

USE OF INDOCYANINE GREEN IN THE PREVENTION OF ANASTOMOTIC LEAK IN COLORECTAL SURGERIES: A SYSTEMATIC REVIEW

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ABSTRACT

Anastomotic leak is a serious complication in colorectal surgery, with an incidence of up to 19% and significant mortality. Indocyanine green (ICG) allows intraoperative assessment of bowel perfusion through fluorescence imaging, but its effectiveness in reducing leaks remains controversial. This systematic review aimed to evaluate whether ICG use reduces anastomotic leak rates in colorectal surgery compared to conventional visual inspection. The search was performed in PubMed using MeSH terms, identifying 198 articles. After applying inclusion and exclusion criteria, 7 randomized controlled trials were analyzed. Two studies demonstrated significant leak reduction with ICG (Alekseev et al., 2020: 16.3% vs 9.1%, $p=0.04$; Watanabe et al., 2023: 11.8% vs 7.6%, $p=0.041$), while five studies showed no statistically significant difference, although with a numerical trend favoring ICG. Subgroup analyses suggest ICG benefit in low anastomoses (rectal). No serious adverse events were reported. ICG is safe, but its clinical efficacy remains uncertain. Routine use for all colorectal surgeries is not recommended, although it may be promising in high-risk scenarios, such as low rectal surgery.

Keywords: Anastomotic leak, Colorectal surgery, Disease Management, Fluorescence, Indocyanine green.

INTRODUCTION

Anastomotic leak (AL) is one of the most feared complications following colorectal surgery with primary anastomosis. Its incidence ranges from 1% to 19%, depending on the level of the anastomosis and the patient's clinical condition, and it is associated with mortality rates that may reach 35%.¹ In addition to its clinical impact, AL significantly increases length of hospital stay, healthcare costs, and the need for surgical reinterventions, constituting an important public health problem.

Currently, the decision regarding the ideal site for anastomosis is based primarily on the surgeon's subjective visual inspection, assessing parameters such as serosal color, bleeding at the edges, and pulsation of the vascular arcades. However, this method has low sensitivity and specificity for detecting inadequate tissue perfusion² and is widely recognized as imprecise and dependent on the surgeon's experience.

Indocyanine green (ICG) has emerged as a promising alternative to overcome these limitations. It is a fluorescent tricarbo-cyanine dye administered intravenously that rapidly binds to plasma proteins. When

illuminated with near-infrared light, it emits fluorescence detectable by specific cameras, allowing the surgeon to assess perfusion of the bowel edge in real time before performing the anastomosis.³ Studies have shown that ICG identifies inadequate perfusion and changes the anastomotic site in approximately 10% of cases⁴, potentially preventing the occurrence of anastomotic leak.

Initial evidence regarding the effectiveness of ICG was promising. Meta-analyses published between 2023 and 2024 demonstrated a significant reduction in AL with the use of fluorescence angiography, with odds ratios ranging from 0.46 to 0.586 in colorectal and rectal surgery.^{5,6} However, more recent randomized controlled trials (RCTs) have yielded conflicting results, with some studies showing significant benefit^{7,8} and others finding no statistically significant differences.^{9,10} This heterogeneity of findings maintains the debate regarding the actual role of ICG in surgical practice.

Given this scenario of uncertainty and the recent publication of new RCTs, an updated systematic review is justified. The present study aims to evaluate whether the intraoperative use of indocyanine green for assessment of bowel perfusion reduces the rate of anastomotic leak in patients undergoing colorectal surgery compared with the conventional method based on subjective visual inspection.

OBJECTIVES

The general objective of this study is to evaluate whether the intraoperative use of indocyanine green (ICG) for assessment of bowel perfusion reduces the rate of anastomotic leak in patients undergoing colorectal surgery compared with the conventional method based on subjective visual inspection.

The specific objectives are to compare the incidence of anastomotic leak between the ICG and control groups; analyze the impact of ICG on surgical reintervention rates and length of hospital stay; and describe adverse effects related to the use of indocyanine green reported in the literature.

METHODS

This is a systematic literature review conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist guidelines.

Studies were included if they met the following criteria:

- (1) original studies designed as randomized clinical trials, non-randomized clinical trials, or cohort studies (prospective or retrospective);
- (2) adult patients undergoing colorectal surgery with primary anastomosis;
- (3) intraoperative use of indocyanine green (ICG) for assessment of bowel perfusion;
- (4) comparison with the conventional method based on subjective visual inspection;
- (5) primary outcome reporting the anastomotic leak rate;
- (6) articles published in English, Portuguese, or Spanish; and
- (7) publication between January 2015 and April 2026.

The following were excluded:

- (1) review studies (systematic, integrative, or narrative), meta-analyses, editorials, letters to the editor, case reports, and case series;
- (2) animal or cadaver studies;
- (3) studies without a control group;

- (4) studies without full-text access; and
- (5) duplicate articles.

The search was conducted in May 2026 in the PubMed/MEDLINE database. English-language descriptors based on MeSH (Medical Subject Headings) and Boolean operators were used according to the following PubMed search strategy: ("Indocyanine Green" [Mesh] OR "ICG" OR "indocyanine green") AND ("Colorectal Surgery" [Mesh] OR "colorectal resection" OR "colorectal anastomosis") AND ("Anastomotic Leak" [Mesh] OR "anastomotic leakage" OR "anastomotic leak").

The following filters were applied: randomized clinical trials, controlled clinical trials, observational studies, cohort studies, publications from the last 10 years, and articles in English, Portuguese, or Spanish.

Two reviewers independently screened the titles and abstracts. Disagreements were resolved by consensus or with the assistance of a third reviewer. Full texts of potentially eligible articles were retrieved and evaluated according to the inclusion criteria.

Data were extracted using a standardized form containing:

- (1) study identification (author, year, country);
- (2) study design;
- (3) sample size (ICG group and control group);
- (4) population characteristics (age, sex, type of surgery);
- (5) anastomotic leak rate in each group; and (6) secondary outcomes (reintervention, length of hospital stay, adverse effects).

The methodological quality of the included studies was assessed according to each study design: for randomized clinical trials, the Cochrane RoB 2 (Risk of Bias 2) tool was used; for cohort studies, the Newcastle-Ottawa Scale was used. Two reviewers performed the assessment independently.

The results were synthesized descriptively (narratively) and presented in tables. A meta-analysis was not performed due to methodological heterogeneity among the studies.

RESULTS AND DISCUSSIONS

The initial PubMed search identified 198 articles using the defined descriptors. After applying the publication date filter for the last 10 years (2015–2025), 192 articles were retrieved. Of these, 12 controlled clinical trials and 8 observational studies were selected for abstract review. After application of the inclusion and exclusion criteria, 7 randomized controlled trials (RCTs) were included in this systematic review. The flowchart of the study selection process is presented in Figure 1 (PRISMA).

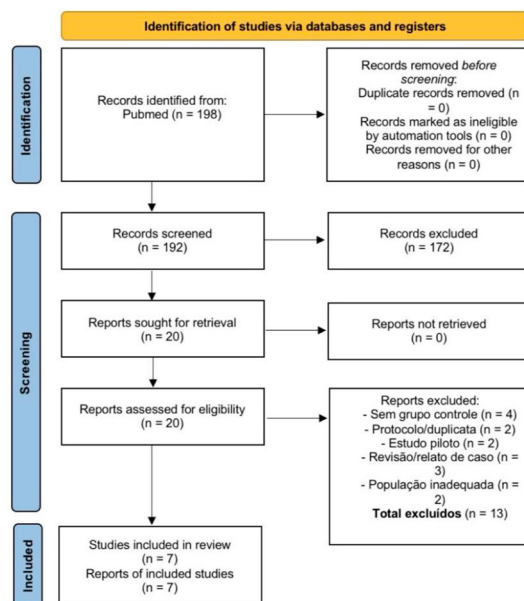


Figure 1: PRISMA Flowchart of the Study Selection Process.

Source: Prepared by the authors based on the PRISMA 2020 model.¹¹

Table 1 presents the characteristics and main findings of the 7 RCTs included. The studies were published between 2020 and 2025, with sample sizes ranging from 240 to 931 patients. All studies compared the intraoperative use of indocyanine green (ICG) for assessment of bowel perfusion with the conventional method based on subjective visual inspection. The primary outcome in all studies was the anastomotic leak rate. Six studies were multicenter, and one was conducted at a single center.

Table 1: Characteristics of the Included Studies.

	Author (year)	Typo	N (ICG)	N (control)	ICG leak (%)	Control leak (%)	p value	Sign ificant
1	Faber, 2024	RCT	463	468	6.9%	9.0%	0.04	No
2	Rinne, 2025	RCT	567	569	5.8%	7.9%	0.16	No
3	Watanabe, 2023	RCT	422	417	7.6%	11.8%	0.041	Yes
4	Jayne, 2025	RCT	343	355	10.5%	15.2%	0.087	No
5	Alekseev, 2020	RCT	187	190	9.1%	16.3%	0.04	Yes
6	De Nardi, 2020	RCT	118	122	5.1%	9.0%	n.s.	No
7	Jafari, 2021	RCT	178	169	9.0%	9.6%	0.37	No

Legend: RCT = randomized controlled trial; ICG = intraoperative indocyanine green.

Table 1: Prepared by the authors.

Of the 7 RCTs included, two studies (28.6%) demonstrated a statistically significant reduction in the anastomotic leak rate with the use of ICG. The study by Alekseev et al.⁷ reported a reduction from 16.3% to 9.1% ($p=0.04$), while the study by Watanabe et al.⁸ showed a reduction from 11.8% to 7.6% ($p=0.041$). The remaining five studies found no statistically significant difference between the ICG and control groups, although most demonstrated a numerical trend favoring ICG.^{2,9,10,12,13}

Two studies performed subgroup analyses suggesting a benefit of ICG in specific populations. Alekseev et al.⁷ observed that ICG significantly reduced anastomotic leak in low colorectal anastomoses (4–8 cm from the anal verge): 14.4% in the ICG group versus 25.7% in the control group ($p=0.04$), whereas no benefit was observed for high anastomoses ($p=0.37$). Rinne et al.¹² demonstrated a trend toward benefit in left-sided surgery (OR 0.55; 95% CI 0.29–1.05), although without statistical significance.

Watanabe et al.⁸ reported that the reoperation rate was significantly lower in the ICG group (0.5% vs. 2.4%; $p=0.021$). De Nardi et al.² observed that ICG angiography led to a change in surgical strategy (extended bowel resection) in 11% of patients due to the identification of inadequate perfusion. None of the studies reported serious adverse events related to the use of ICG.^{2,7-10,12,13}

This systematic review synthesized the available evidence on the use of indocyanine green (ICG) in the prevention of anastomotic leak in colorectal surgery, based on 7 randomized controlled trials totaling 3,195 patients. The results demonstrated that two studies (28.6%) found a significant reduction in the leak rate with the use of ICG^{7,8}, while five studies did not show a statistically significant benefit^{2,9,10,12,13}, although most showed a numerical trend favoring the intervention.

The heterogeneity of the results reflects the current state of knowledge regarding ICG in colorectal surgery. The positive studies share some characteristics: both predominantly included low rectal surgery, a procedure associated with a higher risk of anastomotic leak^{7,8}. In contrast, the negative studies included a mixture of right-sided colon, left-sided colon, and rectal surgeries, which may have diluted the effect of ICG.^{2,9,10,12,13} This observation is supported by the subgroup analyses: Alekseev et al.⁷ demonstrated that ICG significantly reduced anastomotic leak in low anastomoses (14.4% vs. 25.7%; $p=0.04$), but not in high anastomoses. Rinne et al.¹² also observed a trend toward benefit in left-sided surgery (OR 0.55; 95% CI 0.29–1.05). These findings suggest that ICG may be more useful in settings with a higher risk of anastomotic leak, where bowel perfusion is more critical.

Several factors may explain the variation in results among the studies: type of surgery (rectal versus colonic), differences in ICG administration protocols (dose, timing of injection, criteria for modifying the resection), experience of the surgical centers, and variations in the definition of anastomotic leak (grades A, B, and C). The largest study included, with 931 patients¹², was negative, whereas smaller studies with more selected populations were positive^{7,8}, suggesting that the benefit of ICG may be more evident in specific high-risk subgroups.

The largest study included, with 931 patients, was negative, whereas smaller studies with more selected populations were positive.⁹ This raises a critical question: could the benefit of ICG, when present, be a false-positive finding related to selection bias or insufficient sample size? Smaller studies have a greater risk of overestimating effects, and the lack of confirmation in a large multicenter RCT is a warning sign that cannot be ignored.

Despite the lack of statistical significance in some studies, secondary outcomes suggest a benefit of ICG. Watanabe et al.⁸ reported a significant reduction in the reoperation rate (0.5% vs. 2.4%; $p=0.021$). De Nardi et al.² observed that ICG led to a change in surgical strategy in 11% of cases, potentially avoiding anastomoses in poorly perfused areas. No study reported serious adverse events related to ICG^{2,7-10,12,13}, confirming its safety.

This review has limitations that should be considered. The search was restricted to PubMed, although it is the most comprehensive database in biomedical sciences. Methodological heterogeneity among the studies, including differences in ICG protocols and definitions of anastomotic leak, limited comparability and prevented the performance of a meta-analysis. In addition, most studies did not adequately describe blinding, and some are very recent^{9,10,12}, with no independent replication to date.

Based on the findings, routine use of ICG cannot be recommended for all colorectal surgeries. However, ICG appears promising in low rectal surgery (anastomoses less than 8 cm from the anal verge), where the risk of anastomotic leak is higher and subgroup analyses have shown significant benefit⁷. Future research should standardize ICG administration and interpretation protocols, focus specifically on low rectal surgery, and evaluate the cost-effectiveness of the technology, considering the potential reduction in reoperations and length of hospital stay.

Indocyanine green (ICG) is a safe tool for intraoperative assessment of bowel perfusion in colorectal surgery.^{2,7-10,12,13} Although most randomized controlled trials have not demonstrated a statistically significant reduction in anastomotic leak, there is a consistent numerical trend toward benefit and a significant benefit in higher-risk subgroups, such as low anastomoses.⁷ ICG may be more useful in low rectal surgery, where it modifies the surgical strategy in approximately 10% of cases.² Additional studies focused on high-risk populations are needed to establish its actual role in clinical practice.

CONCLUSION

This systematic review demonstrated that indocyanine green (ICG) is a safe tool for intraoperative assessment of bowel perfusion in colorectal surgery. Although most randomized controlled trials did not demonstrate a statistically significant reduction in anastomotic leak in general populations, there was a consistent numerical trend toward benefit, as well as significant benefit in higher-risk subgroups, particularly in low rectal anastomoses, where ICG modified the surgical strategy in approximately 10% of cases.

A major limitation was the methodological heterogeneity among the studies, which prevented the performance of a meta-analysis. Future research should standardize ICG administration and interpretation protocols, focus specifically on low rectal surgery, and evaluate the cost-effectiveness of the technology. Based on the findings, routine use of ICG cannot be recommended for all colorectal surgeries, but it appears promising in settings with a high risk of anastomotic leak.

REFERENCES

1. Soares AS, Bano S, Clancy NT, Stoyanov D, Lovat LB, Chand M. Intraoperative bowel perfusion assessment methods and their effects on anastomotic leak rates: meta-analysis. *Surgery*. 2022;172(1):69-73. doi: 10.1016/j.surg.2021.12.021.
2. De Nardi P, Elmore U, Maggi G, Maggiore R, Boni L, Cassinotti E, Fumagalli U, Gardani M, De Pascale S, Parise P, Vignali A, Rosati R. Intraoperative angiography with indocyanine green to assess anastomosis perfusion in patients undergoing laparoscopic colorectal resection: results of a multicenter randomized controlled trial. *Surg Endosc*. 2020;34(1):53-60. doi: 10.1007/s00464-019-06730-0.
3. Borg L, Portelli M, Testa L, Andrejevic P. The use of indocyanine green for colorectal anastomoses: a systematic review and meta-analysis. *Ann R Coll Surg Engl*. 2025 Jul;107(6):390-396. doi: 10.1308/rcsann.2024.0002.
4. Alekseev MV, Rybakov EG, Achkasov SI. Fluorescence angiography in colorectal surgery. *Khirurgiia (Mosk)*. 2023;(9 Vyp 2):58-62. doi: 10.17116/hirurgia202309258.
5. Kazi M, Ajith A, Bhojar A, Yelamanchi R. Fluorescence imaging in reducing anastomotic leak after left-sided colorectal resections: a systematic review and updated meta-analysis. *ANZ J Surg*. 2024;94(12):2128-2136. doi: 10.1111/ans.19201.

6. Xia S, Wu W, Luo L, Ma L, Yu L, Li Y. Indocyanine green fluorescence angiography decreases the risk of anastomotic leakage after rectal cancer surgery: a systematic review and meta-analysis. *Front Med (Lausanne)*. 2023;10:1157389. doi: 10.3389/fmed.2023.1157389.
7. Alekseev M, Rybakov E, Shelygin Y, Chernyshov S, Zarodnyuk I. A study investigating the perfusion of colorectal anastomoses using fluorescence angiography: results of the FLAG randomized trial. *Colorectal Dis*. 2020;22(9):1147-1153. doi: 10.1111/codi.15037.
8. Watanabe J, Takemasa I, Kotake M, Noura S, Kimura K, Suwa H, Tei M, Takano Y, Munakata K, Matoba S, Yamagishi S, Yasui M, Kato T, Ishibe A, Shiozawa M, Ishii Y, Yabuno T, Nitta T, Saito S, Saigusa Y, Watanabe M. Blood Perfusion Assessment by Indocyanine Green Fluorescence Imaging for Minimally Invasive Rectal Cancer Surgery (EssentiAL trial): A Randomized Clinical Trial. *Ann Surg*. 2023;278(4):e688-e694. doi: 10.1097/SLA.0000000000005907.
9. Faber RA, Meijer RPJ, Droogh DHM, Jongbloed JJ, Bijlstra OD, Boersma F, Braak JPB, Meershoek-Klein Kranenbarg E, Putter H, Holman FA, Mieog JSD, Neijenhuis PA, van Staveren E, Bloemen JG, Burger JWA, Aukema TS, Brouwers MAM, Marinelli AWKS, Westerterp M, Doornebosch PG, van der Weijde A, Bosscha K, Handgraaf HJM, Consten ECJ, Sikken DJ, Burggraaf J, Keereweer S, van der Vorst JR, Hutteman M, Peeters KCMJ, Vahrmeijer AL, Hilling DE. Indocyanine green near-infrared fluorescence bowel perfusion assessment to prevent anastomotic leakage in minimally invasive colorectal surgery (AVOID): a multicentre, randomised, controlled, phase 3 trial. *Lancet Gastroenterol Hepatol*. 2024;9(10):924-934. doi: 10.1016/S2468-1253(24)00198-5.
10. Jayne D, Croft J, Corrigan N, Quirke P, Cahill RA, Ainsworth G, Meads DM, Kirby A, Tolan D, Gordon K, Hompes R, Spinelli A, Foppa C, Wolthuis AM, D'Hoore A, Vignali A, Tilney HS, Moriarty C, Vargas-Palacios A, Young C, Kelly R, Stocken D. Intraoperative fluorescence angiography with indocyanine green to prevent anastomotic leak in rectal cancer surgery (IntAct): an unblinded randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2025;10(9):806-817. doi: 10.1016/S2468-1253(25)00101-3.

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