Original Article

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Indocyanine green fluorescence imaging in gastrointestinal surgery

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Abstract

Background: Prevention of post-operative anastomotic leak (AL) is significant challenge for surgeons, with roughly half of all AL cases linked to insufficient vascular supply, often undetectable during anastomosis. Recently, indocyanine green fluorescence (ICG) emerged as promising tool in visceral surgery due to its low cost, ease of use, wide availability, and low toxicity. In gastrointestinal surgery, ICG is primarily used for real-time intraoperative angiography, allowing surgeons to assess anastomotic stumps' perfusion before and after procedure.

Objectives: To assess efficacy of ICG as an adjunct in preventing AL.

Methods: This descriptive study conducted after ethical approval at Kathmandu Medical College Teaching Hospital from 2022 February 15 to 2023 January 30 included 111 patients enrolled via convenience sampling. During operation, surgeon used ICG fluorescence angiography on patients to determine perfusion status, which allowed for evaluation of transection line and post-anastomotic viability. Data were entered in Microsoft Excel sheet 2019 and descriptive analysis done regarding demographic data, changes in the transection line, and post-operative anastomotic leaks.

Results: Total 111 patients with age 55.41 ± 13.63 years and male-female ratio of 2:1 participated in this study. ICG use resulted in changes to proximal resection margin for five (4.5%) patients. Clinical judgment and ICG fluorescence imaging showed a difference in bowel transection line of 0.5-1.5 cm. None of the patients who underwent proximal resection margin revision with the assistance of ICG experienced post-operative anastomotic leaks.

Conclusion: ICG fluorescence can be used as an adjunct in determining the viability of anastomosis and prevent post-operative anastomosis leak.

Key words: Anastomotic leak; Indocyanine green; Surgical margin.

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INTRODUCTION

The rate of Anastomotic Leak (AL) varies depending on type of gastrointestinal anastomosis, with an ileocolic anastomosis having leak rate of 1% to 4% compared to a 0.5% to 18% colorectal or a 5% to 19% leak rate in coloanal anastomoses.[1] About half of ALs are related to insufficient vascular supply, which cannot be detected with naked eye during anastomosis.[2] Adequate perfusion is a critical factor for anastomotic healing.[3,4] Previous assessment methods of anastomosis perfusion based on color, temperature, pulsation, peristalsis, and bleeding pattern were subjective and at best, mediocre surrogates of good bowel perfusion.[5] Although proximal diverting stoma can minimise consequences of a leak, it does not reduce risk.[6]

Recently, indocyanine green fluorescence (ICG)-guided visualisation has gained predominant role in visceral surgery due to its low cost, ease of use, wide availability, and negligible toxicity. The main role of ICG in gastrointestinal surgery is in real-time intraoperative angiography, which allows for assessment of anastomotic stumps' perfusion before and after anastomosis.[7] This study describes our experience using ICG fluorescence in determining resection margin in gastrointestinal surgery and its outcome in changing risk of AL. The objective was to assess efficacy of ICG as an adjunct in preventing AL.

METHODOLOGY

A descriptive observational study was conducted on 111 patients who received bowel resection and anastomosis treatment at Kathmandu Medical College (KMC) Teaching Hospital, Sinamangal, Kathmandu, Nepal between 2022 February 15, and 2023 January 30. All patients over the age of 18 years who were undergoing bowel resection and anastomosis were included whereas patients under 18 years of age, patients who were pregnant or lactating, patients with a history of adverse reaction or allergy to ICG or Iodine, patients who were taking steroids, patients who were undergoing emergency exploratory laparotomy for peritonitis with bowel perforation were excluded from the study. A proposal was first submitted to the Institutional Review Committee of KMC and ethical approval was taken (Ref. 1001202204) before data collection. Sample size was calculated based on prevalence of colorectal malignancy needing bowel resection and anastomosis from previous studies as mentioned below and all the patient that fit the inclusion criteria were included in the study.[8]

Using the Cochrane Formula for sample size determination (n) $=(Z^2 * p * q)/e^2$. Here, $Z = 1.96$ (taking 95% confidence interval); $p = 0.046$ (4.6% prevalence of colorectal cancer in Nepal using a previous study finding);[8] $q = 1 – p = 0.954$; $e = 0.05$ (margin of error 5%). Thus, sample size $= 34.40 \approx 35$.

The study assessed the necessity for revision of resection margin during the intraoperative period using ICG fluorescence angiography and evaluated the occurrence of post-operative anastomotic leak. Preoperative physical status was graded according to the American Society of Anaesthesiologists (ASA) guidelines, and when required, preoperative contrast-enhanced computed tomography (CECT) scan images were obtained. Informed consent was obtained from all patients for the utilisation on of their data for research purposes. Before anastomosis, the primary surgeon either one YL, SR, RG, DKM, or PBT determined the bowel transection level and marked it with a tissue pen, taking into account the perfusion, proximal margin, and ability to fashion a tension-free anastomosis. Then, a bolus of 5 mg ICG was injected intravenously, followed by 10 ml of normal saline flush. The Karl Storz© light source and near-infrared compatible camera and lens (Karl Storz TM343 model ®) were used for real-time visual assessment of superficial blood flow and tissue perfusion, at the discretion of the surgeon when performing fluorescence imaging. All operating room lights were switched off during the fluorescence imaging, blinding the surgeon to his/her prior decision. The primary surgeon YL, SR, RG, DKM, or PBT determined the level of transection based on the analysis of the fluorescence angiogram on the bowel serosa. The areas of good perfusion were identified by the presence of fluorescence, while the areas with no perfusion were indicated by the absence of fluorescence, appearing dark. At the end of the procedure, the surgeon was asked whether the findings from ICG fluorescence angiogram had altered the decision to revise the resection margin. The final transection level was compared to the originally planned one, and the difference in length was measured and noted. The post-operative occurrence of AL was recorded in proforma which was entered in Microsoft Excel spread sheet (2019) and analysed in IBM SPSS Statistics for Windows, version 20 (IBM Corp., Armonk, N.Y., USA).

RESULTS

The study comprised patients with age of 55.41 ± 13.63 years, with minimum age of 18 years and maximum age of 88 years, all of whom had an ASA physical status classification of 1 or 2. Preoperative evaluation involved a combination of clinical judgment and appropriate imaging modalities such as X-ray, ultrasonography, and computed tomography scan. Preoperative resuscitation was administered to all patients as needed. All patients underwent segmental gastrointestinal resection and anastomosis for the pathology listed in the given table (Table 1). Prior to anastomosis, ICG dye was used to perform vascular angiography in all patients (Figure 1).

A total of 111 patients underwent gastrointestinal segmental resection and anastomosis, with most surgeries (58, 52.3%) being performed in the lower gastrointestinal region (Figure 2). Out of all these patients, five (4.5%) required revision surgery of the proximal resection margin based on ICG imaging.

The surgeon determined any necessary changes in the transection line based on ICG fluorescence and noted them down. Final evaluation was performed after anastomosis to confirm the anastomotic vascular angiography (Figures 3, 4).

The difference in bowel transection line determined by clinical judgment and ICG fluorescence imaging ranged from 0.5-1.5 cm in this study. Among the five (4.5%) patients who required revision of the resection margin, two (1.8%) cases were related to strangulated hernia, two (1.8%) cases were of mid rectal carcinoma undergoing anterior resection and one (0.9%) was a case of bowel ischaemia secondary to Superior Mesenteric Artery thrombosis. None of these patients experienced anastomotic leak post-operatively, and the mean duration of hospital stay was six days. Two anastomotic leaks occurred in the study, one in patient with tubercular perforation who was in septic shock post operatively and the other in a patient with SMA thrombosis where thrombus propagation is the presumed cause of the anastomotic failure.

Figure 1: Normal indocyanine green vascular angiography of distal ileum

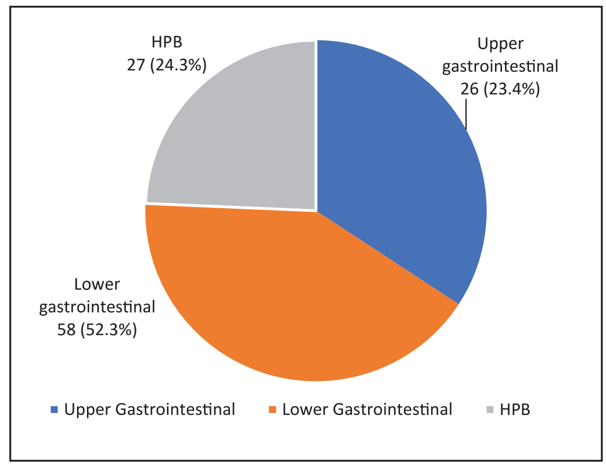

Figure 2: Disease category undergoing operative procedure

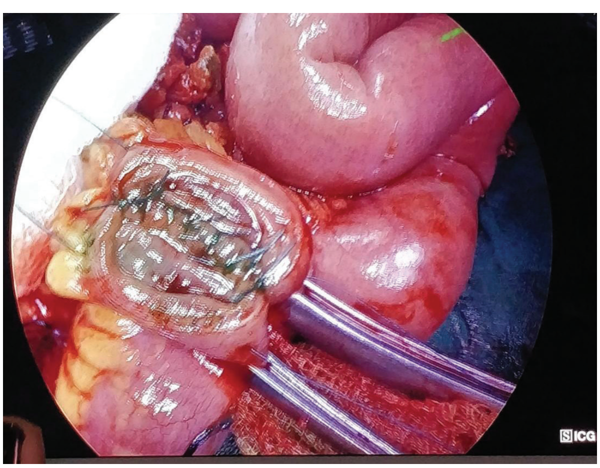

Figure 3: Anastomotic segment on white light of distal ileum

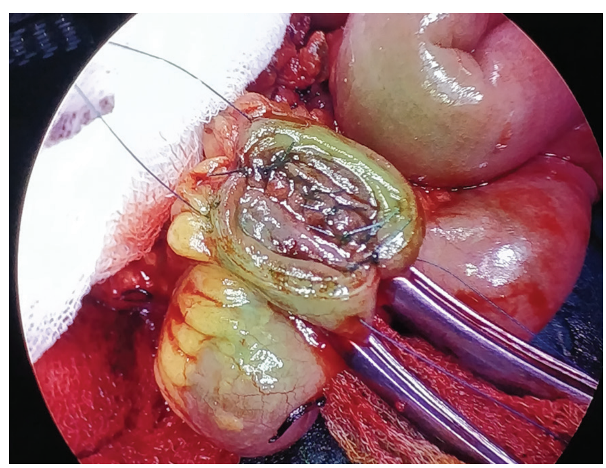

Figure 4: Anastomotic segment with indocyanine green dye on near infrared light

Table 1: Disease category and outcome

Category	Diagnosis	No of patients	Operative procedure	Revision of proximal resection margin, Number (%)	Difference In bowel transection line based on clinical judgement and ICG imaging (cm)	Post-operative anastomotic leak, Number (%)
Upper gastrointestinal	Gastric carcinoma	21	Gastro-jejunostomy or Esophago-jejunostomy	-	-	-
	Gastrointestinal stromal tumor	3	Gastro-jejunostomy	-	-	-
	Second part of duodenal perforation	2	Duodenorrhaphy with Gastro-jejunostomy with Braun anastomosis	-	-	-
Lower gastrointestinal	Strangulated ileal hernia	6	Segmental resection anastomosis	2 (1.8)	1 and 1.5 cm	-
	Traumatic jejunal perforation	5	Jejuno-jejunal resection anastomosis	-	-	-
	Traumatic ileal perforation	6	Ileocolic resection anastomosis	-	-	-
	Superior mesenteric artery thrombosis	6	Ileo-colic resection anastomosis	1 (0.9)	1.5 cm	1 (0.9)
	Diverticular perforation	2	Colo-colic resection anastomosis	-	-	-
	Intussusception	3	Ileocolic resection anastomosis	-	-	-
	Tubercular perforation	1	Ileocolic resection anastomosis	-	-	1 (0.9)
	Upper rectal carcinoma	6	Anterior resection	-	-	-
	Middle rectal carcinoma	3	Low anterior resection	2 (1.8)	0.5 and 1 cm	-
	Sigmoid carcinoma	4	Colo-colic resection anastomosis	-	0.5 cm	-
	Diverting stoma	9	Stoma reversal	-	-	-
	Acute large bowel obstruction	5	Diverting stoma	-	-	-
	Ileal gastrointestinal stromal tumor	2	Ileo-ileal resection anastomosis	-	0.5	-
Hepatopancreatobiliary	Periampullary carcinoma/carcinoma head of pancreas/ uncinate process carcinoma/distal cholangiocarcinoma	27	Whipples procedure	-	-	-

DISCUSSION

In this study, all patients' anastomotic margins were evaluated for adequate vascularity using indocyanine green dye under near-infrared fluorescence imaging. In five (4.5%) cases, the resection margin was revised based on ICG imaging. In all these cases, although the naked eye appearance showed good vascularity at the anastomotic margin, Near Infrared Fluorescence (NIR) imaging with ICG showed decreased ICG staining at the presumed anastomotic site prompting to refresh the margin. This process could have potentially prevented anastomotic failure in these cases.

The ICG is a water-soluble solution with anionic properties that contains relatively hydrophobic and tricarbocyanine molecules with a weight of 775 Da. It absorbs light between 790 and 805 nm and re-emits it with an excitation wavelength of 835 nm, which allows it to act as a fluorophore in response to near infrared irradiation.[9] When administered intravenously, ICG rapidly and extensively binds to plasma proteins with minimal leakage into the interstitium. It has a half-life of three to five minutes and is cleared by the liver in 15-20 minutes with no known metabolites. Intravenous use of ICG is generally considered to be very safe, and severe allergic reactions such as anaphylactic shock, hypotension, tachycardia, dyspnoea, or urticaria are exceedingly rare. These characteristics make ICG an excellent agent for acquiring high-quality images of the circulatory and lymphatic.[10–12] The newly developed IGFI technology enables easy implementation of intraoperative fluorescence angiography and has been utilised to evaluate real-time perfusion of the resection margin during laparoscopic surgery.[13–15] Anastomotic leakage has multifactorial cause, and these leaks have considerable effect on clinical and economic burden on the patient and health care system, as well as a predisposition to local cancer recurrence.[16–18] Numerous studies have evaluated the application of ICG fluorescence in colorectal surgery; however, the majority of them consist of case series with a limited number of participants. The use of fluorescence imaging has been documented in surgical interventions for both malignant and benign conditions, as well as different surgical techniques such as robotic colorectal surgery, transanal rectal surgery, and minimally invasive surgery.[19,20]

In a meta-analysis, ICG fluorescence has shown potential for detecting the necessity of modifying the surgical plan, expanding resection margins, or requiring revision of anastomosis. Among 555 patients in the ICG group, a change in the intended anastomotic level was made in 7.4% of cases. Generally, the decision to make changes is based on the detection of bowel hypoperfusion using fluorescence, even if the bowel appeared well-perfused on visual examination. On the other hand, ICG fluorescence can also be useful in confirming sufficient perfusion in cases where there is clinical suspicion of hypoperfusion, indicating that resection margins do not need to be extended further.[21] The exact objective measurement of acceptable or insufficient pre-anastomotic perfusion is not precisely defined, primarily due to a lack of quantifiable tissue perfusion capability in most imaging systems. Nevertheless, this problem is being addressed with some experimental studies that assess fluorescence quantification in animal models.[22] Furthermore, in a study by Sherwinter et al., a fluorescence score based on the sequence of fluorescence uptake and time of maximum excitation was used to quantify tissue perfusion at the anastomotic site.[23] Likewise, there are investigations seeking to measure fluorescence angiography, such as the study conducted by Nerup and colleagues that aimed to quantify perfusion by employing ICG in a porcine model.[24] Another study by Wada and colleagues utilised video images and constructed a time fluorescence intensity curve to measure ICG fluorescence.[25]

The limitations of this study include a small sample size study done at single centre, subjective evaluation of fluorescence intensity, and the absence of a quantitative method to measure tissue perfusion.

CONCLUSION

This study illustrates the potential utility of ICG fluorescence imaging as a promising clinical tool to reduce the incidence of anastomotic leakages in patients undergoing bowel resection for benign or malignant disease. However, there is currently a lack of published randomised controlled trials (RCTs) on the topic, and larger, well-designed RCTs are necessary to determine the efficacy of incorporating ICG fluorescence imaging into routine gastrointestinal surgery. Such studies could help determine whether the use of ICG fluorescence imaging can indeed decrease the incidence of anastomotic leakages in clinical practice.

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REFERENCES

1. McKenna NP, Bews KA, Cima RR, Crowson CS, Habermann EB. Development of a risk score to predict anastomotic leak after left-sided colectomy: Which patients warrant diversion? J Gastrointest Surg. 2020 Jan;24(1):132. [PubMed | Full Text | DOI]
2. Baiocchi GL, Guercioni G, Vettoretto N, Scabini S, Millo P, Muratore A, et al. ICG fluorescence imaging in colorectal surgery: A snapshot from the ICRAL study group. BMC Surg. 2021 Apr 10;21(1):190. [PubMed | Full Text | DOI]
3. Vignali A, Gianotti L, Braga M, Radaelli G, Malvezzi L, Di Carlo V. Altered microperfusion at the rectal stump is predictive for rectal anastomotic leak. Dis Colon Rectum. 2000 Jan;43(1):76-82. [PubMed | Full Text | DOI]
4. Sheridan WG, Lowndes RH, Young HL. Tissue oxygen tension as a predictor of colonic anastomotic healing. Dis Colon Rectum. 1987 Nov;30(11):867-71. [PubMed | Full Text | DOI]
5. Karliczek A, Harlaar NJ, Zeebregts CJ, Wiggers T, Baas PC, van Dam GM. Surgeons lack predictive accuracy for anastomotic leakage in gastrointestinal surgery. Int J Colorectal Dis. 2009 May;24(5):569-76. [PubMed | Full Text | DOI]
6. Alberts JC, Parvaiz A, Moran BJ. Predicting risk and diminishing the consequences of anastomotic dehiscence following rectal resection. Colorectal Dis. 2003 Sep;5(5):478-82. [PubMed | Full Text | DOI]
7. Jafari MD, Wexner SD, Martz JE, McLemore EC, Margolin DA, Sherwinter DA, et al. Perfusion assessment in laparoscopic left-sided/anterior resection (PILLAR II): A multi-institutional study. J Am Coll Surg. 2015 Jan;220(1):82-92. [PubMed | Full Text | DOI]
8. Shrestha G, Khanal S, Mulmi R, Sapkota G. Five-year trend of colorectal cancer incidence in B.P. Koirala Memorial Cancer Hospital of Central Nepal: A cross-sectional study. International Journal of Surgery: Global Health. 2020;3(6):e30. [Full Text]
9. Boni L, Fingerhut A, Marzorati A, Rausei S, Dionigi G, Cassinotti E. Indocyanine green fluorescence angiography during laparoscopic low anterior resection: Results of a case-matched study. Surg Endosc. 2017 Apr;31(4):1836-40. [PubMed | Full Text | DOI]
10. Alander JT, Kaartinen I, Laakso A, Pätilä T, Spillmann T, Tuchin VV, et al. A review of indocyanine green fluorescent imaging in surgery. Int J Biomed Imaging. 2012;2012:940585. [PubMed | Full Text | DOI]
11. Burnier P, Niddam J, Bosc R, Hersant B, Meningaud JP. Indocyanine green applications in plastic surgery: A review of the literature. J Plast Reconstr Aesthet Surg. 2017;70(6):814-27. [PubMed | Full Text | DOI]
12. Aslim EJ, Lee FJ, Gan VHL. The utility of intraoperative near infrared fluorescence (NIR) imaging with indocyanine green (icg) for the assessment of kidney allograft perfusion. J Transplant. 2018 Aug 19;2018:6703056. [PubMed | Full Text | DOI]
13. Mizrahi I, Abu-Gazala M, Rickles AS, Fernandez LM, Petrucci A, Wolf J, et al. Indocyanine green fluorescence angiography during low anterior resection for low rectal cancer: Results of a comparative cohort study. Tech Coloproctol. 2018 Jul;22(7):535-40. [PubMed | Full Text | DOI]
14. Son GM, Kwon MS, Kim Y, Kim J, Kim SH, Lee JW. Quantitative analysis of colon perfusion pattern using indocyanine green (ICG) angiography in laparoscopic colorectal surgery. Surg Endosc. 2019 May;33(5):1640-9. [PubMed | Full Text | DOI]
15. Watanabe J, Ota M, Suwa Y, Suzuki S, Suwa H, Momiyama M, et al. Evaluation of the intestinal blood flow near the rectosigmoid junction using the indocyanine green fluorescence method in a colorectal cancer surgery. Int J Colorectal Dis. 2015 Mar;30(3):329-35. [PubMed | Full Text | DOI]
16. Hyman NH, Osler T, Cataldo P, Burns EH, Shackford SR. Anastomotic leaks after bowel resection: what does peer review teach us about the relationship to postoperative mortality? J Am Coll Surg. 2009 Jan;208(1):48-52. [PubMed | Full Text | DOI]
17. Choi HK, Law WL, Ho JW. Leakage after resection and intraperitoneal anastomosis for colorectal malignancy: analysis of risk factors. Dis Colon Rectum. 2006 Nov;49(11):1719-25. [PubMed | Full Text | DOI]
18. Chadi SA, Fingerhut A, Berho M, DeMeester SR, Fleshman JW, Hyman NH, et al. Emerging trends in the etiology, prevention, and treatment of gastrointestinal anastomotic leakage. J Gastrointest Surg. 2016 Dec;20(12):2035-51. [PubMed | Full Text | DOI]
19. Hellan M, Spinoglio G, Pigazzi A, Lagares-Garcia JA. The influence of fluorescence imaging on the location of bowel transection during robotic left-sided colorectal surgery. Surg Endosc. 2014 May;28(5):1695-702. [PubMed | Full Text | DOI]
20. Bae SU, Min BS, Kim NK. Robotic low ligation of the inferior mesenteric artery for rectal cancer using the firefly technique. Yonsei Med J. 2015 Jul;56(4):1028-35. [PubMed | Full Text | DOI]

21. Blanco-Colino R, Espin-Basany E. Intraoperative use of ICG fluorescence imaging to reduce the risk of anastomotic leakage in colorectal surgery: a systematic review and meta-analysis. Tech Coloproctol. 2018 Jan;22(1):15-23. [PubMed | Full Text | DOI]
22. Diana M, Agnus V, Halvax P, Liu YY, Dallemagne B, Schlagowski AI, et al. Intraoperative fluorescence-based enhanced reality laparoscopic real-time imaging to assess bowel perfusion at the anastomotic site in an experimental model. Br J Surg. 2015 Jan;102(2):e169-76. [PubMed | Full Text | DOI]
23. Sherwinter DA, Gallagher J, Donkar T. Intra-operative transanal near infrared imaging of colorectal anastomotic perfusion: A feasibility study. Colorectal Dis. 2013 Jan;15(1):91-6. [PubMed | Full Text | DOI]
24. Nerup N, Andersen HS, Ambrus R, Strandby RB, Svendsen MBS, Madsen MH, et al. Quantification of fluorescence angiography in a porcine model. Langenbecks Arch Surg. 2017 Jun;402(4):655-62. [PubMed | Full Text | DOI]
25. Wada T, Kawada K, Takahashi R, Yoshitomi M, Hida K, Hasegawa S, et al. ICG fluorescence imaging for quantitative evaluation of colonic perfusion in laparoscopic colorectal surgery. Surg Endosc. 2017 Oct;31(10):4184. [PubMed | Full Text | DOI]