



Evaluation of anastomotic blood supply during digestive tract reconstruction with the use of the oxygen saturation index: A pooling up analysis

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Abstract

Purpose Anastomotic leakage (AL) is one of the most serious clinical complications in digestive tract reconstruction (DTR) surgery, and it is currently hypothesized that this may be related to insufficient anastomotic blood supply. Thus, Therefore, we aimed to assess the ability of tissue oxygen saturation(StO_2) as a measure to evaluate anastomotic blood supply.

Methods A comprehensive literature search was performed using Embase, PubMed and Cochrane Library. StO_2 was used as an evaluation index of anastomotic blood supply after DTR to analyze the potential association between this index and the occurrence of AL in the postoperative period.

Results A total of eleven articles involving 867 participants were included in this systematic review and meta-analysis. After pooling the standardized mean difference (SMD) and 95% confidence intervals (CIs), low StO_2 was found to be an independent risk factor for AL ($P < 0.00001$; 95%CI: 1.02 [0.53–1.51]). The mean StO_2 in the AL group (62.3%) was significantly lower than that in the non-AL group (74.3%); AL incidence increased with the reduction of StO_2 to a certain value to 201.8% and 338.1% respectively.

Conclusion Oxygen saturation index can be utilized in DTR to accurately and quantitatively evaluate the anastomotic blood supply to reduce the probability of postoperative AL.

Keywords Oxygen saturation · Digestive System Surgical Procedures · Anastomotic Leak; Meta-analysis

Introduction

Cancer of the digestive tract is one of the cancers with a high incidence rate in clinical practice, and in recent years there has been a trend of gradual increase. The latest statistics published by the American Cancer Society indicate that in 2023, there will be nearly 170,000 people in the United States who will die from cancer of the digestive tract [1]. As the preferred option for treatment, digestive tract reconstruction (DTR) surgery still has many complications, and the most fatal complication is anastomotic leakage (AL) [2,

3]. The rate of AL after colorectal anastomosis ranges from 1%–19% and gastric conduit reconstruction after esophagectomy is as high as 6.2%–27% statistically [4, 5]. Whereas postoperative AL significantly increases perioperative morbidity and mortality [4, 6–8]. Therefore, the prevention of AL is a key issue after DTR reconstruction, whether colorectal anastomosis or gastric conduit reconstruction.

AL may be a multifactorial event [9, 10], including patient's gender, age, body mass index(BMI), nutritional status, history of neoadjuvant therapy, tumor site, operative duration, intraoperative bleeding, surgeon's experience, and anastomotic tension [11–14], of which insufficient anastomotic blood supply is considered to be one of the possible risk factors for the development of AL. Up to the present, surgeons mostly adopt competent assessment to determine anastomotic vascular perfusion by visual observation, which includes observation of the color of the tube wall, peristalsis, pulsation of vessels at the margins, and hemorrhage from the cut edge. However, it has been demonstrated that this method is poorly predictive [15].

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Currently, techniques for evaluating the intraoperative anastomotic site blood supply have matured, representative of which is the indocyanine green fluorescence angiography (ICG-FA), and the use of which significantly reduces the incidence of AL [16]. Although it has been shown that the routine use of ICG-FA in colorectal anastomosis can result in cost savings [17]. We would like to find a technique that is even less costly and has a predictive effect that is equivalent to or even superior to ICG-FA. In recent years, the feasibility of tissue oxygen saturation measurement has been confirmed in animal models and human models [18–20]. The technique of determining anastomotic blood supply by measuring StO_2 has received widespread attention by virtue of being rapid, quantitative, noninvasive, and low-cost [21–23]. This technology has the potential to replace or combine indocyanine green, which is safer, more economical, and accurately determines the condition of anastomotic perfusion, and reduce the incidence of AL.

Therefore, the aim of this meta-analysis was to analyze the ability of StO_2 to predict AL after DTR reconstruction by combining data from multiple studies. We hypothesized that low anastomotic StO_2 was one of the factors predisposing to AL, and that the lower the anastomotic StO_2 , the higher the probability that the patient would develop AL after surgery.

Materials and methods

Technical background

This systematic review was conducted in accordance with the PRISMA Checklist (Supplementary Information) and was pre-registered with PROSPERO (registration number: 42023458764).

StO_2 is the percentage of the volume of oxygen-bound oxygenated hemoglobin (HbO_2) in the tissue blood to the volume of all bindable hemoglobin (Hb, hemoglobin), StO_2 is an important physiological parameter of the respiratory cycle. The oxygen saturation of normal human arterial blood is 98%, and venous blood is 75%. Oxygen saturation tends to be significantly affected when the digestive tract blood supply is poor [24, 25].

Inclusion and exclusion criteria

The studies included in this meta-analysis were performed according to the PICOS principle, the inclusion criteria were: the study population was required to be human patients who underwent digestive tract reconstruction surgery (P); The exposure factor was the occurrence of AL in

the postoperative period (I); The AL group and the non-AL group were used as the control (C); The outcome of the study was the anastomotic StO_2 value (O); The types of the study were the RCT (Randomized Controlled Trial) study, the single arm studies, and cohort studies (S); The language of publication was limited to English. There was no limit on the sample size and time of publication;

The exclusion criteria were as follows: 1, studies with incomplete data; 2, data was repeated (When two studies had overlapped data, the study with a larger sample size would be included); 3, wrong site of StO_2 measurement (any part except the digestive tract); 4, change the anastomosis position after the measurement; 5, ischemic pretreatment was performed prior to surgery; 6, case reports, case series, letters to the editor, comments, conferences, and reviews.

Search strategy

The databases searched included Embase, Cochrane library, Pubmed. The StO_2 search terms utilized were “oxygen saturation” OR “Blood Oxygen Level” OR “Saturation of Peripheral Oxygen” OR “Peripheral Oxygen Saturation” OR “ SpO_2 ” OR “ StO_2 ” OR “tissue oxygenation”; AL search terms are: “Anastomotic Leak” OR “Anastomotic Leakage” OR “Leakage, Anastomotic” OR “anastomotic complication”; DTR search terms were “Digestive System Surgical Procedures” OR “Anastomosis, Roux-en-Y” OR “Colectomy” OR “Endoscopy, Digestive System” OR “Enterostomy” OR “Esophagectomy” OR “Esophagoplasty” OR “Esophagostomy” OR “Fundoplication” OR “Gastrectomy” OR “Gastroenterostomy” OR “Gastropexy” OR “Gastropasty” OR “Jejunioileal Bypass” OR “ancreaticoduodenectomy” OR “Pancreaticojejunostomy” OR “Proctectomy” OR “Colorectal Surgery” OR “colorectal resection”; The search was conducted until July 23, 2023,

Data extraction

Extracted data included: first author, year, country, study design content, and measurement device, number of patients, age, sex, and BMI, American Society of Anesthesiologists (ASA) grade, cardiopulmonary disease, smoking status, alcohol abuse, neoadjuvant therapy, diabetes mellitus (DM), surgical site, anastomotic StO_2 , the location of the anastomosis, the time of the anastomosis, and the method of anastomosis. The selected articles were independently evaluated by two researchers who completed the data extraction. Both extractors were trained before starting the work. Disagreements that arose during the process were resolved by negotiation.

Assessment of risk of bias in included studies

The quality of the included literature was assessed by using the Newcastle–Ottawa Quality Assessment Scale (NOS), which was independently scored by two investigators, with a third investigator adjudicating when there was a large discrepancy in the ratings. Studies with a NOS score < 7 points were classified as having a risk of bias. Specific scoring details of the included studies can be found in the Supplementary Materials.

Statistical analysis

The primary outcome of the study was anastomosis StO₂ in the AL group versus the non-AL group. Used a random effects model (dersimon-laird method). Selected Standardized Mean Difference (SMD) as the effect scale index. The secondary outcome was the occurrence of AL in StO₂ at different intervals. The grouping approach of M. Salusjärvi in his study was considered [22], and StO₂ was divided into three groups: excellent group StO₂ ∈ [100–90), qualified group StO₂ ∈ [90–80), and low group StO₂ ≤ 80. RR was chosen as the effect scale indicator using a random effects model. Considering the possible differences in StO₂ measured in the intestine and the stomach and esophagus. We pre-planned a subgroup analysis, we divided the data into an intestinal group and an esophagogastric group according to the surgical site and analyzed the data separately.

A sensitivity analysis of the primary endpoint (StO₂) of this systematic review was performed, excluding low-quality studies after assessment using the NOS scale and excluding studies with small sample sizes (defined as those with fewer than 30 patients) in order to maximize the validity of the metric to StO₂. Due to the small number of included studies, funnel plots were not used to check for potential publication bias in the outcome measures; Forest plots were used to illustrate the presence or absence of heterogeneity in the studies. The degree of heterogeneity of the studies was quantified by the I² statistic, which was considered to be moderately to highly heterogeneous when I² was greater than 50%. When included studies reported continuous data in the form of median (range) or median (IQR: Interquartile Range), the mean (SD: Standard Deviation) was calculated using the methods suggested by Hozo et al. and Wan et al. [26, 27]. All data in this paper were analyzed using Stata statistically (version 18.0).

Results

Study characteristics

A total of 178 studies were initially retrieved, and after removing 33 duplicate articles, the abstracts of the remaining 145 articles were screened, and a total of 124 studies were excluded. After a further full-text review, 10 studies were excluded, resulting in a total of eleven studies that were included in the present systematic review [21–23, 28–35] (Fig. 1).

The eleven included studies were all single-center studies, including nine cohort studies [21, 23, 28, 30–35], one single-arm study [22], and one medical record series [29]. A total of 867 patients were involved, including 87 patients with AL, with a mean incidence of AL of 10.0%; The primary outcomes of the studies included 10 studies with a total of 445 patients divided into the AL group (65 patients) and the non-AL group (380 patients). In the subgroup analysis, six studies with 267 cases of gastroesophageal reconstruction and four studies with 178 cases of colorectal anastomosis were included; The secondary outcome was addressed in five studies, which included a total of 616 patients divided into an excellent group (StO₂ ∈ [100–90), 388 cases), a qualified group (StO₂ ∈ [90–80), 147 cases), and a low group (StO₂ ≤ 80, 81 cases). Five of the included studies were defined as having a high risk of bias [29, 31, 34, 35]. (Appendix for more detailed information on key assessments).

The studies came from a total of six countries, including four studies conducted in Japan, three studies conducted in the United States, and one each from Germany, Switzerland, Finland, and the Netherlands in the remaining countries included in the study. The publication years range from 2006 to 2022; The equipment used in the studies basically covers commercially available oximetry instruments and is not limited to those developed independently by the investigators (Table 1). The equipment used, the timing of the coincidence, the location and the method used vary from study to institute (Table 2).

Outcome assessment

A total of 11 studies were included in this study containing 867 patients, the baseline characteristics of the patients were: mean age 67.4 (n = 8), male percentage 72.1% (305/423, n = 9), mean BMI was 24.7 (n = 4); ASA grade 2 and above was 65.0% (72/206, n = 3). Among the risk factors for AL: mean operative time was 148.3 min (n = 3), the average intra-operative blood loss was 172.1 ml (n = 2), the percentage of

DM was 11.4% (34/298, $n=5$), having respiratory disease was 7.7% (17/221, $n=4$), and the hypertensive population was 41.2% (63/153, $n=2$); The percentage of people receiving neoadjuvant treatment was 50.9% (142/279, $n=2$), other specific patient information is detailed in Table 3.

The main outcome of this meta-analysis was the anastomotic StO₂ after DTR reconstruction, and 10 studies involving 445 individuals were included, including 65 patients with AL, and the mean AL rate was 14.6%. The results showed: after DTR reconstruction, there was a statistically significant difference in the anastomotic StO₂ in the AL group (65) compared with the non-AL group (380) ($P<0.0001$; 95% CI: 1.02 [0.53–1.51]). The mean StO₂ in the AL group was 62.3%, which was significantly lower than that in the non-AL group, which was 74.3%, with a high degree of heterogeneity between the data ($I^2=62.7\%$, $P=0.004$) (Fig. 2).

After excluding highly biased studies and performing sensitivity analyses, there was still a statistically significant difference in StO₂ between the AL group and the non-AL group ($P=0.004$; 95% CI: 1.02 [0.53–1.51]). There was no heterogeneity between the data ($I^2=0\%$, $P=0.667$) (Fig. 3).

In subgroup analysis, anastomotic StO₂ in the intestinal subgroup was statistically different between the two groups ($P=0.018$; 95% CI: 0.85 [0.15–1.56]); There was significant heterogeneity between studies ($I^2=63.3\%$, $P=0.043$); In the gastroesophageal subgroup it was also statistically different ($P=0.002$, 95% CI: 1.17 [0.43–1.91]), with significant inter-study variability ($I^2=66.8\%$, $P=0.001$). Evidently, our data support the application of StO₂ as an indicator of anastomotic blood supply evaluation for predicting AL in patients undergoing DTR reconstruction, whether it is intestinal reconstruction or reconstruction of the gastric conduit after esophagectomy (Fig. 4, Fig. 5).

Fig. 1 PRISMA 2020 study selection flow diagram

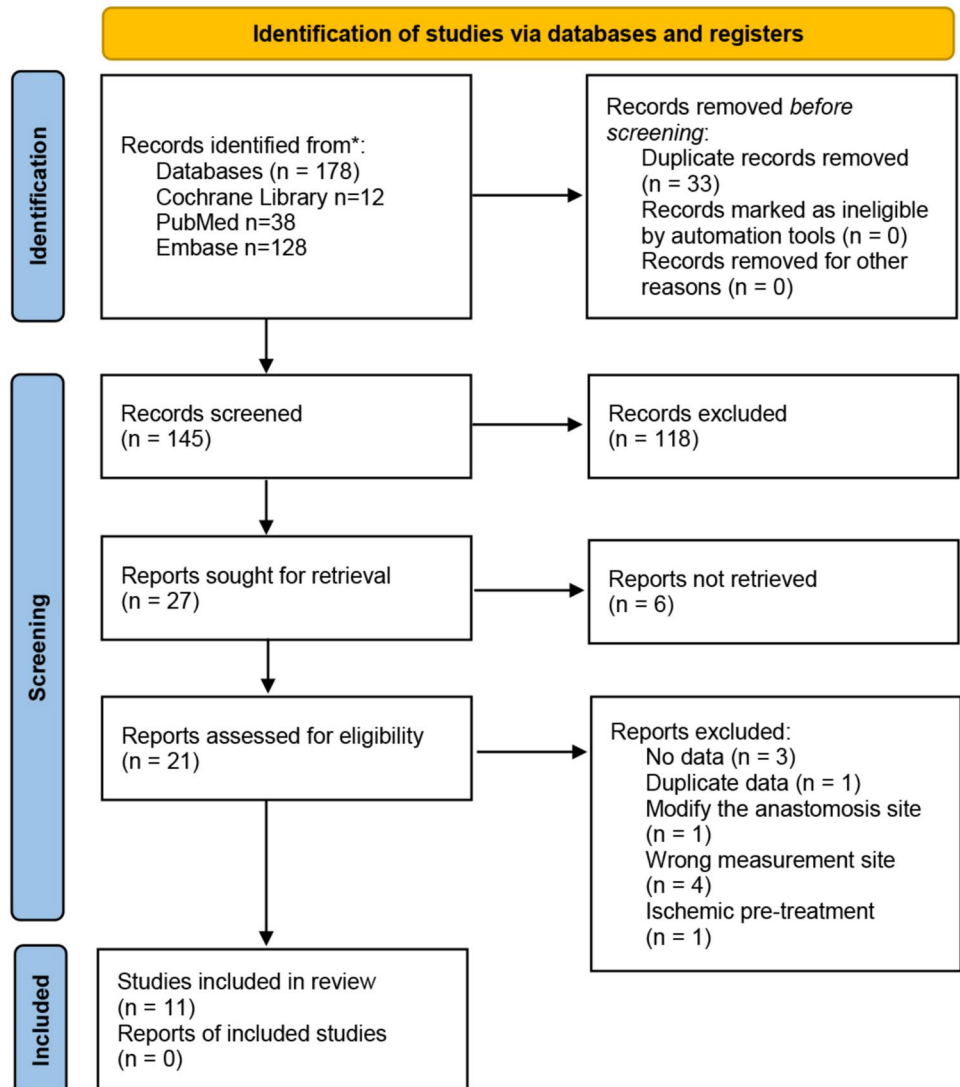


Table 1 Characteristics of included studies

Author	Year	Country	Study Design	Equipment	Surgical site	N	N(AL)	Number of men	Age	Mean BMI(kg/m ²)	StO ₂ (%)		NOS
											non-AL	AL	
Salusjärvi, J. M	2018	Finland	Single-arm Single center	Datex Ohmeda S/5, Finland	Colorectal	422	22	NA	NA	NA	NA	NA	7
Adusumilli, P. S	2020	USA	Retrospective cohort	WiPOX, USA	Gastroesophagus	114	7	97(85%) ^a	NA	NA	92.7 ± 12.8 ^b	91.2 ± 12.9 ^b	0.764
Gräffisch, A	2021	Switzerland	Single center Retrospective cohort	T-Stat, USA	Colorectal	50	8	34(68%) ^a	66.0 ^c	23.6 ^c	67.9 ± 10.8 ^b	62.1 ± 16.1 ^b	0.203
Ishii, K	2022	Japan	Single center A Case Series	Toccare, Japan	Gastroesophagus	18	6	12(67%) ^a	73.0 ^c	20.4 ^d	54.9 ± 4.6 ^b	46.3 ± 6.7 ^b	0.005
Fujita, T	2022	Japan	Single center Retrospective cohort	EP-0002, Japan	Gastroesophagus	51	3	40(78%) ^a	69.9 ^d	21.5 ^d	57.1 ± 7.9 ^b	48.3 ± 7.3 ^b	0.065
Tsutsumi, R	2019	Japan	Single center Retrospective cohort	Multispectral Cam- eras, Japan	Gastroesophagus	39	2	31(79%) ^a	65.9 ^d	NA	92.6 ± 4.1 ^b	79.0 ± 1.4 ^b	<0.001
Darwich, I	2019	Germany	Single center Retrospective cohort	O2C, Germany	Colorectal	31	9	15(48%) ^a	66.7 ^d	NA	88.0 ± 17.5 ^b	73.0 ± 26.0 ^b	0.068
Pham, T. H	2011	USA	Single center Retrospective cohort	Combined devices, USA	Gastroesophagus	23	8	17(74%) ^a	63.0 ^d	28.3 ^d	84.9 ± 42.2 ^b	47.5 ± 16.8 ^b	0.025
Karliczek, A	2010	Holland	Single center Retrospective cohort	T-Stat, USA	Colorectal	77	14	42(55%) ^a	68.0 ^d	26.8 ^d	76.7 ± 8.0 ^b	73.1 ± 7.4 ^b	0.126
Garcia, D. S	2010	USA	Single center Retrospective cohort	Combined devices, USA	Gastroesophagus	22	6	NA	NA	NA	42.1 ± 19.4 ^b	21.0 ± 15.1 ^b	0.025
Hirano, Y	2006	Japan	Single center Retrospective cohort	PSA-500, Japan	Colorectal	20	2	17(85%) ^a	67.0 ^d	NA	71.0 ± 4.2 ^b	58.0 ± 2.4 ^b	0.001

Abbreviations: BMI, body mass index; StO₂, tissue oxygen saturation; AL, anastomotic leakage; NA, measurement not available; NOS, Newcastle–Ottawa Scale^a means (percentage)^b means ± standard^c median^d means*

p < 0.05, AL versus non-AL

Table 2 Method, time and location of StO₂ measurements in the included studies

Author	Equipment	Surgical site	Time	Location	Method
Salusjärvi, J. M Adusumilli, P. S	Datex Ohmeda S/5, Finland WiPOX, USA	Colorectal Gastroesophagus	After the division of the mesentery After the gastric conduit was mobilized and the anastomotic site was identified by the surgeon	StO ₂ of the colonic anastomosis On the serous surface of the planned anastomotic site	NA The measurement was deemed accurate when the heart rate reading by the device matched the heart rate on the operating room monitors
Gräfftsch, A	T-Stat, USA	Colorectal	Three measurements: ①before mobilization ②after mobilization ③after anastomosis	Five parts: ①Caecum ②Prox. Planned resection ③Distal planned resection ④1 cm prox. Anastomosis ⑤1 cm distal anastomosis	Using a 5-mm sensor above the intestine until the values stabilized within a 5% margin
Ishii, K	Toccare, Japan	Gastroesophagus	When The gastric tube was raised to the cervical site via the retrosternal route	StO ₂ was measured at the tip, and 2, 4, and 6 cm on the distal side of the tip of the gastric tube Then, StO ₂ was measured at the anastomotic site	NA
Fujita, T	EP-0002, Japan	Gastroesophagus	After gastric tube preparation	At each site on the gastric tube (pre-pylorus, gastric angle, end of right gastroepiploic vessel area of the conduit, demarcation line of the conduit, demarcation line of the conduit, and tip of the conduit)	An oxygen saturation imaging evaluation of the gastric tube obtained in real time during surgery
Tsutsumi, R	Multispectral Cameras, Japan	Gastroesophagus	Preserving the right gastric artery/vein and the bilateral gastroepiploic arteries/veins was created. The gastric tube was placed on the body surface anterior to the sternum	StO ₂ of the anastomosis	The oxygen saturation imaging system
Darwich, I	O2C, Germany	Colorectal	After the mesentery is separated and the bowel is severed	StO ₂ of the anastomosis	Utilizing laser Doppler flowmetry as well as tissue spectrometry, was used to measure three different parameters: SO ₂ , rHb and blood flow velocity A minimal time cost of 3–4 min per measurement

Table 2 (continued)

Author	Equipment	Surgical site	Time	Location	Method
Pham, T. H	Combined devices, USA	Gastroesophagus	Four measurements: ①Short gastric vessel division ②Left gastric vessel division ③Completion of conduit ④Pull-up	Five independent recordings were taken at each of three adjacent locations in the region of the anastomosis and averaged	NA
Karliczek, A	T-Stat, USA	Colorectal	Before taking the descending colon down into the pelvis, and were repeated after completion of the anastomosis	Measurements were taken approximately 1.5 cm away from the cut edge of the proximal and distal colon and simultaneously at the caecal serosa	A sterile handheld probe was placed in the operative field and held a few millimeters above the gauze-cleaned serosal or adventitial surface until values stabilized within a 5% margin
Gareau, D. S	Combined devices, USA	Gastroesophagus	Spectra were collected at five time points during the surgery: ①a baseline value ②after division of the short gastric arteries ③after division of the left gastric artery ④after creation of the gastric conduit ⑤after completion of the anastomosis	At each time point, five measurements were taken in rapid succession at each of three locations within 2 cm of a marking stitch	The endoscope light was turned off for spectral measurements The integration time for each measurement was about 200 ms
Hirano, Y	PSA-500, Japan	Colorectal	After completion of the anastomosis	Except for patients with anterior resection, StO ₂ measurements were obtained at two points (proximal and distal side of anastomosis) on the anti-mesenteric position of the bowel	Each StO ₂ measurement was performed for 10 s and was duplicated. The mean of the two values was used for StO ₂ . When StO ₂ measurements were obtained at two points, the lower value was used

Abbreviations: StO₂, tissue oxygen saturation; AL, anastomotic leakage; NA, not available

Table 3 Summary of characteristics between AL group and non-AL group

Characteristics	Studies	Participants(AL/non-AL)	SMD/OR (95% CI)	Heterogeneity
Basic information of patients				
Male	6	263/47	0.755 [0.374, 1.528]; P=0.435 *	I ² =0%; P=0.462 †
Age	2	54/14	0.330 [-0.273, 0.933]; P=0.284 *	I ² =0%; P=0.650 †
Risk factors of AL				
DM	5	260/38	1.082 [0.341, 3.431]; P=0.894 *	I ² =0%; P=0.658 †
Respiratory dysfunction	4	197/24	1.163 [0.303, 4.457]; P=0.826 *	I ² =0%; P=0.478 †
Cardiovascular	2	148/16	2.798 [0.615, 12.737]; P=0.183 *	I ² =39.6%; P=0.198 †
Smoking history	3	160/22	0.839 [0.315, 2.238]; P=0.726 *	I ² =0%; P=0.602 †
Post radiation therapy	5	240/39	1.447 [0.514, 4.079]; P=0.484 *	I ² =34.4%; P=0.192 †
Hypercholesterinemia	2	79/10	0.986 [0.155, 6.262]; P=0.988 *	I ² =0%; P=0.448 †
Hypertension	2	143/10	2.210 [0.592, 8.251]; P=0.238 *	I ² =0%; P=0.705 †
Surgery-related information				
Thoracotomy	4	94/25	0.956 [0.328, 2.788]; P=0.935 *	I ² =0%; P=0.566 †
Thoracoscope	4	94/25	1.046 [0.359, 3.048]; P=0.935 *	I ² =0%; P=0.566 †
ASA Grade: 1–2	2	103/22	0.507 [0.153, 1.675]; P=0.265 *	I ² =0%; P=0.329 †
ASA Grade: 3–4	2	103/22	1.974 [0.597, 6.528]; P=0.265 *	I ² =0%; P=0.329 †
Hand sewn	2	104/21	1.390 [0.247, 7.821]; P=0.708 *	I ² =34.6%; P=0.216 †
Stapler	2	104/21	0.719 [0.128, 4.046]; P=0.708 *	I ² =47.4%; P=0.216 †

Abbreviations: AL, anastomotic leakage; OR, Odds ratio; SMD, standardized mean difference; CI, confidence intervals; DM, diabetes mellitus; ASA, American Society of Anesthesiologists classification of physical status

* p < 0.05, AL versus non-AL

† p > 0.1, AL versus non-AL

The secondary outcome of the study was the probability of AL. We divided the collected StO₂ into three groups, excellent (StO₂ ∈ [100–90]), normal (StO₂ ∈ [90–80]), and low (StO₂ ≤ 80), to determine whether there was an obvious relationship between reduced StO₂ and AL (Table 4).

A total of 616 patients were included in the secondary results, of which 42 patients had AL after surgery, with a mean AL rate of 6.82%; There were 388 patients in the excellent StO₂ group (17 AL patients), 147 patients in the normal StO₂ group (13 AL patients), and 81 patients in the poor StO₂ group (12 AL patients) (Table 4).

The results showed that there was a statistically significant difference in the incidence of AL between the StO₂-excellent group and the normal group (P = 0.034); RR = 0.47 (95%CI: 0.29 to 2.67); There was no inter-study heterogeneity (I² = 0%, P = 0.933); The incidence of AL in the StO₂-excellent group was 47% of that in the normal group (Fig. 6).

There was no statistically markedly discrepancy in the incidence of AL between the normal and low StO₂ groups (P = 0.837); RR = 0.83 (95%CI: 0.14 to 5.03), with significant between-study heterogeneity (I² = 57.2%, P = 0.072). The incidence of AL in the normal StO₂ group was 83% of that in the low group.

The test for the incidence of AL between the StO₂ superior and low groups (P = 0.337) found no significant differences; RR = 0.31 (95%CI: 0.03 to 3.38). There was significant heterogeneity between the studies (I² = 68.6%, P = 0.041); The incidence of AL in the StO₂ superior group was 31% of that in the low group.

From the above results, there was a significant difference in the probability of AL only between the StO₂ excellent group and the normal group. However, according to statistics, the probability of AL in the StO₂ excellent group was 4.38% (17/388), the probability of AL in the StO₂ normal group was 8.84% (13/147), and the probability of AL in the low StO₂

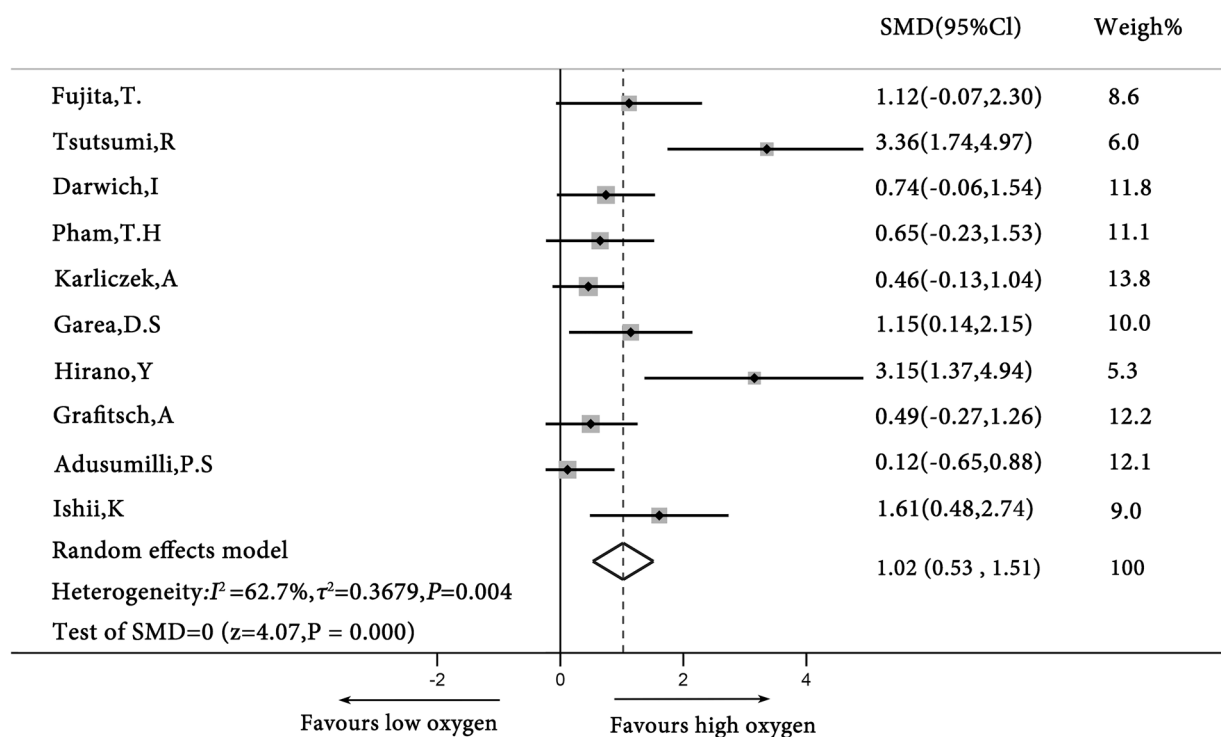


Fig. 2 Anastomotic StO₂ in the AL group versus the non-AL group

group was 14.81% (12/81). Using the StO₂ excellent group as a control, the incidence of AL was elevated to 201.8% and 338.1% after the anastomotic StO₂ was lowered respectively to the [90–80) and [80–0] intervals. The incidence of AL tended to be significantly higher with the reduction of StO₂.

Discussion

This meta-analysis included 867 patients from 11 studies, and we found that anastomotic low StO₂ was an independent risk factor for developing AL. Further subgroup analyses showed that low StO₂ was a potential predictor of postoperative AL in both bowel cancer patients, esophageal cancer patients. In addition, there was a correlation between the incidence of AL and reduced StO₂.

Cancer of the digestive tract is one of the most common cancers in clinical practice today. The prognosis of DTR reconstruction is particularly important as a means of radical treatment, and AL is still the most serious postoperative complication of this procedure. Considering the patient's intestines after performing a break-end anastomosis, the formation of the anastomosis depends on the healing of collagen connections to form a stable ductal structure. Kivisaari J in his study pointed out that there exists a threshold level of tissue oxygen tension for collagen synthesis (15–20mmHg), below which collagen synthesis is markedly impaired in experimental wounds [36–38]. The collagen synthesis is an important process in the healing of scar and its synthesis also depend on the supply of oxygen up to the threshold level, which predicts that StO₂ may be used as a predictor of anastomotic healing.

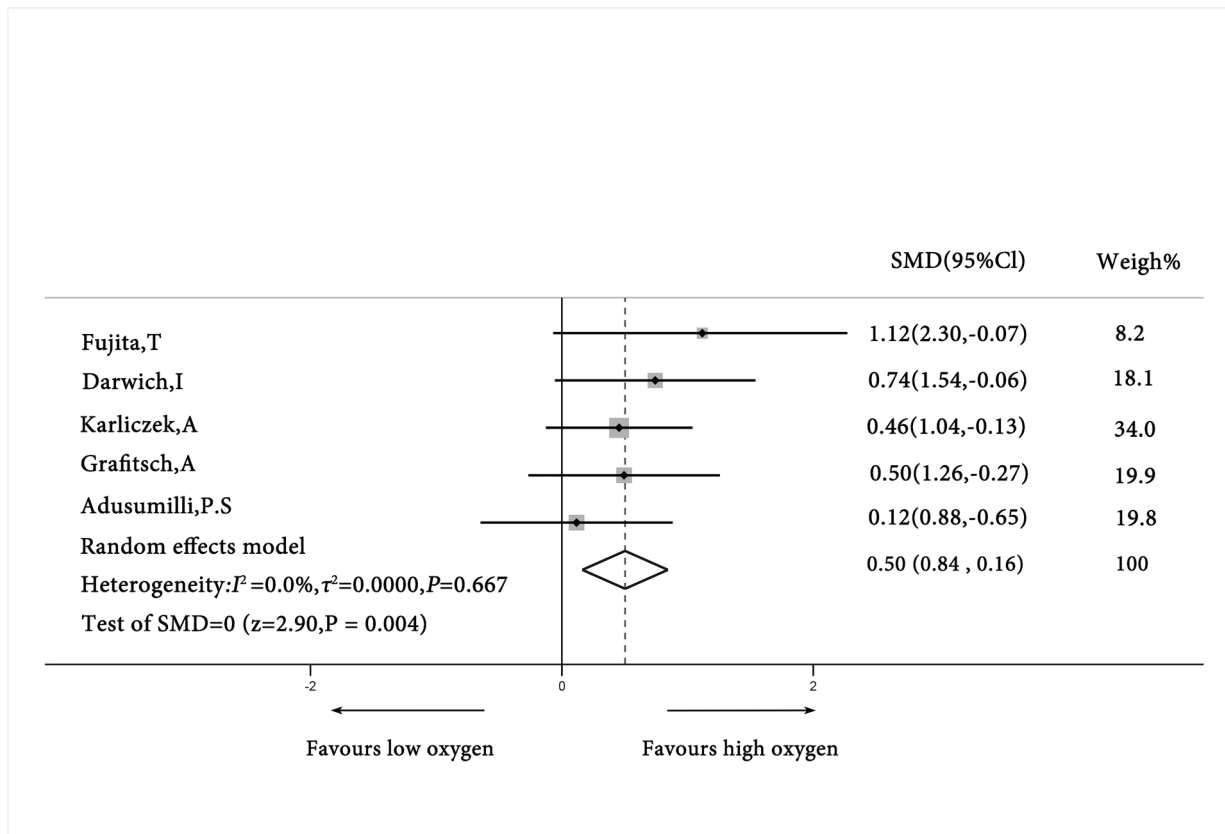


Fig. 3 The predefined sensitivity analysis of anastomotic StO₂ in the AL group versus the non-AL group

Current studies are controversial regarding the predictive value of StO₂. Adusumilli, P. S. et al. and Gräfitzsch, A. et al. concluded after their experiments that anastomotic StO₂ did not significantly correlate with postoperative AL formation [28, 30]. In turn, Salusjärvi, J. M. et al. and Ishii, K. et al. concluded that this method seems to be useful in assessing anastomotic viability [22, 29]. Therefore, further comprehensive analysis of the potential relationship between AL and StO₂ is needed.

For evaluating anastomotic blood supply, there are two main clinical approaches. One is the clinician's visual judgment, but in addition to the disadvantage of the surgeon's low predictive value of the anastomosis in DTR [15]. When performing NOSES and NOTES surgeries in the upcoming minimally invasive surgical era, the abdominal wall is not opened and the intestinal tubes have not been dragged out of the peritoneal cavity. Therefore, it is difficult to directly visualize and evaluate the color, mobility, and bleeding of the

severed ends of the digestive tract. In addition to extracorporeal surgery, the surgeon needs to use an endoscope to make indirect observations of the digestive tract in most cases.

The second is the ICG-FA, which, according to literature reports In laparoscopic colorectal cancer surgery, ICG-FA can enhance the visualization of tumor lesions, improve the detection rate of lymph nodes, and reduce the incidence of AL [39]. In addition, the quantitative measurement of ICG-FA is also an area of concern, but most of the studies are unable to achieve real-time decision-making [40–42]. The study of Kim, J. C., and Gomez-Rosado, J. C. closed this gap and demonstrated that quantitative ICG-FA can help prevent anastomotic complications more precisely [39, 43]. On the contrary, there are still some problems with ICG-FA, such as the need to give fluorescent substances, the possibility of ICG allergies, and the cost problem [19]. And the judging criteria and operation specifications need to be supported by multicenter, large-sample, and high-level evidence-based medical evidence.

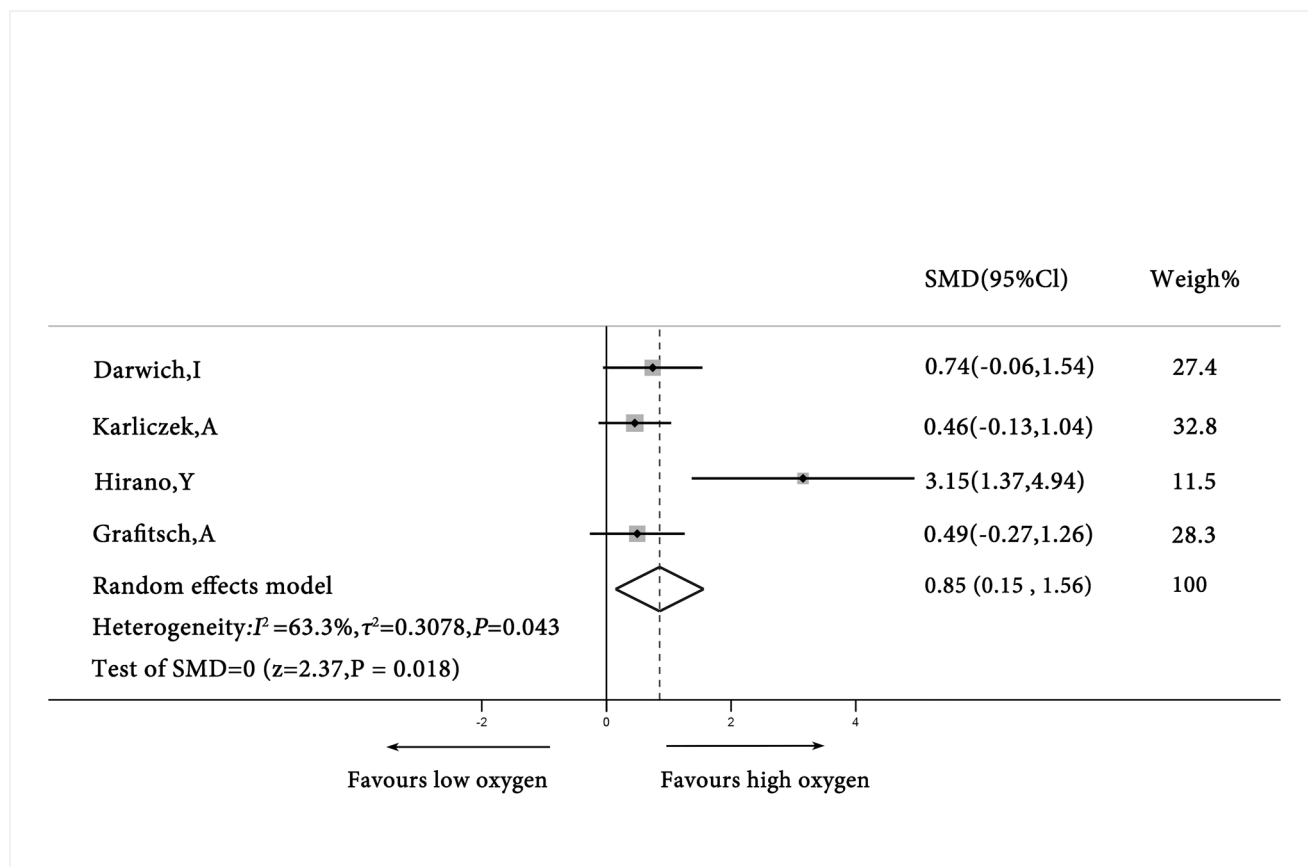


Fig. 4 Forest plot assessment of anastomotic StO₂ in the AL versus non-AL groups in the intestinal subgroups

In addition to ICG-FA and StO₂, there are several other intraoperative techniques for measuring tissue perfusion at anastomosis sites, such as laser speckle contrast imaging (LSCI), Doppler flow, and angiography. However, these methods have not been widely accepted and research data is limited due to limited feasibility, reproducibility issues, or cost issues [44].

Comparing the above two ways of judging anastomotic blood supply, using StO₂ as an evaluation index seems to be a better solution. This technique can realize qualitative and quantitative evaluation of blood supply at the anastomosis, and output the results in the form of images or numerical values to assist clinicians in choosing the anastomotic margins. The measurement process does not require the injection of any substance, and the measurement method is safe and convenient. Several oxygen saturation measurement instruments are currently available on the market: IntraOx (USA) and WiPOX (USA) have been used in preliminary clinical trials [28, 45].

To the best of our knowledge, this is the first meta-analysis to analyze the use of StO₂ as an indicator to evaluate blood supply after DTR reconstruction. We resolved the controversy of whether StO₂ can be an independent risk factor for AL. In addition, we included studies from multiple countries and multiple measurement devices, which means that the results are not limited to a particular geographic region or device and have broad applicability.

However, this meta-analysis still has some limitations. First, only 867 patients from 11 studies were included in the statistics, not including any large RCT, which leads to possible bias in the results. Second, due to the lack of standardization, different studies varied regarding specific intraoperative measurements, which can lead to a certain degree of heterogeneity between studies. Third, we were unable to compare the distance of the tumor from the anal margin or its location in the esophagus between the two groups, as this part of the data was missing from some studies. Finally,

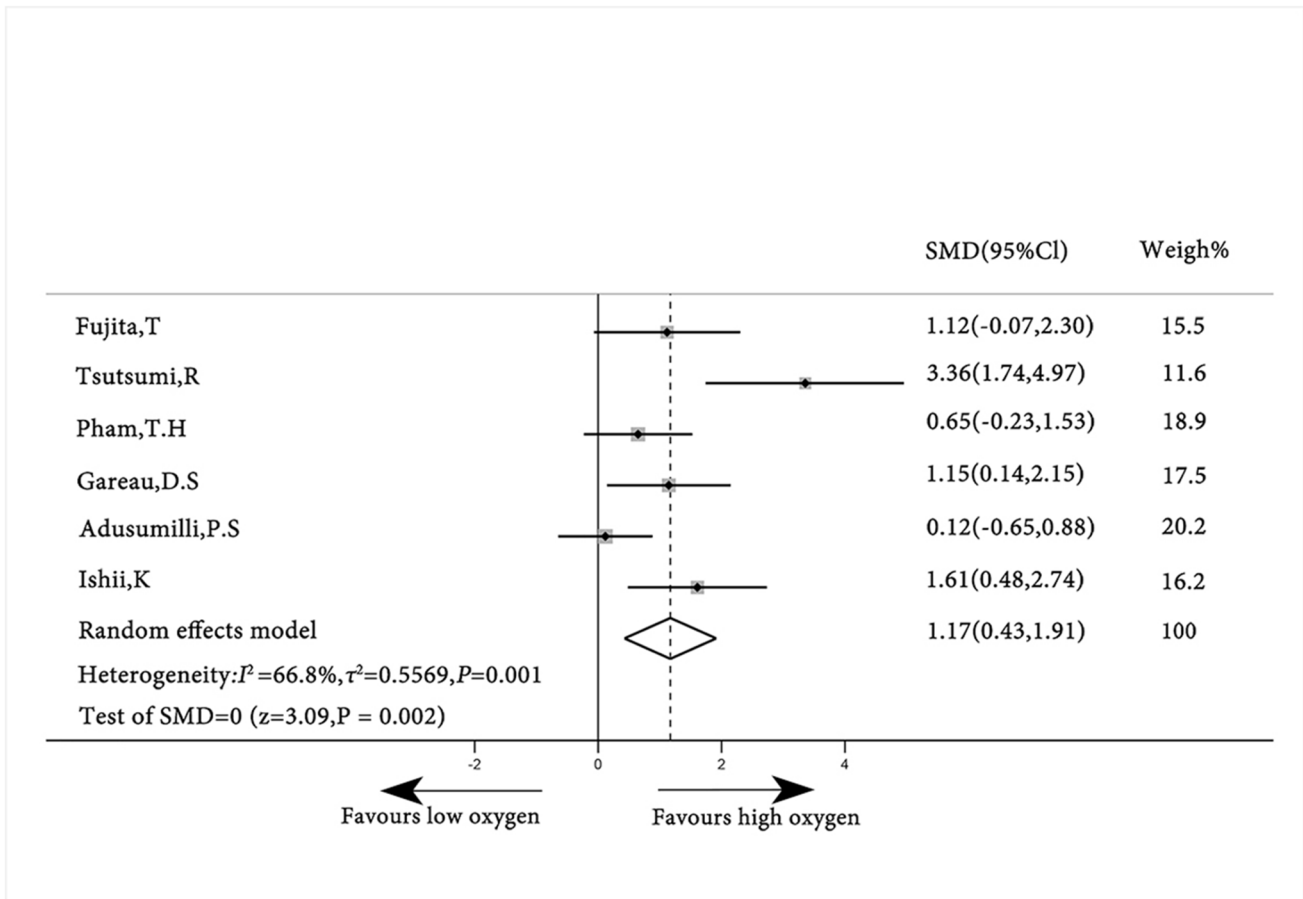


Fig. 5 Forest plot assessment of anastomotic StO₂ in gastroesophageal subgroups in the AL and non-AL groups

Table 4 Number of people with different StO₂ ranges and number of people with AL

Author	N	N(AL)	StO ₂ > 90%		80% < StO ₂ ≤ 90%		StO ₂ ≤ 80%	
			N	N(AL)	N	N(AL)	N	N(AL)
Salusjärvi, J. M	422	22	293	11	111	9	18	2
Hirano, Y	20	2	0	0	1	0	19	2
Tsutsumi, R	49	2	25	0	12	0	2	2
Adusumilli, P. S	113	10	70	6	23	4	20	0
Gareau, D. S	22	6	0	0	0	0	22	6
Summary	626	42	388	17	147	13	81	12

Abbreviations: AL, anastomotic leakage; StO₂, tissue oxygen saturation

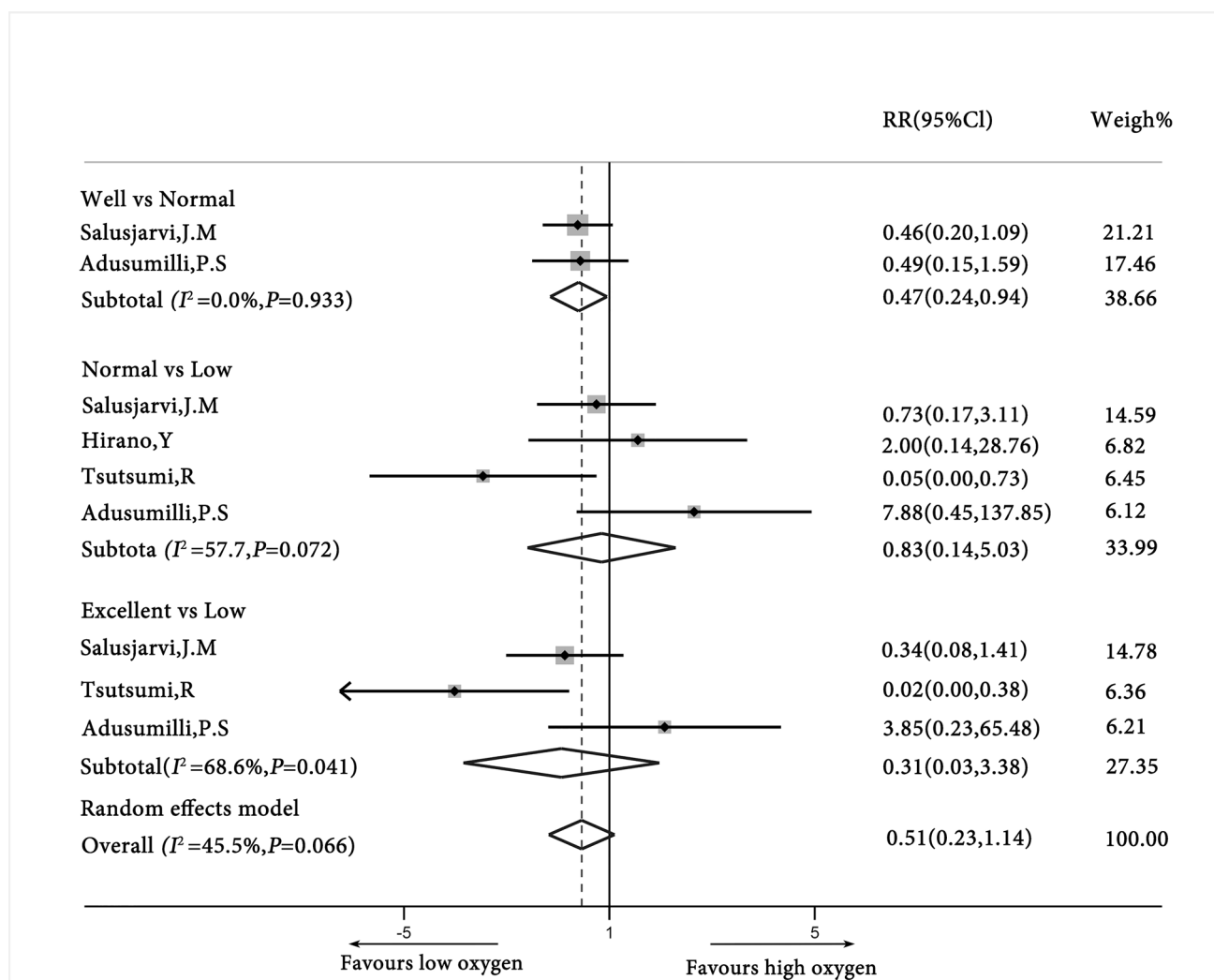


Fig. 6 Integrated estimation of AL incidence with forest plots at different intervals of StO_2

although different measurement devices indicate generalizability of the study results, the total number of measurement devices as well as missing device parameters reduces the confidence in the data (which is a likely source of inter-study heterogeneity).

Currently, there are no uniform international standards for measurement of DTR oxygen saturation and no measurement instruments that are widely recognized internationally, and the timing of measurements, the site of measurement, and the sensitivity of the measurement instruments have varied from study to study. Further clinical trials of this technique in the future will require international organizations

to develop standardized protocols to facilitate the collection and use of data. Surgical centers wishing to adopt the new technique should consider these factors.

Conclusion

StO_2 can be utilized to accurately and quantitatively evaluate anastomotic blood supply in DTR. It can help clinicians select anastomotic margins with adequate blood supply to reduce the probability of postoperative AL.

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Declarations

Ethics approval and consent to participate Not appliance.

Consent to publish Not appliance.

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