolaparotomy, laparoscopic surgery	Radical7(7.4.0.9,Rev C)	HB (Rapidlab 860)	Total	20	92	No funding
Causey et al.	2011	General surgery, maxillofacial surgery, orthopedic surgery, general surgery, urology, vascular surgery, neurosurgery, orthopedic surgery, otolaryngology	Radical7 (7.5.3.1) R1 25 RevC	HB	Overall	25	101	No funding
Skelton et al.	2013	Elective cesarean section	Radical7 (7.6.0.1,Rev E)	Hb Advia 2120	Preoperative Postoperative	137	247	Masimo
Miyashita et al.	2014	Elective abdominal surgery	Radical7(R1 25 R1 25a)	Thb ALB700	R1-25 R1-25a	19	70	No funding
Kim sung-Hoon et al.	2014	Double-jaw surgery	Radical7 (7.8.0.1) R2-25, Rev E	Thb pHOx	Pre Lefort BSSO POSTo	51	51	Institutional or departmental source

Table 1 (continued)

Author	Year	Type of surgery	Test device (software version, sensor version)	Laboratory hemoglobin analyzer	Stage measurements	Sample size	Measurement pairs	Funding source
Patino et al.	2014	Spinal surgery, cardiac craniectomy-cranio liver resection	Radical7 (R1 20L or R1 25L,revision E) (R2 20 or R2 25, revision E)	HB Cell-Dyn sapphire	Total	46	140	Masimo
Awada et al.	2015	Reduces red blood cell transfusion during neurosurgery	Radical 7 v7748 (R2-25 Rev E)	HB GEN-S	Total	106	?	Masimo
Yamaura et al.	2014	Urologic oncology, gynecological oncology, others	Radical7 (R-25, Rev C)	HB ABL 800	0–1 1, 2 2, 3 3, 4	28	175	Departmental funding
Frasca et al.	2015	Total hip or knee, replacement (redux, hepatectomy, spinal surgery, aortic aneurysm repair, nephrectomy, prostatectomy, meningioma	Radical7 (R2-25, Revision G)	HB Sysmex™XT-2100i	Total	41	173	Masimo
Giraud et al.	2013	Major surgery with expected significant blood los	Radical7 (7.6.0.1) R2-25Rev E	HB Sysmex™XT-2100i	Total	53	219	University Hospital of and Masimo
Park et al.	2015	General surgery, maxillofacial surgery, orthopedic surgery, gynecology, otolaryngology, eye surgery, urology	Radical7 (7.8.0.1) R2-25Rev E	HB XE-2100®	Pre Post	26	26	Not report
Saito et al.	2015	Radical prostatectomy, nephrectomy, radical hysterectomy, semiradical hysterectomy	Radical7 (7601) ReSposable TM	HB KX-21N	Dilution Transfusion	24	228	Department of Anaesthesia
Toyoda et al.	2014	Major gastrointestinal, vascular, gynecological, urological, neurosurgical	Radical-7	HB ABL725	tHBlow thbMed thbHigh	56		JSPS KAKENHI Grant Number 24592361
Colquhoun	2012	Spine surgery	Radical-7 R1 25 (Rev E)	HB RapidPoint 405	Total	20	88	Masimo
Huang et al.	2016	Liver transplantation	Radical 7 ((1.1.6.3i) R225, revE)	HB gas analyzer	Total	40	161	Not report
Riess et al.	2016	Undergoing cardiac surgery	Radical 7 (7.7) R2 25a R2-25r	HB i-STAT CG8+	Before CPB	35	–	Institutional funding
Baulig et al.	2015	Sever traumatized and surgical bleeding patients	Radical 7 Type RDS-1 (R1 25 (revision F and G))	CoOxHb ABL 825	Total	35	141	Masimo
Khanna	2014	Undergoing intracranial surgery	Radical7	Thb hematology analysers	Total	30	–	Not funding
Kayhan	2017	Liver transplantation	Software v. 7.8.0.1, Masimo Corp.	Coulter LH 780	Total	53	282	Not funding
Namrata Gupta	2018	Oncosurgery	Radical7	Beckman Coulter	Total	50	66	Not funding

Test device (software version, sensor version) noninvasive Hb-monitoring devices: Radical-7 and Rad-57 (Masimo Corporation, Irvine, CA, USA) SpHb invasive blood Hemoglobin Measurement Hb: Laboratory Hb analyzer

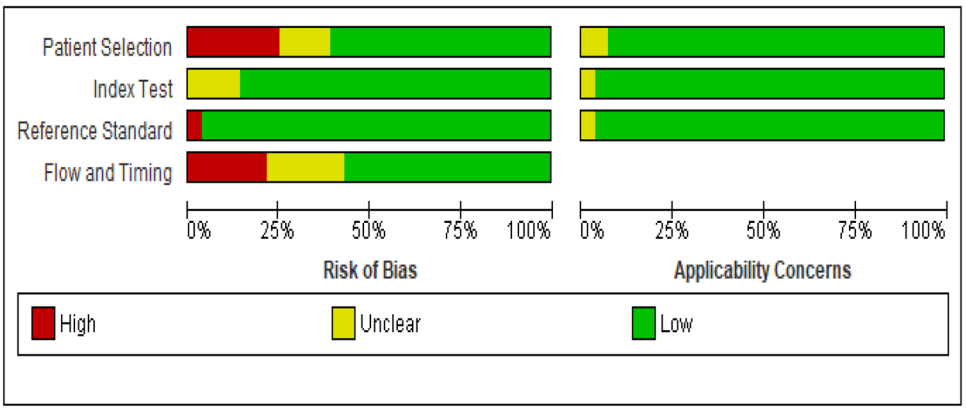

Fig. 2 Risk of bias and applicability concern graph between the noninvasive Hb (hemoglobin) monitoring and laboratory Hb analyzer

Fig. 3 A summary table of review authors' ratings of risk of bias and applicability concerns for each study between the noninvasive Hb (hemoglobin) monitoring and laboratory Hb analyzer

was added. After the Trim and fill, the bias value (95% LOA) is equal to: −0.44 (−0.77; −0.17). Also, the funnel plot for assessing publication bias and funnel plot-related trim and fill in Figs. 5 and 6 showed that the symmetry of the graph indicated the absence of a publication bias.

Discussion

One of the most important determinants of blood transfusion is the measurement of blood hemoglobin. It is very important to use devices that can provide this information to the medical staff quickly and continuously [42]. In recent years, noninvasive hemoglobin measurements have been used to manage patients and administer blood [43]. Several studies have examined the accuracy and precision of noninvasive Hb measurement compared to gold standard central laboratory Hb measurement in various conditions, such as various surgeries as well as ICU [21, 44–46].

In our meta-analysis, 2000 people participated in 28 independent studies to verify the accuracy and precision of noninvasive hemoglobin measurements compared to the Hb laboratory method. In this study based on quality of evidence, the bias between the two methods of measuring hemoglobin in all studied subgroups was less than 1 g/dl.

The results of the random effects model meta-analysis studies showed the mean difference and 95% LOA, between two methods of measurement, was blood hemoglobin −0.27(−0.44, −0.1) g/dl. The heterogeneity among studies was not significant for mean difference. Kim et al., in their systematic review of the evaluation of an agreement between the invasive and noninvasive Hb measurements in various healthcare settings, indicate the limits of agreement reached were consistent with the current meta-analysis, but bias (noninvasive-invasive) was negative, contrary to our study. It should be taken into account, however, that the studies included in the study, Kim et al., were conducted in various settings, and only 13 were in the operating room. Also, the studies performed in the operating room were not

Table 2 Grading of recommendation assessment, development and evaluation (GRADE) bias between the two methods of noninvasive Hb monitoring and laboratory Hb analyzer

Sdss subgroup	No of study	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Strength (95% LOA)	Quality
Age								
< 20	4	Very serious	No serious	No serious	Serious	Undetected	0.18 (− 1.04; 1.40)	⊗⊗ Low
20–33	7	Serious	No serious	No serious	Serious	Undetected	0.27 (− 0.47; 1.00)	⊗⊗⊗ Moderate
33–45	6	No serious	No serious	No serious	Serious	Undetected	0.95 (− 2.02; 0.13)	⊗⊗⊗⊗ High
> 45	25	Serious	No serious	No serious	No serious	Detected	− 0.27 (− 0.45; − 0.09)	⊗⊗⊗ Moderate
Continent								
America	13	Very serious	No serious	No serious	Serious	Detected	− 0.26 (− 0.86; − 0.34)	⊗ very low
Asia	20	No serious	No serious	No serious	Serious	Undetected	− 0.22 (− 0.63; 0.19)	⊗⊗⊗⊗ High
Europe	8	No serious	No serious	No serious	Serious	Undetected	0.03 (− 0.88; 0.93)	⊗⊗⊗⊗ High
Method								
Venous	6	Serious	No serious	No serious	Serious	Undetected	− 0.26 (− 1.45; − 0.92)	⊗⊗⊗ Moderate
Arterial	35	No serious	Serious	No serious	No serious	Detected	− 0.26 (− 0.43; − 0.09)	⊗⊗⊗ Moderate
Funding								
Funding	13	No serious	No serious	No serious	Serious	Undetected	0.357 (− 0.253; 0.967)	⊗⊗⊗⊗ High
No funding	27	Serious	No serious	No serious	No serious	Undetected	− 0.348 (− 0.656; − 0.041)	⊗⊗⊗⊗ High
Measurement								
Multi	22	Very serious	No serious	No serious	Serious	Undetected	− 0.122 (− 0.600; 0.355)	⊗⊗ Low
Single	19	Serious	No serious	No serious	No serious	Undetected	− 0.291 (− 0.472; − 0.110)	⊗⊗⊗⊗ High

homogeneous ($I^2 = 93\%$), which could provide bias results. While, in the present meta-analysis, researchers just include 28 studies conducted in operating rooms and there was no significant heterogeneity among them.

All noninvasive devices measuring hemoglobin in our meta-analysis study were Radical-7 (Masimo Corporation, Irvine, CA, USA), The Hiscock et al. meta-analysis study, recently performed to evaluate two Masimo pulse co-oximeters and HemoCue® devices compared to an invasive measurement method, showed that Masimo device has a lower accuracy and precision than HemoCue®. Also, the bias and 95% LOA of noninvasive Massimo and laboratory methods in the Hiscock study were − 0.03 (− 3.0, 2.9). There was no clinically significant difference and the results were consistent with our research results.

In the subgroups analysis on age variables, it was found that bias 95% LOA was significant in the age group of above 45 years. Several studies with the mean age of participants over 45 years of age have been consistent with the results of this study [1, 36, 37, 39]. In some studies, there was no significant relationship between bias and limit of agreement, which could be due to the low number of participants or the difference in the type of surgery [26, 27, 34].

In subgroup analysis for venous and arterial blood sampling, it was found that there was an agreement between arterial and venous blood values. For clinical evaluation, arterial blood samples are usually used, but considering that the ABG (Arterial Blood Gas) compared to (Venous Blood Gas) VBG, in addition to being more painful, there is a possibility of complications such as hematoma, thrombosis or embolization. According to the results of the subgroup analysis of the present study, there is no difference between venous and arterial blood samples [47]. To interpret the results of 95% LOA of noninvasive Hb measurements compared to invasive central laboratory measurements, several studies have considered the value of 1 g/dl as the significant threshold between methods [1, 29, 35]. According to these studies, which consider 1 g/dl as a clinical threshold, the

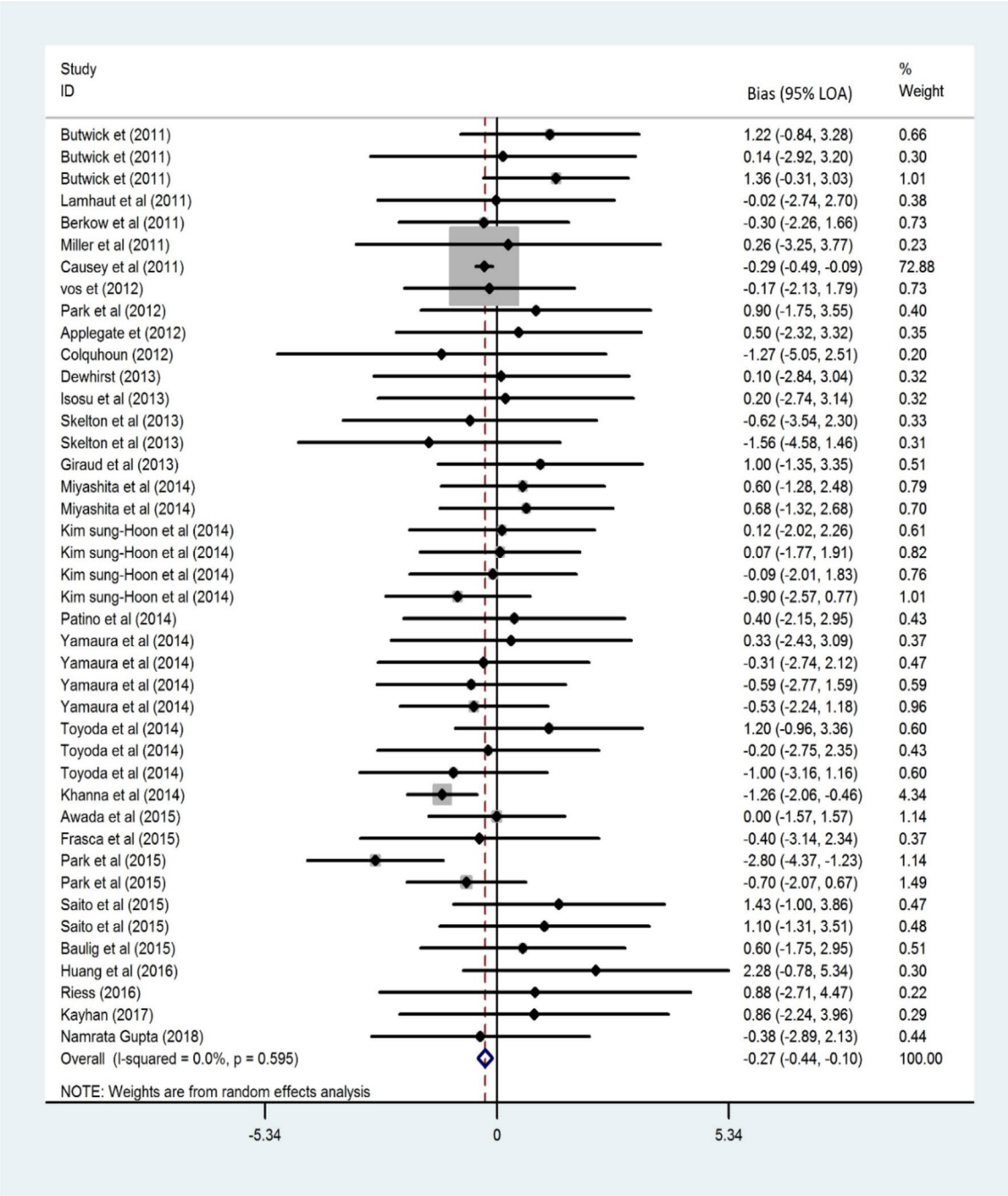

Fig. 4 Forest plot mean difference and 95% limits of agreement (LOA) for studies comparing noninvasive hemoglobin monitoring with laboratory hemoglobin analyzer

Table 3 The analysis of subgroups for age variables was classified into four groups and the continental location was considered for studies

Age (categories)	Number study	Pooled mean difference (bias)	95% LOA	*P* value	*I*-squared (%)
< 20	4	0.18	(− 1.04, 1.40)	0.786	0.0
20–33	5	0.27	(− 0.47, 1.00)	0.479	0.0
33–45	8	0.95	(− 2.02, 0.13)	0.084	40.4
> 45	25	− 0.27	(− 0.45,− 0.09)	0.003	0.0
Total	43	− 0.27	(− 0.44, − 0.10)	0.002	0.0

Table 4 Subgroup analysis continent for mean difference between the noninvasive Hb monitoring and laboratory Hb analyzer

Continent	Number study	Pooled mean difference (bias)	95% LOA	*P* value	*I*-squared (%)
America	14	−0.26	(−0.86, 0.34)	0.390	30.4
Europe	8	0.03	(−0.88, 0.93)	0.951	0.0
Asia	21	−0.22	(−0.63, 0.19)	0.285	0.0
Overall	43	−0.27	(−0.44, −0.10)	0.002	0.0

Table 5 The analysis of subgroups for based method mean difference between the noninvasive Hb monitoring and laboratory Hb analyzer

Based method	Number study	Pooled mean difference (bias)	95% LOA	*P* value	*I*-squared (%)
Arterial	22	−0.26	(−1.45, 0.92)	0.014	62.6
Venous	5	−0.26	(−0/43, −0/09)	0.927	0.0
Arterial/venous	1	−0.30	(−2/26, 1/66)	0	0
Overall	28	−0.27	(−0.44, −0.10)	0.595	0.0

Table 6 The analysis of subgroup-based funding method mean difference between the noninvasive Hb monitoring and laboratory Hb analyzer

Based funding	Number study	Bias	95% LOA	*P* value	*I*-squared (%)
Funding	13	0.357	(−0.253; 0.967)	0.251	0.00
Non-funding	27	−0.348	(−0.656; −0.041)	0.026	8.3
Overall	41	−0.270	(−0.437; −0.103)	0.002	0.00

Table 7 The analysis of subgroups by number of paired measurements method mean difference between the noninvasive Hb monitoring and laboratory Hb analyzer

Based measurement	Number study	Bias	95% LOA	*P* value	*I*-squared (%)
Multiple	21	−0.122	(−0.600; 0.355)	0.615	15.4
Single	19	−0.291	(−0.472; −0.110)	0.002	0.00
Overall	41	−0.270	(−0.437; −0.103)	0.002	0.00

result of our study is an acceptable result. Based on our meta-analysis results, bias in studies that received funding was not statistically significant. It can be said that no significant difference exists between the mean of hemoglobin measured by two methods. This is while in studies without funding resources, the mean of Hb between two methods was statistically significant. Perhaps the difference between the results based on the funding resources may be due to the availability of those funding resources which ever in favor of the measurement method with the noninvasive device. However, the difference between the two methods of measuring hemoglobin in two groups of studies was less than 1 g/dl, which could indicate acceptable results.

The goal of this systematic review and meta-analysis was to assess the agreement between noninvasive Hb measurements and central laboratory Hb measurements in surgery and providing a general interpretation of the results. Therefore, the importance of the accuracy of noninvasive continuous hemoglobin measurements is apparent in reducing transfusion. Awada et al. in their study showed that in the noninvasive hemoglobin measurement group, blood transfusion rates dropped 0.1 versus 1.9 in the invasive group [18].

Due to the limitations of this systematic review according to the diagnostic accuracy studies, the sensitivity and specificity were not counted [48]. Since the strength of the evidence is greater in the clinical trial study, it is necessary to use clinical trial studies to compare noninvasive hemoglobin measurement compared to the gold standard of the laboratory, otherwise, some of the influential variables would not be analyzed for example, peripheral perfusion is one of the variables that have influence on invasive and noninvasive measurements. In a study that measured SpHb by Radical7, it was shown that if the peripheral perfusion value is more than 1.4, the accuracy of the SpHb device is less than that when PI > 4.0 [31]. The laboratory measurement method was the reference in this study, but the difference was not considered in laboratory methods.

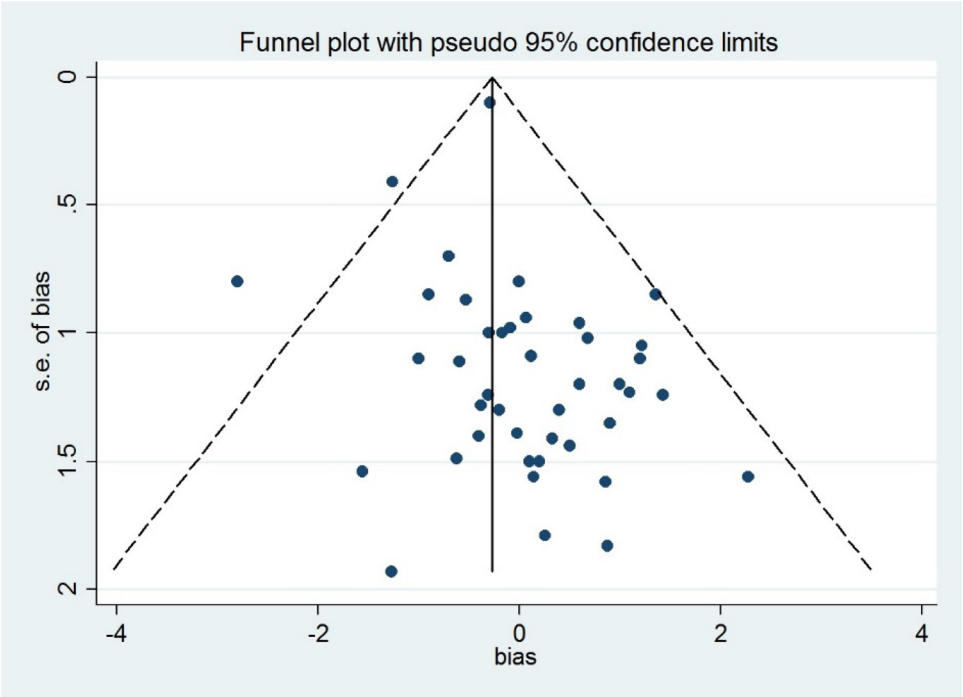

Fig. 5 Funnel plot for assessing publication bias between the articles entered into the study for the comparison of noninvasive Hb monitoring and laboratory Hb analyzer

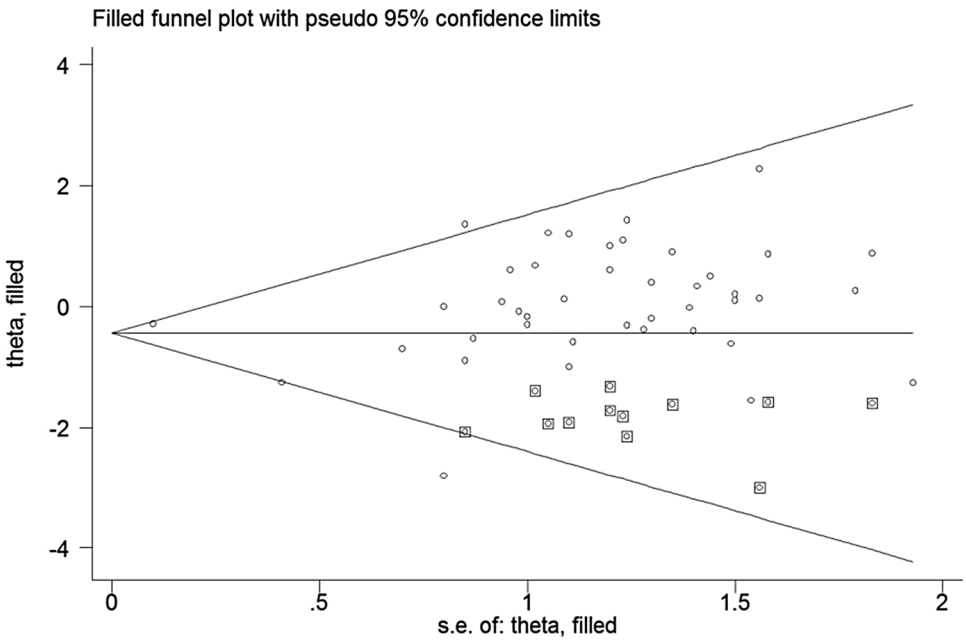

Fig. 6 Funnel plot adjusted based on trim and fill. After the studies have been fill

Conclusions

Our meta-analysis showed that with a conservative view of point and stringent, regarding an acceptable agreement between invasive and noninvasive Hb measurements, based on clinical significance 1 g/dl, the clinician after first Hb assessment by both methods can follow the trend of variations in Hb using the noninvasive method.

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