Comparing near-infrared spectroscopy—measured cerebral oxygen saturation and corresponding venous oxygen saturations in children with congenital heart disease: a systematic review and meta-analysis

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Background: Near-infrared spectroscopy (NIRS) is a non-invasive approach that measures cerebral regional oxygen saturation ($rScO_2$). In this study, we evaluated the evidence on the validity of NIRS and the interchangeability between NIRS and common invasive approaches by exploring the correlation and consistency and comparing the mean and standard deviation between the NIRS $rScO_2$ and jugular bulb venous oxygen saturation ($SjvO_2$) as well as central venous oxygen saturation ($ScvO_2$) in the perioperative period of children with congenital heart disease (CHD).

Methods: We searched electronic bibliographic databases (PubMed, The Cochrane Library and Embase) and screened the studies that met the inclusion criteria. We included cross-sectional studies of CHD pediatric patients in the perioperative period receiving both tests for NIRS $rScO_2$ and $SjvO_2$ or NIRS $rScO_2$ and $ScvO_2$. Methodological quality assessment and heterogeneity analyses were performed. We qualitatively summarized the results of Bland-Altman's analysis. Meta-regression, subgroup analyses, and sensitivity analyses were carried out to explore the causes of heterogeneity.

Results: There was no significant difference in Cohen's d between $rScO_2$ and $ScvO_2$ or between $rScO_2$ and $SjvO_2$ (Cohen's d =0.06, 95% CI: –0.16 to 0.28; Cohen's d =0.03, 95% CI: –0.25 to 0.31, respectively) and notable heterogeneity existed (I^2=76.0%, P<0.001; I^2=73.6%, P<0.001, respectively). A positive linear correlation was present between $rScO_2$ and $ScvO_2$ or between $rScO_2$ and $SjvO_2$ (r=0.58, 95% CI: 0.54 to 0.63; r=0.60, 95% CI: 0.54 to 0.66, respectively) and the heterogeneity was not significant (I^2=36.7%, P=0.065; I^2=12.7%, P=0.328, respectively). In most studies, the 95% limits of agreements of Bland-Altman's analysis were large. No evidence of publication bias was observed.

Conclusions: The $rScO_2$ measured by NIRS reflected the $SjvO_2$ and $ScvO_2$ monitored by invasive measurements in the perioperative period of children with CHD to some extent. However, wide limits of agreements between $rScO_2$ and $SjvO_2$ as well as $ScvO_2$ indicated that NIRS and $SjvO_2$ as well as $ScvO_2$ are not interchangeable. Whether NIRS plays a prominent role in monitoring cerebral oxygen saturation in children with CHD needs further research.

Introduction

In the past several years, the postoperative survival rate of children with congenital heart disease (CHD) has improved, but whether their postoperative quality of life has also improved is not known (1-3). For CHD patients undergoing cardiac surgery or cardiac catheterization, brain injury could occur before and after interventions, and neurodevelopmental impairment could affect patients' cognition, motor skills, social interaction and behavior, language, concentration, and executive function (4,5). Preoperative and postoperative hypotension and hypoxemia are significant risk factors for brain injury in pediatric CHD patients (6,7). Thus, real-time neurological monitoring is necessary for children with CHD undergoing cardiac surgery or cardiac catheterization (5). Cerebral perfusion and oxygen saturation are important factors affecting neurological functions that must be monitored perioperatively to assure satisfactory patient outcomes.

Direct or indirect invasive approaches are used to monitor cerebral oxygen saturation. The best indicator reflecting global tissue oxygen saturation is mixed venous saturation, but it is inconvenient to acquire. Central venous oxygen saturation (ScvO$_2$) is considered the gold standard substitute for mixed venous oxygen saturation to monitor tissue oxygen saturation in pediatric cardiac surgery (8-10). Pulmonary artery catheters can provide ScvO$_2$ directly. In the absence of pulmonary artery catheters, superior vena cava saturation can be used to reflect cardiac index and mixed venous oxygen saturation after cardiac surgery as a measure of tissue oxygen saturation. Sampling through retrograde cannulation of the jugular vein and measuring jugular bulb venous oxygen saturation (SjvO$_2$) by reflectance oximetry is another accepted invasive method for measuring global cerebral oxygen saturation. An SjvO$_2$ below 50% indicates that insufficient oxygen is supplied to the brain, and treatment to increase cerebral oxygen supply and/or decrease metabolic demand is needed (11).

Near-infrared spectroscopy (NIRS) is a non-invasive method for the measurement of cerebral regional oxygen saturation (rScO$_2$) (12). Invented by Jöbsis *et al.* in 1997 (12), NIRS is a widely used and reliable tool for the measurement of cerebral hypoperfusion in infants with CHD (13). The NIRS monitoring system is based on tissue transmission and absorption of near-infrared light (wavelength 700–950 nm) via biomolecules, for example, oxygenated and deoxygenated hemoglobin. Owing to different optical densities in the near-infrared spectrum, the concentrations of hemoglobin molecules can be determined by their relative absorption wavelength (14). In addition, rScO$_2$ measures the oxygen saturation of brain tissue after weighting that of arteries, veins, and capillaries, and it is simultaneously related to physiological variables such as arterial oxygen saturation, partial pressure of arterial carbon dioxide (PCO$_2$), blood pressure, hematocrit, cerebral blood flow, cerebral blood volume, and cerebral metabolic rate (15,16). In pediatric cardiac surgery, it is recommended that NIRS oxygenation monitoring start before delivery of oxygen and continue to the postoperative period (7). As a sustainable, rapid, and non-invasive monitoring tool for rScO$_2$ measurement, NIRS may yield improved measurement of cerebral oxygen saturation. Nevertheless, due to the lack of generally accepted reference values and assumption of fixed arterio-venous ratio as well as diverse algorithms, the accuracy of NIRS remains controversial (17). The paradox is that biologic variation exists in arterio-venous ratio related to hypoxia while manufacturers hypothesize a fixed arterio-venous ratio, which will inevitably affect the results of NIRS (18). Besides, readings of NIRS vary considerably between repeated measurement of the same subjects and between subjects with different cerebral oximeters (19). Currently, the Food and Drug Administration (FDA) have not regulated the standards for accuracy of cerebral oximeters. A systematic review and meta-analysis is needed to validate the accuracy of NIRS and assess whether rScO$_2$ can replace SjvO$_2$ and ScvO$_2$ to monitor cerebral oxygen saturation.

This systematic review and meta-analysis intended to assess the validity of NIRS in measuring cerebral oxygen saturation in children with CHD undergoing surgery and evaluate the interchangeability between noninvasive

NIRS and common invasive approaches in observational studies. Our specific objectives were to compare Cohen's d between NIRS $rScO_2$ and $ScvO_2$ as well as $SjvO_2$ and explore the correlation and consistency between NIRS $rScO_2$ and $ScvO_2$ and $SjvO_2$. We hypothesized that the validity of NIRS is comparable to that of $ScvO_2$ and $SjvO_2$ measurements. We presented the following article in accordance with the MOOSE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-345/rc) (20).

Methods

Search strategy

A literature search was conducted by 2 investigators independently from the inception of the relevant databases until February 2022. The electronic bibliographic databases of PubMed, The Cochrane Library, and Embase were searched. We searched these databases using the search strategies described in Supplementary Appendix 1, Appendix 2, and Appendix 3. All the retrieved results were crosschecked by Y Ma, L Zhao.

Inclusion criteria

Types of studies
Cross-sectional analyses.

Types of participants
CHD pediatric patients younger than 18 years of age undergoing cardiac surgery or cardiac catheterization.

Types of examination method
(I) Cerebral oxygen saturation of patients was monitored perioperatively by NIRS and $SjvO_2$. (II) Patients were monitored perioperatively by NIRS and $ScvO_2$ as an assessment of cerebral oxygen saturation. (III) All included studies provided details of the NIRS devices used.

Statistics
The included studies reported mean difference (MD), standard deviation (SD), and correlation coefficient (r) values between $rScO_2$ and $SjvO_2$ and between $rScO_2$ and $ScvO_2$.

Study selection

After removal of duplicate papers, the remaining articles retrieved in the databases were screened through the titles and abstracts according to the inclusion criteria. Editorials, reviews, animal experiments, commentaries, conference papers, non-English language articles, abstracts, unpublished articles, and irrelevant articles were excluded. Articles with unobtainable original texts were also excluded. Full text articles were assessed for eligibility, and articles that lacked the data mentioned stipulated by the inclusion criteria were excluded. The screening was performed manually and independently by 2 reviewers, and differences were resolved through discussion and consensus.

Data extraction

The following data were extracted from the included studies: author, publication year, study design, number of patients, data points, median age, types of treatment, diagnosis, sites of NIRS, types of NIRS device, types of venous oxygen saturation measurement, MD, SD, r values between 2 methods, and 95% limits of agreement (LOA). Data extraction was conducted by 4 experienced investigators.

As the MD and SD were not provided in some studies, we extracted $rScO_2$, $ScvO_2$, and $SjvO_2$ values from scatter diagrams created by MATLAB® (MathWorks, Inc., Natick, MA, USA) instead of contacting authors and then calculated the MD and SD between $rScO_2$ and $ScvO_2$ and between $rScO_2$ and $SjvO_2$. To standardize effect size, we used Cohen's d to evaluate the difference between the 2 methods. Cohen's d was calculated as the MD divided by the SD (21). Most studies used Pearson's correlation coefficients to describe the correlation between the 2 methods. For several studies that used Spearman's correlation coefficients, we converted the Spearman's correlation coefficients into Pearson's correlation coefficients for the sake of uniformity (22). Before calculating the pooled Pearson's correlation coefficient, we transformed the correlation coefficients into Fisher's Z, as the variance or standard error was closely related to the r values.

Methodological quality assessment

Considering that all the included articles were cross-sectional studies, we used the 11-item checklist for methodological quality assessment of cross-sectional studies recommended by the Agency for Healthcare Research and Quality (AHRQ) (23). When the answer was 'NO' or

'UNCLEAR', the item was scored '0'; if it was answered 'YES', then the item was scored '1'. Studies rated as 8–11 scores were regarded as high-quality studies; scores of 4–7 indicated intermediate-quality; and scores of 0–3 suggested low-quality (24).

Statistical analysis

We divided all the studies into $rScO_2$ versus $ScvO_2$ and $rScO_2$ versus $SjvO_2$ groups to estimate the difference and correlation among methods. For continuous variables, we evaluated the pooled Cohen's d and r values with their 95% confidence intervals (95% CIs) in the $rScO_2$ *vs.* $ScvO_2$ and $rScO_2$ *vs.* $SjvO_2$ groups, respectively, using the Stata 15.0 software (Stata Corporation, College Station, TX, USA). We then performed heterogeneity analyses by I^2 test with Stata under a fixed effects model. A score of $25\%<I^2<50\%$ suggested low heterogeneity, and $50\%<I^2<75\%$ and $I^2<75\%$ indicated intermediate heterogeneity and high heterogeneity, respectively (25). When the heterogeneity was significant, meta-analysis was performed under a random effects model. The results were presented in the form of forest plots; when the results suggested high heterogeneity, we carried out meta-regression subgroup analyses and sensitivity analyses to explore the cause of heterogeneity. Meta-regression and subgroup analyses were performed based on the types of NIRS devices used, number of patients, and types of treatment. We drew a funnel plot to detect publication bias only when more than 10 studies were included and used Egger's test to assess funnel plot asymmetry quantitatively (26). For all analyses, $P<0.05$ was considered statistically significant.

Results

The search and methodological quality assessment

Based on our search strategy, 1,590 articles were retrieved from the PubMed, Cochrane Library, and Embase databases (*Figure 1*). The number of papers remaining after removing duplicates was 1,115. A total of 47 papers were left after we excluded editorials, reviews, animal experiments, comments, conference papers, non-English language articles, and irrelevant articles through reading of the titles and abstracts. After full text screening of the remaining articles, and additional 24 articles were excluded. Two articles lacked a description of NIRS devices; 8 articles included patients without CHD; 8 articles lacked a comparison

between $rScO_2$ and $SjvO_2$ as well as $ScvO_2$; and data in 6 articles could not be extracted. A total of 23 studies with 997 children from 1995 to 2022 were eligible for inclusion (8,10,27-47). The search flowchart of this meta-analysis is shown in *Figure 1*. Since we excluded non-English language articles, there was language bias in this study.

Regarding the methodological quality assessment, the scores of the included studies as assessed by the 11-item checklist recommended by AHRQ are given in *Table 1*. Among them, 4 studies were of high quality, and the remainder were of intermediate quality.

Descriptors

The studies included in this meta-analysis are listed in *Table 1*. All 23 included articles were cross-sectional studies. There were a total of 997 participants in the 23 included studies. The sample sizes ranged from 5 to 186. The ages of patients were spread over a broad range in each study. The mean age ranged from 7.9 days to 8.6 years. Studies were carried out in diverse countries, including the UK, USA, Germany, Italy, Argentina, Canada, and Japan. The treatment for CHD involved 2 approaches: 9 studies used cardiac catheterization; 13 studies used cardiac surgery under cardiopulmonary bypass; and 1 study included patients undergoing cardiac surgery or cardiac catheterization. The devices of NIRS mentioned in the involved studies were the NIRO 500/300/200 (Hamamatsu Photonics, Hamamatsu, Japan), the INVOS 3100/5100 (Somanetics Corp., Troy, MI, USA), the INVOS (Covidien, Boulder, CO, USA), the INVOS 5100C (Covidien, Tokyo, Japan), the FORE-SIGHT (CAS Medical Systems, Inc, Branford, CT, USA), and the FORE-SIGHT ELITE (CAS Medical Systems, Inc., Branford, CT, USA). The INVOS 5100C and FORE-SIGHT were approved by the FDA for use in pediatric patients. The NIRS probes were placed over the forehead of patients.

Main outcomes

The pooled Cohen's d with 95% CIs as well as the I^2 for the $rScO_2$ *vs.* $ScvO_2$ group and the $rScO_2$ vs $SjvO_2$ group were performed under a random effects model (*Figures 2,3*).

The pooled Cohen's d was 0.06 (95% CI: –0.16 to 0.28; *Figure 2*) in the $rScO_2$ versus the $ScvO_2$ group and 0.03 (95% CI: –0.25 to 0.31; *Figure 3*) in the $rScO_2$ versus the $SjvO_2$ group, which indicated no statistically significant difference between the Cohen's d of $rScO_2$ measured by NIRS and
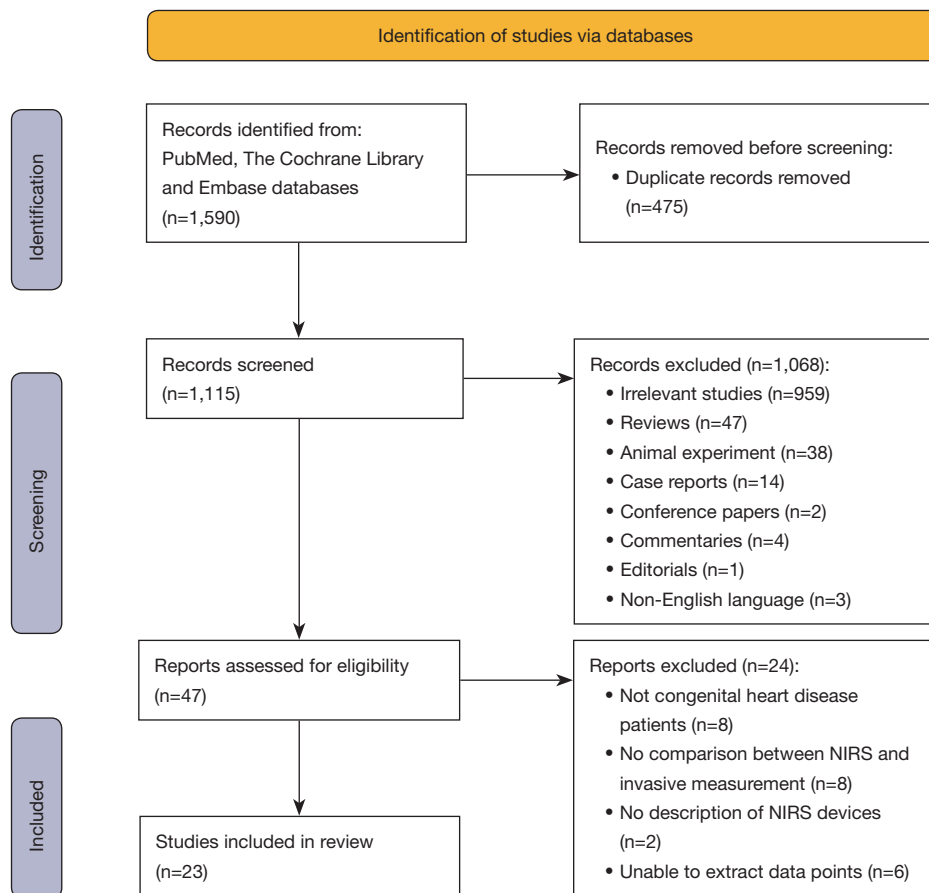
Figure 1 Search flowchart.

ScvO$_2$ as well as SjvO$_2$ measured by invasive approaches. The heterogeneity for the rScO$_2$ *vs.* ScvO$_2$ group was high (I^2=76.0%, P<0.001), and the heterogeneity for the rScO$_2$ *vs.* the SjvO$_2$ group was intermediate (I^2=73.6%, P<0.001). The fixed effects model showed that the rScO$_2$ was positively correlated with the ScvO$_2$ (Fisher's Z =0.67, 95% CI: 0.60 to 0.74; *Figure 4*) with an r value of 0.58 (95% CI: 0.54 to 0.63) after Fisher's Z transformation. Accordingly, rScO$_2$ and SjvO$_2$ were correlated (Fisher's Z =0.70, 95% CI: 0.61 to 0.79; r=0.60, 95% CI: 0.54 to 0.66; *Figure 5*). The heterogeneity was within the acceptable range in the rScO$_2$ *vs.* ScvO$_2$ group (I^2=36.7%, P=0.065) and the rScO$_2$ *vs.* SjvO$_2$ group (I^2=12.7%, P=0.328).

Sixteen of the included studies performed Bland-Altman's analysis to discuss the consistencies between rScO$_2$ and SjvO$_2$ or rScO$_2$ and ScvO$_2$. The 95% LOA of each study is summarized in *Table 1*, and it was fairly wide in most studies. Among them, 3 studies postulated that a difference of ±5%

was considered clinically acceptable (8,29,36). Apparently, consistencies between rScO$_2$ and SjvO$_2$ or rScO$_2$ and ScvO$_2$ were poor in these studies with this standard. With one exception, Shimizu *et al.* declared that rScO$_2$ and SjvO$_2$ showed a reasonable consistency because the difference in the two parameters within the limits of ±10% accounted for 86% (30). Notably, this study only included 5 patients with 14 data points which was unrepresentative.

Publication bias

To assess publication bias, we drew funnel plots for the meta-analyses of Cohen's d and Fisher's Z only in the rScO$_2$ *vs.* ScvO$_2$ group (*Figure 6*). Since there were fewer than 10 studies in the rScO$_2$ *vs.* SjvO$_2$ group, we did not analyze publication bias in this group. Egger's tests revealed no evidence of publication bias (P=0.76 for Cohen's d analysis between rScO$_2$ and ScvO$_2$; P=0.067 for Fisher's Z analysis

Table 1 Characteristics of the included studies

Author	Year	Study design	Cases	Data points	Median age (range)	Types of treatment	Diagnosis [n]	Sites of NIRS	NIRS devices	Types of venous oxygen saturation	95% LOA (%)	Quality scores
Yoxall (27)	1995	Cross-sectional study	15	150	2 (0.3–14.0) y	Cardiac catheterization	PDA [3], VSD [4], after corrective surgery [3], PH [1], complex cyanotic banalities [4]	Right fronto-temporal	NIRO 500 (Hamamatsu Photonics, Japan)	SjvO$_2$	−18.8 to 20.5	6
Daubeney (28)	1996	Cross-sectional study	40	147	4.5 (0.04–14.5) y	Cardiac catheterization or cardiac surgery under CPB	Acyanotic and cyanotic forms of congenital heart disease	Bilateral forehead	INVOS 3100 (Somanetics Corp., Troy, MI, USA)	SjvO$_2$	NA	6
Nagdyman (10)	2004	Cross-sectional study	43	70	2.8 (0.02–16.8) y	Cardiac corrective surgery	ASD [16], VSD [13], complete endocardial cushion defect [1], AS [6], MS [3], CoA [1], complex congenital heart defect [9], HOC [1], PS [2]	Supra-orbital region	NIRO 300 (Hamamatsu Photonics, Japan)	ScvO$_2$	NA	6
Nagdyman (29)	2005	Cross-sectional study	60	60	4.4 (0.1–16.0) y	Cardiac Catheterization	ASD [14], VSD [6], complete endocardial cushion defect [7], AS [3], MS [2], CA [2], complex congenital heart defects [8], HCM [2], TGA [6], TOF [10]	Right forehead	NIRO 300 (Hamamatsu Photonics, Japan)	SjvO$_2$	−15.3 to 11.7	8
Shimizu (30)	2005	Cross-sectional study	5	14	0.6 (0.2–1.3) y	Cardiac surgery under CPB	TGA [1], VSD [1], AVSD [1], TOF [2]	Forehead	NIRO 300 (Hamamatsu Photonics, Japan)	SjvO$_2$	−17.8 to 11.0	7
Tortoriello (31)	2005	Cross-sectional study	20	100	0.8 (0.4–8.0) y	Reparative or palliative cardiac surgery under CPB	HLHS [5], PA [6], BTS [7], BDG [4], PHTN [3], CAVC [3]	Right, left, or bilateral forehead	INVOS 5100 (Somanetics Corp., Troy, MI, USA)	ScvO$_2$	−10.1 to 13.4	6
Bhutta (32)	2007	Cross-sectional study	29	52	8.6 (1.3–17.0) y	Cardiac catheterization, myocardial biopsy	post-orthotopic heart transplant [29]	Forehead	INVOS 5100B (Somanetics Corp., Troy, MI, USA)	ScvO$_2$	−12.5 to 16.3	7
Kirshbom (33)	2007	Cross-sectional study	20	20	0.6 (NA) y	Cardiac catheterization	HLHS [8], PA or TA [10], DORV variants [2]	Bilateral forehead	INVOS (Somanetics Corp., Troy, MI)	ScvO$_2$	NA	6
McQuillen (34)	2007	Cross-sectional study	70	NA	0.3 (0.01–1.2) y	Cardiac surgery under CPB	AVSD [10], TGA [8], TOF [8], VSD [5], ASD [3], PA [3], truncus arteriosus [2], TAPVD [2], PS [1], PDA [1], AI [1], CoA [4], IAA [1], TA/PA [5], RAI [2], TA [1], Ebstein's anomaly [1], HLHS [7], uAVSD [2], HRV [2]	Left forehead	INVOS 5100 (Somanetics Corp., Troy, MI, USA)	ScvO$_2$	−25.6 to 23.5	7
Knirsch (35)	2008	Cross-sectional study	60	120	4.3 (0.2–16.0) y	Cardiac catheterization	CHD [60]	Right forehead	INVOS 5100 (Somanetics Corp., Troy, MI, USA)	ScvO$_2$ SjvO$_2$	−15.5 to 15.9 −18.6 to 17.4	6
Nagdyman (36)	2008	Cross-sectional study	30	36 60	3.1 (0.1–16.0) y	Cardiac catheterization	ASD [6], VSD [2], PDA [1], heart transplantation [5], complex congenital heart defects [8], cardiomyopathy [2], TGA [1], TOF [6]	Left forehead	NIRO 200 (Hamamatsu Photonics, Tokyo, Japan)	ScvO$_2$ SjvO$_2$	−20.1 to 10.3 −20.1 to 15.7	8
Ranucci (37)	2008	Cross-sectional study	15	117	1.5 (0.02–7.0) y	Cardiac surgery under CPB	ASD [2], VSD [3], TOF [5], TAPVR [1], CPC [2], AS [2]	Forehead	INVOS (Somanetics Corp., Troy, MI, USA)	ScvO$_2$	−15.2 to 26.4	8
Ricci (38)	2010	Cross-sectional study	100	890	13.0 (NA) days	Cardiac surgery under CPB	TGA [39], HLHS and UVH [26], TOF [24], other diagnosis [11]	Right forehead	INVOS 5100 (Somanetics Corp., Troy, MI, USA)	ScvO$_2$	−25.0 to 25.0	5
Ginther (39)	2011	Cross-sectional study	8	690	8.1 (2.0–15.0) y	Bicaval cardiac catheterization	PS [2], AS [2], VSD [1], ASD [1], MR [1], RV-PA conduit insufficiency and stenosis [1]	Right forehead	INVOS 5100 (Somanetics Corp., Troy, MI, USA)	ScvO$_2$	NA	6
Marimón (40)	2012	Cross-sectional study	20	605	4.5 (0.02–16.3) y	Cardiac surgery under CPB	TOF [4], atrioventricular canal defect [4], VSD [2], TA [1], aortic vascular ring [1], AS [1], CoA [1], ASD [1], HLHS [3], TOF with MAPCA and VSD [2]	Forehead	INVOS 5100 (Somanetics Corp., Troy, MI, USA)	ScvO$_2$	NA	6
Hansen (41)	2013	Cross-sectional study	32	NA	0.2 (0.1–0.80) y	Superior cavopulmonary anastomosis with CPB	HLHS [26], MA [2], TGA [1], DILV [1], DORV [1], AS [1]	Midline forehead	INVOS 5100 (Somanetics Corp., Troy, MI, USA)	ScvO$_2$	−17.9 to 19.8	5
Moreno (8)	2013	Cross-sectional study	23	980	12.0 (2–46) d	Open heart surgery	HLHS [8], TGA [6], TAPVC [5], IAA with VSD [2], multiple VSD [1], TA [1]	Forehead	INVOS 5100 (Somanetics Corp., Troy, MI, USA)	ScvO$_2$	−17.2 to 38.1	7
Iodice (42)	2014	Cross-sectional study	10	36	2.2 (0.1–8.5) y	Cardiac surgery under CPB	MR [1], PA with VSD [1], TGA [2], IAA [1], TA [2], TOF [1], MS [1], univentricular heart with HAA [1]	Forehead	INVOS 5100 (Somanetics Corp., Troy, MI, USA)	ScvO$_2$	−13.0 to 10.0	5
Kussman (43)	2017	Cross-sectional study	57	NA	4.8 (NA) y	Cardiac catheterization	Acyanotic or cyanotic congenital heart disease [57]	Forehead	FORE-SIGHT (CASMED, Inc., Branford, CT, USA)	SjvO$_2$	−7.7 to 9.9	7
Naguib (44)	2017	Cross-sectional study	34	361	3.5 (NA) y	Cardiac surgery utilizing CPB and require bicaval cannulation	VSD [24], ASD [6], ASD + VSD [12], AVSD [9], BDG [3], Fontan [3], valve replacement [18], TOF [12], subaortic membrane resection [3], cortriatriatum [6], Ebstein's anomaly [3], aortic arch augmentation [3]	Right and left forehead	FORE-SIGHT (P/N 01-06-2030C; CASMED, Inc., Branford, CT, USA)	SjvO$_2$	NA	8
Rescoe (45)	2017	Cross-sectional study	73	520	7.9 (NA) d	Stage 1 palliation under CPB	HLHS [73]	Forehead	FORE-SIGHT (CASMED, Inc., Branford, CT, USA)	ScvO$_2$	−17.6 to 34.1	7
Gagnon (46)	2020	Cross-sectional study	47	506	11.3 (NA) d	Stage 1 palliation under CPB	HLHS [38], DILV [4], TA [3], others [2]	Forehead	FORE-SIGHT ELITE (CASMED, Inc., Branford, CT, USA)	ScvO$_2$	−10.6 to 38.6	6
Terada (47)	2022	Cross-sectional study	186	NA	6.0 (NA) y	Cardiac catheterization	ASD [16], VSD [54], AVSD [9], AS [8], PA [2], PDA [4], TAPVR [3], TGA [15], TOF [16], DORV [1], Single right ventricle [14], Single left ventricle [18], others [10]	Forehead	INVOS 5100C (Covidien, Tokyo, Japan)	ScvO$_2$, Sjv$_C$2	NA	4

NIRS, near-infrared spectroscopy; LOA, limits of agreement; PDA, patent ductus arteriosus; VSD, ventricular septal defect; PH, pulmonary hypertension; SjvO$_2$, jugular bulb venous oxygen saturation; CPB, cardiopulmonary bypass; ASD, atrial septal defect; AS, aortic stenosis; MS, mitral stenosis; ScvO$_2$, central venous oxygen saturation; HOC, hypertrophic obstructive cardiomyopathy; PS, pulmonary stenosis; HCM, hypertrophic cardiomyopathy; TGA, transposition of great arteries; TOF, tetralogy of Fallot; AVSD, atrioventricular septal defect; NA, not available; HLHS, hypoplastic left heart syndrome; PA, pulmonary atresia; BTS, Blalock-Taussig shunt; BDG, bidirectional Glen; PHTN, pulmonary hypertension; CAVC, complete atrioventricular canal; TA, tricuspid atresia; DORV, double outlet right ventricle; TAPVD, total anomalous pulmonary venous drainage; AI, aortic insufficiency; CoA, coarctation of aorta; IAA, interrupted aortic arch; RAI, right atrial isomerism; uAVSD, unbalanced atrioventricular septal defect; HRV, hypoplastic right ventricle; CHD, congenital heart disease; TAPVR, total anomalous pulmonary venous return; CPC, cavo-pulmonary connection; MA, mitral atresia; DILV, double inlet left ventricle; TAPVC, total anomalous pulmonary venous connection; INVOS, a type of NIRS device; NIRO, a type of NIRS device; FORE-SIGHT, a type of NIRS device.
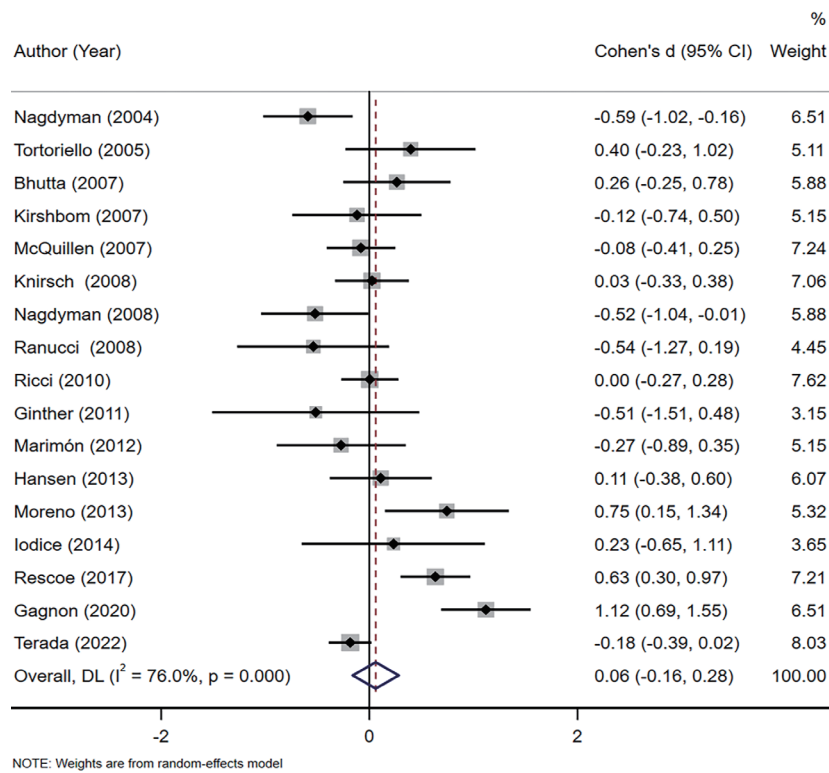
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Figure 2 Cohen's d between rScO$_2$ and ScvO$_2$. CI, confidence interval; rScO$_2$, cerebral regional oxygen saturation; ScvO$_2$, central venous oxygen saturation.
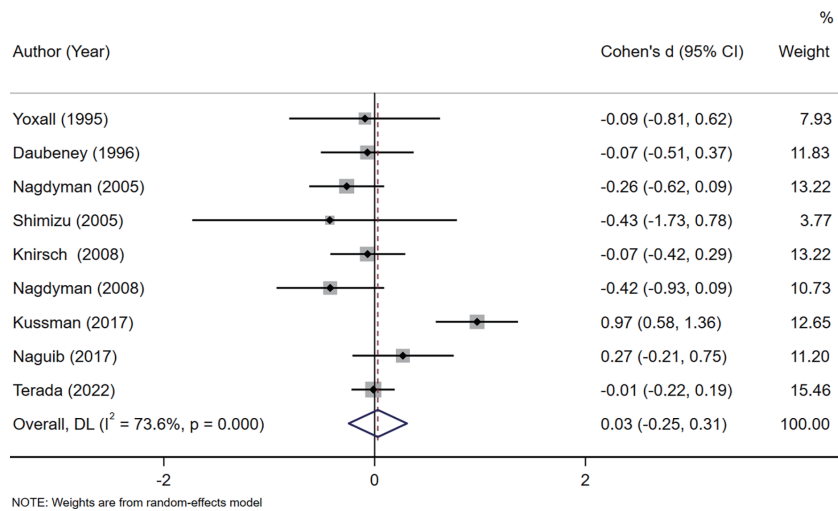

Figure 3 Cohen's d between rScO$_2$ and SjvO$_2$. CI, confidence interval; rScO$_2$, cerebral regional oxygen saturation; SjvO$_2$, jugular venous oxygen saturation.
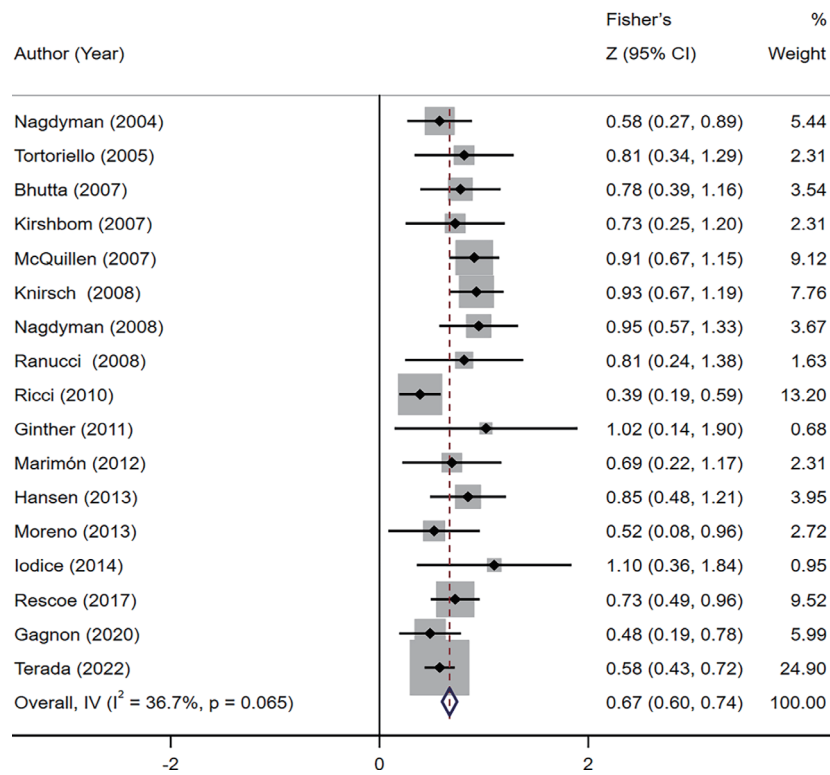
Figure 4 Fisher's Z between $rScO_2$ and $ScvO_2$. CI, confidence interval; $rScO_2$, cerebral regional oxygen saturation; $ScvO_2$, central venous oxygen saturation.
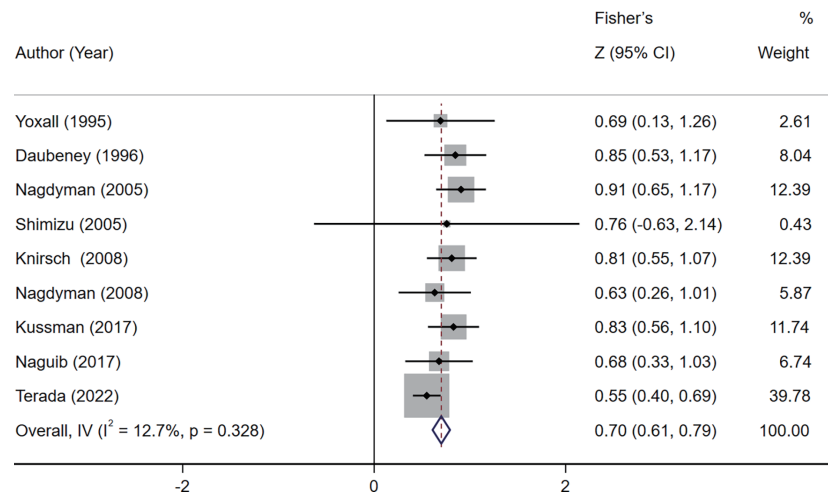

Figure 5 Fisher's Z between $rScO_2$ and $SjvO_2$. CI, confidence interval; $rScO_2$, cerebral regional oxygen saturation; $SjvO_2$, jugular venous oxygen saturation.
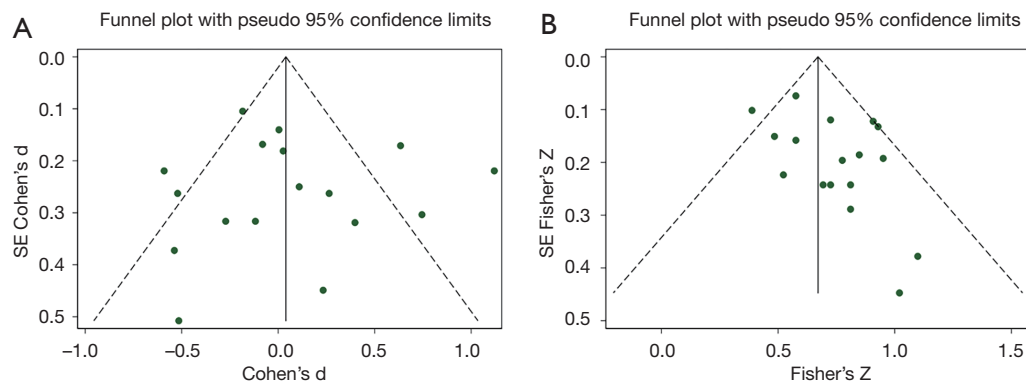
Figure 6 Funnel plot with pseudo 95% confidence limits for Cohen's d and Fisher's Z. (A) Cohen's d between $rScO_2$ and $ScvO_2$; (B) Fisher's Z between $rScO_2$ and $ScvO_2$. $rScO_2$, cerebral regional oxygen saturation; $ScvO_2$, central venous oxygen saturation.

between $rScO_2$ and $ScvO_2$).

Sensitivity analyses, meta-regression, and subgroup analyses

Removal of any one of the studies alone did not significantly affect the overall results, which suggested that the results of this meta-analysis were stable (Figures S1-S4). In view of the low heterogeneity of Fisher's Z analyses, further analysis was not carried out. As relatively significant heterogeneity existed in Cohen's d analyses in both the $rScO_2$ versus $ScvO_2$ and the $rScO_2$ versus $SjvO_2$ groups, we conducted meta-regression to explore the cause. As a result, the types of NIRS devices were related to high heterogeneity of Cohen's d in the $rScO_2$ versus $ScvO_2$ group (P<0.001), whereas the number of patients (P=0.67) and the types of treatment (P=0.46) were not related. The meta-regression result of Cohen's d in the $rScO_2$ versus $SjvO_2$ group also indicated that the types of NIRS devices were responsible for the heterogeneity (P<0.001), and that the number of patients (P=0.98) and types of treatment (P=0.88) were not responsible.

In the analyses of the $rScO_2$ versus $ScvO_2$ group, significant heterogeneity was noted between the 3 subgroups of types of NIRS devices (P<0.001), and, among them, the FORE-SIGHT subgroup had the highest heterogeneity (I^2=67.3%, P<0.001). After removal of studies using the FORE-SIGHT device (45,46), the I^2 was reduced to 43.9% (P=0.04). Similarly, in the analyses of the $rScO_2$ versus $SjvO_2$ group, heterogeneity between different types of NIRS devices was significant (P=0.03, and the heterogeneity of the FORE-SIGHT subgroup was high (I^2=79.9%, P=0.03). The I^2 decreased to 0.0% (P=0.76)

when studies of the FORE-SIGHT subgroup were removed (43,44). No significant heterogeneity existed between the number of patients and the types of treatment subgroups. The results of subgroup analyses can be found in *Table 2*.

Discussion

This systematic review and meta-analysis assessed the validity of NIRS in measuring $rScO_2$ in children with CHD undergoing surgery and the interchangeability between NIRS and common invasive approaches that measure $SjvO_2$ and $ScvO_2$. After removing studies that met the exclusion criteria, such as reviews, animal experiments, non-English language articles, unpublished articles and irrelevant articles, we included 23 studies of intermediate to high quality. No evidence of publication bias was observed. No statistically significant difference was found between $rScO_2$ and $SjvO_2$ and between $rScO_2$ and $ScvO_2$ in the pediatric patients with CHD and NIRS $rScO_2$ was positively correlated with the saturation of jugular bulb blood and central venous blood. The results indicated that NIRS exhibited comparative accuracy to a certain extent. Nevertheless, significant heterogeneity was found in the results, which could be attributed to variation in the diverse NIRS devices, especially the FORE-SIGHT device, used in the measurement of $rScO_2$. This shortcoming detracted from the validity of the research. Besides, in terms of Bland-Altman's analysis, the 95% LOAs of most studies were wide, which suggested that the interchangeability between NIRS and $SjvO_2$ as well as $ScvO_2$ was up for debate.

Through the application of sensitivity analyses, meta-regression, and subgroup analyses to investigate the cause of heterogeneity, we learned that different NIRS

Table 2 Subgroup analysis

Subgroup	Number of studies	Cohen's d, (95% CI)	P value	I^2	Heterogeneity between subgroups, P
Number of patients					
$rScO_2$ *vs.* $ScvO_2$					0.264
Patients ≤20	6	−0.10 (−0.40, 0.20)	0.496	6.30%	
Patients >20	11	0.13 (−0.15, 0.40)	0.362	83.40%	
$rScO_2$ *vs.* $SjvO_2$					0.508
Patients ≤20	2	−0.17 (−0.80, 0.45)	0.583	0.00%	
Patients >20	7	0.06 (−0.25, 0.37)	0.7	79.80%	
Types of treatment					
$rScO_2$ *vs.* $ScvO_2$					0.108
Cardiac surgery under CPB	11	0.17 (−0.15, 0.49)	0.294	80.60%	
Cardiac catheterization	6	−0.13 (−0.32, 0.05)	0.166	17.10%	
$rScO_2$ *vs.* $SjvO_2$					0.639
Cardiac surgery under CPB	2	0.17 (−0.29, 0.64)	0.467	2.40%	
Cardiac catheterization	6	0.03 (−0.34, 0.40)	0.869	82.50%	
Types of NIRS devices					
$rScO_2$ *vs.* $ScvO_2$					<0.001
NIRO	2	−0.56 (−0.89, −0.23)	0.001	0.00%	
INVOS	13	−0.00 (−0.15, 0.14)	0.952	25.30%	
FORE-SIGHT	2	0.86 (0.38, 1.33)	<0.001	67.30%	
$rScO_2$ *vs.* $SjvO_2$					0.032
NIRO	4	−0.29 (−0.55, −0.03)	0.031	0.00%	
INVOS	3	−0.03 (−0.20, 0.13)	0.699	0.00%	
FORE-SIGHT	2	0.63 (−0.05, 1.32)	0.071	79.90%	

NIRS, near-infrared spectroscopy; CI, confidence interval; $rScO_2$, cerebral regional oxygen saturation; $ScvO_2$, central venous oxygen saturation; $SjvO_2$, jugular venous saturation; CPB, cardiopulmonary bypass; NIRO, a type of NIRS device; INVOS, a type of NIRS device; FORE-SIGHT, a type of NIRS device.

devices calculate $rScO_2$ through different algorithms. The NIRO device calculates the tissue oxygenation index (TOI) through spatially resolved spectroscopy by the equation $TOI = HbO_2/(HbO_2 + HHb) \times 100$ (48,49). The INVOS device calculates $rScO_2$ according to the ratio of oxyhemoglobin to total hemoglobin (47,50). In the FORE-SIGHT device, cerebral mixed arterial-venous oxygen saturation is measured by the different absorption of oxygenated and deoxygenated hemoglobin to near-infrared light, thus detecting $rScO_2$ by the formula $rScO_2 = 0.3\ SaO_2 + 0.7\ ScvO_2$ or $rScO_2 = 0.3SaO_2 + 0.7\ SjvO_2$ according to a 30% arterial to 70% venous ratio (45,51,52).

The effectiveness of monitoring cerebral oxygen saturation varies from device to device. Theoretically, NIRS monitors oxygenation saturation at the tissue and cellular level; at the cellular level, cytochrome aa3 is a key variable to measure changes in mitochondrial oxygenation (53). However, the INVOS 3100 device cannot provide information about this parameter on account of technical difficulties, whereas the NIRO 500 device not only measures the level of cytochrome aa3 but also monitors the oxygenation state of hemoglobin (54). In addition, Naguib *et al.* (44) reported that the FORESIGHT device had higher sensitivity, whereas the INVOS device had better specificity. The use

of different algorithms among commercial NIRS devices makes comparing the rScO$_2$ of the devices difficult, and industry standards among devices are lacking.

This study has reference significance for the application of NIRS in clinical practice to monitor cerebral oxygen saturation properly in children with CHD undergoing surgery. The results of our study revealed that rScO$_2$ measured by NIRS reflected the SjvO$_2$ and ScvO$_2$ measured by co-oximetry in the perioperative period of children with CHD to a certain extent. However, the agreement between NIRS and invasive oxygen saturation measurements was below expectation, and the LOA was wide, which indicated that NIRS cannot replace SjvO$_2$ and ScvO$_2$. The NIRS method has inherent limitations that restrict its application. As a monitoring tool, NIRS is affected by factors such as hemoglobin, blood volume, arterial blood pressure (55), cardiac output, arterial oxyhemoglobin saturation, the position of the probe head, body position, and vasoactive drugs (19). Due to the discrepancy in sensor technology, near infrared wavelength, fixed arterio-venous (A/V) ratio, and reference values of different NIRS devices, each manufacturer lacks large sample data to determine reference values of cerebral oxygen, which is the major limitation in NIRS validation. Studies have found that the A/V ratio differed among subjects, which implies that a fixed A/V ratio is not appropriate for validating the technology (56).

Despite the limitations of NIRS, the ability of providing noninvasive continuous monitoring for cerebral oxygen saturation is of importance and the potential to identify cerebral ischemic events is prominent. Venous thrombosis, infection, and extracerebral contamination are common and intractable problems of invasive measurements, which can be avoid by using NIRS (57,58). NIRS has been extensively used in pediatric patients undergoing cardiovascular operations with a high risk of compromised cerebral perfusion (59). Cruz *et al.* (60) reported that the variance of peripheral capillary oxygen saturation (SpO$_2$) was larger than that of NIRS, meaning that NIRS monitoring was more stable and better at predicting events. Similar results were replicated in a 24-hour observational study that found NIRS superior to SpO$_2$ in monitoring hypoxia and ischemic events (61). Moerman *et al.* (62) demonstrated that NIRS monitoring identified compromised cerebral perfusion despite hemodynamic measurements being normal. However, Robust studies, including randomized clinical trials, are needed to prove the clinical benefit of NIRS. There is still no evidence that early monitoring of cerebral oxygenation during pediatric surgery under general anesthesia improves prognosis after surgery (63). A systematic review of surgical treatment of pediatric CHD concluded that the benefit and cost-effectiveness of NIRS monitoring and management capable of improving short-term clinical neurological outcomes has not yet been demonstrated (64). Zheng *et al.* (65) reported that the correlation between decreased rScO$_2$ and postoperative neurological complications was low, and improving rScO$_2$ desaturation in attempts to prevent stroke, delirium, or postoperative cognitive dysfunction could not be supported by available evidence. Future studies should look at solving the heterogeneity problems, that is, setting uniform reference standards among NIRS devices. In addition, more research should attempt to determine whether perioperative monitoring with NIRS can improve postoperative outcomes.

This systematic review and meta-analysis had some limitations. First, the proposed data extraction and analysis method may be inadequate, as the discrepancy in data acquisition led to downstream data issues. We used MATLAB to extract data from images in articles when the MD and SD were not provided. In that case, the ordinate and abscissa values of the scatter points were measured manually, which may have introduced errors. When the scattered points were stacked together, accurately identifying them separately was difficult, and accurately measuring the diameter of the scattered points themselves was challenging. The second limitation was the relatively high heterogeneity in the analyses of Cohen's d. Under normal circumstances, combining effect size in the case of high heterogeneity due to the broad distribution and variation of sample characteristics is not recommended. However, since we discussed the cause of high heterogeneity through sensitivity analyses, meta-regression, and subgroup analyses, the results were still of reference value. Thirdly, the lack of randomized controlled trials reduced the validity of the study. More high-quality studies are required in this field.

Conclusions

This systematic review and meta-analysis revealed that rScO$_2$ measured by NIRS reflects SjvO$_2$ and ScvO$_2$ recorded by invasive measurements in the perioperative period of children with CHD to some extent. Nevertheless, wide LOA indicated that the interchangeability between NIRS and invasive oxygen saturation measurements was below expectation. Despite the technical limitations of NIRS, it provides a non-invasive, convenient approach for

the real-time monitoring of hypoxia, ischemia, and changes in cerebral perfusion. More evidence is needed to prove the possible clinical benefits of NIRS in monitoring cerebral oxygen saturation in children with CHD.

Footnote

Reporting Checklist: The authors have completed the MOOSE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-22-345/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-22-345/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Hirsch JC, Jacobs ML, Andropoulos D, et al. Protecting the infant brain during cardiac surgery: a systematic review. Ann Thorac Surg 2012;94:1365-73; discussion 1373.

2. Flechet M, Güiza F, Vlasselaers D, et al. Near-Infrared Cerebral Oximetry to Predict Outcome After Pediatric Cardiac Surgery: A Prospective Observational Study. Pediatr Crit Care Med 2018;19:433-41.

3. Andropoulos DB, Easley RB, Gottlieb EA, et al. Neurologic Injury in Neonates Undergoing Cardiac Surgery. Clin Perinatol 2019;46:657-71.

4. Kim MJ, Baek JS, Kim JA, et al. Cerebral and Somatic Oxygen Saturation in Neonates with Congenital Heart Disease before Surgery. J Clin Med 2021;10:2455.

5. Zhu S, Sai X, Lin J, et al. Mechanisms of perioperative brain damage in children with congenital heart disease. Biomed Pharmacother. 2020;132:110957.

6. McQuillen PS, Barkovich AJ, Hamrick SE, et al. Temporal and anatomic risk profile of brain injury with neonatal repair of congenital heart defects. Stroke 2007;38:736-41.

7. Yoshitani K, Kawaguchi M, Ishida K, et al. Guidelines for the use of cerebral oximetry by near-infrared spectroscopy in cardiovascular anesthesia: a report by the cerebrospinal Division of the Academic Committee of the Japanese Society of Cardiovascular Anesthesiologists (JSCVA). J Anesth 2019;33:167-96.

8. Moreno GE, Pilán ML, Manara C, et al. Regional venous oxygen saturation versus mixed venous saturation after paediatric cardiac surgery. Acta Anaesthesiol Scand 2013;57:373-9.

9. Tweddell JS, Hoffman GM. Postoperative management in patients with complex congenital heart disease. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2002;5:187-205.

10. Nagdyman N, Fleck T, Barth S, et al. Relation of cerebral tissue oxygenation index to central venous oxygen saturation in children. Intensive Care Med 2004;30:468-71.

11. Milne B, Gilbey T, Gautel L, et al. Neuromonitoring and Neurocognitive Outcomes in Cardiac Surgery: A Narrative Review. J Cardiothorac Vasc Anesth. 2022;36:2098-2113.

12. Jöbsis FF. Noninvasive, infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters. Science 1977;198:1264-7.

13. Hirsch JC, Charpie JR, Ohye RG, et al. Near-infrared spectroscopy: what we know and what we need to know--a systematic review of the congenital heart disease literature. J Thorac Cardiovasc Surg 2009;137:154-9, 159e1-12.

14. Smith M, Elwell C. Near-infrared spectroscopy: shedding light on the injured brain. Anesth Analg 2009;108:1055-7.

1386

Ma et al. Meta-analysis of near-infrared spectroscopy

15. Ghosh A, Elwell C, Smith M. Review article: cerebral near-infrared spectroscopy in adults: a work in progress. Anesth Analg 2012;115:1373-83.

16. Diop M, Verdecchia K, Lee TY, et al. Calibration of diffuse correlation spectroscopy with a time-resolved near-infrared technique to yield absolute cerebral blood flow measurements. Biomed Opt Express 2011;2:2068-81.

17. Nasr VG, Bergersen LT, Lin HM, et al. Validation of a Second-Generation Near-Infrared Spectroscopy Monitor in Children With Congenital Heart Disease. Anesth Analg 2019;128:661-8.

18. Zaleski KL, Kussman BD. Near-Infrared Spectroscopy in Pediatric Congenital Heart Disease. J Cardiothorac Vasc Anesth. 2020;34:489-500.

19. Bickler PE, Feiner JR, Rollins MD. Factors affecting the performance of 5 cerebral oximeters during hypoxia in healthy volunteers. Anesth Analg 2013;117:813-23.

20. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008-12.

21. Kadel RP, Kip KE. A SAS macro to compute effect size (Cohen's) and its confidence interval from raw survey data. South East SAS Users Group (SESUG). 2012.

22. Rupinski MT, Dunlap WP. Approximating Pearson product-moment correlations from Kendall's Tau and Spearman's Rho. Educ Psychol Meas 1996;56:419-29.

23. Rostom A, Dubé C, Cranney A, et al. Rockville (MD): Agency for Healthcare Research and Quality (US); 2004. Available online: https://www.ncbi.nlm.nih.gov/books/NBK35156

24. Hu J, Dong Y, Chen X, et al. Prevalence of suicide attempts among Chinese adolescents: A meta-analysis of cross-sectional studies. Compr Psychiatry 2015;61:78-89.

25. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557-60.

26. Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629-34.

27. Yoxall CW, Weindling AM, Dawani NH, et al. Measurement of cerebral venous oxyhemoglobin saturation in children by near-infrared spectroscopy and partial jugular venous occlusion. Pediatr Res 1995;38:319-23.

28. Daubeney PE, Pilkington SN, Janke E, et al. Cerebral oxygenation measured by near-infrared spectroscopy: comparison with jugular bulb oximetry. Ann Thorac Surg 1996;61:930-4.

29. Nagdyman N, Fleck T, Schubert S, et al. Comparison between cerebral tissue oxygenation index measured by near-infrared spectroscopy and venous jugular bulb saturation in children. Intensive Care Med 2005;31:846-50.

30. Shimizu N, Gilder F, Bissonnette B, et al. Brain tissue oxygenation index measured by near infrared spatially resolved spectroscopy agreed with jugular bulb oxygen saturation in normal pediatric brain: a pilot study. Childs Nerv Syst 2005;21:181-4.

31. Tortoriello TA, Stayer SA, Mott AR, et al. A noninvasive estimation of mixed venous oxygen saturation using near-infrared spectroscopy by cerebral oximetry in pediatric cardiac surgery patients. Paediatr Anaesth 2005;15:495-503.

32. Bhutta AT, Ford JW, Parker JG, et al. Noninvasive cerebral oximeter as a surrogate for mixed venous saturation in children. Pediatr Cardiol 2007;28:34-41.

33. Kirshbom PM, Forbess JM, Kogon BE, et al. Cerebral near infrared spectroscopy is a reliable marker of systemic perfusion in awake single ventricle children. Pediatr Cardiol 2007;28:42-5.

34. McQuillen PS, Nishimoto MS, Bottrell CL, et al. Regional and central venous oxygen saturation monitoring following pediatric cardiac surgery: concordance and association with clinical variables. Pediatr Crit Care Med 2007;8:154-60.

35. Knirsch W, Stutz K, Kretschmar O, et al. Regional cerebral oxygenation by NIRS does not correlate with central or jugular venous oxygen saturation during interventional catheterisation in children. Acta Anaesthesiol Scand 2008;52:1370-4.

36. Nagdyman N, Ewert P, Peters B, et al. Comparison of different near-infrared spectroscopic cerebral oxygenation indices with central venous and jugular venous oxygenation saturation in children. Paediatr Anaesth 2008;18:160-6.

37. Ranucci M, Isgrò G, De la Torre T, et al. Near-infrared spectroscopy correlates with continuous superior vena cava oxygen saturation in pediatric cardiac surgery patients. Paediatr Anaesth 2008;18:1163-9.

38. Ricci Z, Garisto C, Favia I, et al. Cerebral NIRS as a marker of superior vena cava oxygen saturation in neonates with congenital heart disease. Paediatr Anaesth 2010;20:1040-5.

39. Ginther R, Sebastian VA, Huang R, et al. Cerebral near-infrared spectroscopy during cardiopulmonary bypass

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predicts superior vena cava oxygen saturation. J Thorac Cardiovasc Surg 2011;142:359-65.

40. Marimón GA, Dockery WK, Sheridan MJ, et al. Near-infrared spectroscopy cerebral and somatic (renal) oxygen saturation correlation to continuous venous oxygen saturation via intravenous oximetry catheter. J Crit Care 2012;27:314.e13-8.

41. Hansen JH, Schlangen J, Armbrust S, et al. Monitoring of regional tissue oxygenation with near-infrared spectroscopy during the early postoperative course after superior cavopulmonary anastomosis. Eur J Cardiothorac Surg 2013;43:e37-43.

42. Iodice FG, Ricci Z, Haiberger R, et al. Fiberoptic monitoring of central venous oxygen saturation (PediaSat) in small children undergoing cardiac surgery: continuous is not continuous. F1000Res 2014;3:23.

43. Kussman BD, Laussen PC, Benni PB, et al. Cerebral Oxygen Saturation in Children With Congenital Heart Disease and Chronic Hypoxemia. Anesth Analg 2017;125:234-40.

44. Naguib AN, Winch PD, Sebastian R, et al. The Correlation of Two Cerebral Saturation Monitors With Jugular Bulb Oxygen Saturation in Children Undergoing Cardiopulmonary Bypass for Congenital Heart Surgery. J Intensive Care Med 2017;32:603-8.

45. Rescoe E, Tang X, Perry DA, et al. Cerebral near-infrared spectroscopy insensitively detects low cerebral venous oxygen saturations after stage 1 palliation. J Thorac Cardiovasc Surg 2017;154:1056-62.

46. Gagnon MH, Kussman BD, Zhou L, et al. Sensitivity of a Next-Generation NIRS Device to Detect Low Mixed Venous Oxyhemoglobin Saturations in the Single Ventricle Population. Anesth Analg 2020;131:e138-41.

47. Terada K, Nakamura S, Nakao Y, et al. Cerebral hemoglobin oxygenation in children with congenital heart disease. Pediatr Int 2022;64:e14726.

48. Yagi T, Kawamorita T, Kuronuma K, et al. Usefulness of a New Device to Monitor Cerebral Blood Oxygenation Using NIRS During Cardiopulmonary Resuscitation in Patients with Cardiac Arrest: A Pilot Study. Adv Exp Med Biol. 2020;1232:323-329.

49. Gagnon RE, Macnab AJ, Gagnon FA, et al. Comparison of two spatially resolved NIRS oxygenation indices. J Clin Monit Comput 2002;17:385-91.

50. Ziehenberger E, Urlesberger B, Binder-Heschl C, et al. Near-infrared spectroscopy monitoring during immediate transition after birth: time to obtain cerebral tissue

oxygenation. J Clin Monit Comput 2018;32:465-9.

51. Schneider A, Hofstätter E, Brandner J, et al. Benchmarking of Four Near Infrared Spectroscopy Devices for Long Time Use in Neonates. Klin Padiatr. 2018;230:240-244.

52. Benni PB, Chen B, Dykes FD, et al. Validation of the CAS neonatal NIRS system by monitoring vv-ECMO patients: preliminary results. Adv Exp Med Biol 2005;566:195-201.

53. du Plessis AJ, Newburger J, Jonas RA, et al. Cerebral oxygen supply and utilization during infant cardiac surgery. Ann Neurol 1995;37:488-97.

54. Wollert HG, Eckel L. Cerebral oxygenation measured by near-infrared spectroscopy. Ann Thorac Surg 1997;63:292; author reply 292-3.

55. Sørensen H, Secher NH, Rasmussen P. A note on arterial to venous oxygen saturation as reference for NIRS-determined frontal lobe oxygen saturation in healthy humans. Front Physiol 2013;4:403.

56. Watzman HM, Kurth CD, Montenegro LM, et al. Arterial and venous contributions to near-infrared cerebral oximetry. Anesthesiology 2000;93:947-53.

57. Alten J, Mariscalco MM. Critical appraisal of Perez et al: Jugular venous oxygen saturation or arteriovenous difference of lactate content and outcome in children with severe traumatic brain injury. Pediatr Crit Care Med 2005;6:480-2.

58. Berman W Jr, Fripp RR, Yabek SM, et al. Great vein and right atrial thrombosis in critically ill infants and children with central venous lines. Chest 1991;99:963-7.

59. Scheeren TWL, Kuizenga MH, Maurer H, et al. Electroencephalography and Brain Oxygenation Monitoring in the Perioperative Period. Anesth Analg 2019;128:265-77.

60. Cruz SM, Akinkuotu AC, Rusin CG, et al. A novel multimodal computational system using near-infrared spectroscopy to monitor cerebral oxygenation during assisted ventilation in CDH patients. J Pediatr Surg 2016;51:38-43.

61. Koch HW, Hansen TG. Perioperative use of cerebral and renal near-infrared spectroscopy in neonates: a 24-h observational study. Paediatr Anaesth 2016;26:190-8.

62. Moerman A, Meert F, De Hert S. Cerebral near-infrared spectroscopy in the care of patients during cardiological procedures: a summary of the clinical evidence. J Clin Monit Comput 2016;30:901-9.

63. Nielsen HB. Systematic review of near-infrared spectroscopy determined cerebral oxygenation during non-cardiac surgery. Front Physiol 2014;5:93.

64. Deschamps A, Lambert J, Couture P, et al. Reversal of decreases in cerebral saturation in high-risk cardiac surgery. J Cardiothorac Vasc Anesth 2013;27:1260-6.

65. Zheng F, Sheinberg R, Yee MS, et al. Cerebral near-infrared spectroscopy monitoring and neurologic outcomes in adult cardiac surgery patients: a systematic review. Anesth Analg 2013;116:663-76.

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Appendix 1 PubMed search strategy

1# "spectroscopy, near infrared"[MeSH Terms] OR "near-infrared spectroscopy"[Title/Abstract] OR "near infrared spectroscopy"[Title/Abstract] OR "near-infrared spectroscopies"[Title/Abstract] OR "Near-Infrared Spectroscopy"[Title/Abstract] OR "nir spectroscopy"[Title/Abstract] OR "nir spectroscopies"[Title/Abstract] OR ("near infrared"[All Fields] AND "Spectrometries"[Title/Abstract]) OR "near-infrared spectrometry"[Title/Abstract]

2# "cerebral venous oxyhemoglobin saturation"[Title/Abstract] OR "cerebral oxygenation"[Title/Abstract] OR "cerebral saturations"[Title/Abstract] OR "cerebral saturation"[Title/Abstract] OR "tissue oxygenation index"[Title/Abstract] OR "cerebral oximetry"[Title/Abstract] OR "cerebral oximeter"[Title/Abstract] OR "cerebral regional oxygen saturation"[Title/Abstract] OR "regional cerebral oxygenation"[Title/Abstract] OR "venous oxygen saturation"[Title/Abstract]

3# (#1) AND (#2)

4# (#1) AND (#2) Filters: Child: birth-18 years

Appendix 2 The Cochrane Library search strategy

#1→MeSH descriptor: [Spectroscopy, Near-Infrared] explode all trees

#2→((near-infrared spectroscop*) or (NIR spectroscop*) or (near-infrared spectromet*) or (near infrared spectroscop*)): ti,ab,kw

#3→((cerebral venous oxyhemoglobin saturation) or (cerebral oxygenation) or (cerebral saturations) or (cerebral saturation) or (tissue oxygenation index) or (cerebral oximetry) or (cerebral oximeter) or (cerebral regional oxygen saturation) or (regional cerebral oxygenation) or (venous oxygen saturation)): ti,ab,kw

#4→#1 or #2

#5→#3 and #4 with 'Neonatal', 'Child Health' in Cochrane Groups

Appendix 3 Embase search strategy

#1 'near infrared spectroscopy'/exp

#2 'near-infrared spectroscop*' OR 'near infrared spectroscop*' OR 'nir spectroscop*' OR 'near-infrared spectromet*': ab,ti

#3 #1 OR #2

#4 'cerebral venous oxyhemoglobin saturation' OR 'cerebral oxygenation': ab,ti OR 'cerebral saturations' OR 'cerebral saturation' OR 'tissue oxygenation index' OR'cerebral oximetry' OR 'cerebral oximeter' OR 'cerebral regional oxygen saturation' OR 'regional cerebral oxygenation' OR 'venous oxygen saturation':ab,ti

#5 #3 AND #4

#6 #3 AND #4 AND ([newborn]/lim OR [infant]/lim OR [child]/lim OR [adolescent]/lim)

```
---------------------------------------------------------------------------
Study omitted    |   Estimate    [95%  Conf.  Interval]
-----------------+---------------------------------------------------------
Nagdyman (2004)  |   .07593819   -.02669942   .17857581
Tortoriello (2005)|  .03061461   -.07051696   .13174619
Bhutta (2007)    |   .0312417    -.07052172   .13300511
Kirshbom (2007)  |   .04419363   -.05695939   .14534664
McQuillen (2007) |   .05217678   -.05256429   .15691786
Knirsch  (2008)  |   .04118957   -.06284186   .14522099
Nagdyman (2008)  |   .06189227   -.03987115   .16365568
Ranucci  (2008)  |   .05100425   -.0497757    .1517842
Ricci (2010)     |   .04545117   -.06169142   .15259375
Ginther (2011)   |   .04563222   -.05470719   .14597164
Marimón (2012)   |   .04829279   -.05286023   .14944582
Hansen (2013)    |   .03699954   -.06497241   .13897149
Moreno (2013)    |   .01956561   -.08170312   .12083434
Iodice (2014)    |   .03747183   -.06300995   .13795361
Rescoe (2017)    |  -.01790722   -.12249233   .08667788
Gagnon (2020)    |  -.02154422   -.12418184   .0810934
Terada (2022)    |   .10962417   -.00467884   .22392718
-----------------+---------------------------------------------------------
Combined         |   .03998831   -.05984477   .13982138
---------------------------------------------------------------------------
```

Figure S1 Sensitivity analysis of Cohen's d between $rScO_2$ and $ScvO_2$. $rScO_2$, cerebral regional oxygen saturation; $ScvO_2$, central venous oxygen saturation.

```
---------------------------------------------------------------------------
Study omitted    |   Estimate    [95%  Conf.  Interval]
-----------------+---------------------------------------------------------
Yoxall (1995)    |   .03919733   -.08966073   .16805539
Daubeney (1996)  |   .04449827   -.08793661   .17693315
Nagdyman (2005)  |   .07896332   -.05681033   .21473698
Shimizu (2005)   |   .03982654   -.08764096   .16729404
Knirsch  (2008)  |   .0500006    -.08577307   .18577425
Nagdyman (2008)  |   .06519345   -.06573382   .19612074
Kussman (2017)   |  -.07570761   -.20981026   .05839504
Naguib (2017)    |   .01759147   -.11389553   .14907847
Terada (2022)    |   .06486888   -.09653542   .22627318
-----------------+---------------------------------------------------------
Combined         |   .03507014   -.09174492   .1618852
---------------------------------------------------------------------------
```

Figure S2 Sensitivity analysis of Cohen's d between $rScO_2$ and $SjvO_2$. $rScO_2$, cerebral regional oxygen saturation; $SjvO_2$, jugular venous oxygen saturation.

```
---------------------------------------------------------------------
Study omitted    |  Estimate     [95%  Conf.  Interval]
-----------------+---------------------------------------------------
Nagdyman (2004)  |  .67662913    .60228348    .75097477
Tortoriello (2005)| .66786659    .59472138    .7410118
Bhutta (2007)    |  .66735268    .5937447     .74096072
Kirshbom (2007)  |  .6698966     .59675139    .74304175
McQuillen (2007) |  .64745301    .57161975    .72328627
Knirsch  (2008)  |  .64951825    .57424629    .72479022
Nagdyman (2008)  |  .6605196     .58685964    .73417956
Ranucci  (2008)  |  .66885465    .59596282    .74174649
Ricci (2010)     |  .71415955    .63656384    .79175526
Ginther (2011)   |  .66877973    .5962382     .74132121
Marimón (2012)   |  .67065084    .59750569    .74379605
Hansen (2013)    |  .66390949    .59014529    .7376737
Moreno (2013)    |  .67531627    .60201776    .74861479
Iodice (2014)    |  .66706121    .59442008    .73970228
Rescoe (2017)    |  .66550446    .58950031    .7415086
Gagnon (2020)    |  .68304491    .60848433    .75760543
Terada (2022)    |  .7026099     .61918831    .78603148
-----------------+---------------------------------------------------
Combined         |  .67117119    .59887683    .74346555
---------------------------------------------------------------------
```

Figure S3 Sensitivity analysis of Fisher's Z between $rScO_2$ and $ScvO_2$. $rScO_2$, cerebral regional oxygen saturation; $ScvO_2$, central venous oxygen saturation.

```
---------------------------------------------------------------------
Study omitted    |  Estimate     [95%  Conf.  Interval]
-----------------+---------------------------------------------------
Yoxall (1995)    |  .70140219    .60880256    .79400176
Daubeney (1996)  |  .68834889    .59305215    .78364557
Nagdyman (2005)  |  .67198551    .57435274    .76961827
Shimizu (2005)   |  .70093799    .60935485    .79252106
Knirsch  (2008)  |  .68569124    .58805847    .783324
Nagdyman (2008)  |  .70544904    .61125916    .79963893
Kussman (2017)   |  .68417186    .58690047    .78144324
Naguib (2017)    |  .70288646    .60825849    .79751438
Terada (2022)    |  .80152673    .68376392    .91928959
-----------------+---------------------------------------------------
Combined         |  .70118681    .60980302    .79257061
---------------------------------------------------------------------
```

Figure S4 Sensitivity analysis of Fisher's Z between $rScO_2$ and $SjvO_2$. $rScO_2$, cerebral regional oxygen saturation; $SjvO_2$, jugular venous oxygen saturation.