CHAPTER 9
Surgical treatment: fluorescence-guided colorectal surgery

With the collaboration of Alejandro Moreira Grecco, MD, PhD, MAAC, MSACP

Fluorescence, particularly with indocyanine green (ICG), has emerged as a tool that improves the safety and precision of colorectal surgical procedures. It allows for intraoperative identification of anatomical structures and assessment of tissue perfusion in real time, guiding resections and anastomoses, with a potential reduction in postoperative complications.

In fluorescence-guided surgery, a fluorophore (e.g. ICG) is used and evaluated with a specific optical system with an infrared light source and a camera specially adapted to capture the fluorescent signal. The signal is processed by different computer programs that create an image that is evaluated in real time by the surgeon.

Particularly in colorectal surgery, fluorescence is used for the assessment of intestinal perfusion, the localization of lesions with lymphatic mapping, and the identification of the ureters.

Assessment of intestinal perfusión

Fluorescent angiography (FA) is an additional procedure performed during colorectal surgery to achieve real-time assessment of perfusion and blood flow in a bowel segment. It is applicable during conventional, laparoscopic, or robotic surgery.[1–3]

Anastomotic dehiscence is one of the most serious and feared complications of colorectal surgery.[4] To create a safe anastomosis, it is recommended that it be well perfused, not rotated, and without tension.[5] The use of fluorescence allows the perfusion of the bowel ends to be assessed to create anastomoses with optimal perfusion and greater chances of adequate healing, without fistulization.

In 4% to 27% of cases, FA results in a change of the chosen site for the anastomosis.[6-9] In a multicenter study in the USA that included 139 patients, a change in the plan occurred in 11 (7.9%), which did not significantly modify the operative time (with ICG: 214.9 ± 67.5 min vs. without ICG 228.9 ± 66.1 min).[10]

A national case series reported a change in management in 11% of patients, with revision of the anastomosis site in 8.7%, taking a short extra operative time.[11]

An average of 2 cm of proximal colon resection has been reported after FA.[6] This change in intraoperative management is reflected in the lower incidence of fistulas in series using FA.[12] Degget et al.[13] performed a systematic review in which series using FA showed an anastomotic leak rate of 3.8%, compared with 7.6% in series not using FA. The use of FA decreases the risk of fistulas but does not eliminate it, because other factors intervene in their development.

The advantage of using angiography is even more evident in the case of rectal surgeries, in which the colon descended after mobilization of the splenic flexure is most often irrigated only through the vascular arcade connected to the middle colic artery.

In the meta-analysis by Blanco Colino et al.,14 when all colorectal surgeries were analyzed, the use of AF was associated with an OR of 0.5 for the development of anastomotic dehiscence. However, when only rectal surgeries were evaluated, the OR was 0.19, equivalent to an 81% reduction in the risk of colorectal anastomotic dehiscence.

Despite presenting a trend, not all studies found a statistically significant difference for fistula prevention. In this regard, De Nardi et al.[15] reported a rate of 5% in the group with fluorescence compared to 9% in the group without fluorescence, without reaching statistical significance. However, other groups found a difference. The EssentiAL study, in 850 randomized patients, reported an anastomotic dehiscence rate of 7.6% when FA was used vs. 11.8% when it was not used. (RR 0.645; $p = 0.041$).[16] When fistulas requiring some intervention for resolution were analyzed, the difference was even more significant (4.7 vs. 8.2%; $p = 0.044$).[17]

Quantification of the intensity of the fluorescent signal, as well as the speed at which perfusion occurs, allows for an objective measurement of intestinal perfusion, identifying risk groups for performing an anastomosis.[18]

Lesion marking and fluorescent lymphography

Another application of fluorescence in colorectal surgery is lesion marking and fluorescent lymphography. Injection of ICG into the submucosa or subserosa of the colon migrates and produces a real-time lymphography with the possibility of visualizing lymphatic vessels and nodes. In this way, the sentinel node and the lymphatic drainage territory of the intestinal segment under study can be identified.[19,20]

Endoscopic marking prior to or during surgery allows the location of the lesion in a similar way to what happens with a tattoo with Indian ink, but with better visualization.21 The migration of the contrast occurs in an average time of 4-9 minutes and does not progress after 25 minutes of its application.[22,23]

Identification of the sentinel node is possible in 80 to 98% of cases.[22] Aberrant drainage is detected in 25% of patients, especially in lesions located near colon flexures. Detection of aberrant drainage allows the area of previously unsuspected drainage to be included in lymph node dissection and can therefore modify the choice of the central vessel to be ligated.[24,25] Fluorescent lymphography has a sensitivity of 78% and a specificity of 84% for determining the territory of lymphatic drainage.[26]

During rectal surgery, fluorescent lymphography guides the fascial plane of the TME, improves mesorectal and lateral lymph node dissection, and reduces residual mesorectal tissue.[27]

Some factors may affect the results of fluorescent lymphography, such as the presence of a large T3-4 tumor, the use of an inadequate concentration of ICG, the presence of a thick mesocolon, and the use of rigid needles.[10]

Identification of the ureters

An additional application of fluorescence in colorectal surgery includes the identification of the ureters, for which different compounds with urinary excretion have been described.[28] ICG circulates in the bloodstream bound to albumin, so it is not filtered by the kidneys and is not excreted in the urine. However, low-weight compounds with affinity for ICG are being developed to achieve urinary excretion.[29] Currently, visualization of the ureters with ICG requires injection of the dye into the ureter by cystoscopy. This maneuver has resulted in a decrease in operating time in colorectal surgeries by minimizing the time spent searching for the ureter.[30]

In summary, fluorescence-guided surgery offers the possibility of visualizing structures and phenomena that were previously unidentifiable and improves the surgeon's ability to make intraoperative decisions. Although fluorescence does not completely eliminate the risks of colorectal surgery, its systematic use is associated with a significant improvement in outcomes, in particular a reduction in the incidence of anastomotic dehiscence.

REFERENCES

1. Marano A, Priora F, Lenti LM, et al. Application of fluorescence in robotic general surgery: review of the literature and state of the art. *World J Surg*. 2013;37:2800–11.
2. Boni L, Fingerhut A, Marzorati A, et al. Indocyanine green fluorescence angiography during laparoscopic low anterior resection: results of a case-matched study. *Surg Endosc*. 2017;31:1836–40.
3. Kawada K, Hasegawa S, Wada T, et al. Evaluation of intestinal perfusion by ICG fluorescence imaging in laparoscopic colorectal surgery with DST anastomosis. *Surg Endosc*. 2017;31:1061–69.
4. Kingham TP, Pachter HL. Colonic anastomotic leak: risk factors, diagnosis, and treatment. *J Am Coll Surg*. 2009;208:269–78.
5. Hyman N, Manchester TL, Osler T, et al. Anastomotic leaks after intestinal anastomosis: it's later than you think. *Ann Surg*. 2007;245:254–58.
6. Wada T, Kawada K, Hoshino N, et al. The effects of intraoperative ICG fluorescence angiography in laparoscopic low anterior resection: a propensity score-matched study. *Int J Clin Oncol*. 2019;24:394–402.
7. Boni L, David G, Dionigi G, et al. Indocyanine green-enhanced fluorescence to assess bowel perfusion during laparoscopic colorectal resection. *Surg Endosc*. 2016;30:2736–42.
8. Watanabe J, Ishibe A, Suwa Y, et al. Indocyanine green fluorescence imaging to reduce the risk of anastomotic leakage in laparoscopic low anterior resection for rectal cancer: a propensity score-matched cohort study. *Surg Endosc*. 2020;34:202–8.
9. Nishigori N, Koyama F, Nakagawa T, et al. Visualization of lymph/blood flow in laparoscopic colorectal cancer surgery by ICG fluorescence imaging (Lap-IGFI). *Ann Surg Oncol*. 2016;23 Suppl 2:S266–74.
10. Jafari MD, Wexner SD, Martz JE, et al. Perfusion assessment in laparoscopic left-sided/anterior resection (PILLAR II): a multi-institutional study. *J Am Coll Surg*. 2015;220:82–92.e1.
11. Moreira Grecco A, Zapata G, Dip FD, et al. Utilidad de la angiografía fluorescente en la cirugía colorrectal. *Rev Argent Cir*. 2021;112:508–16.
12. Kudszus S, Roesel C, Schachtrupp A, et al. Intraoperative laser fluorescence angiography in colorectal surgery: a noninvasive analysis to reduce the rate of anastomotic leakage. *Langenbecks Arch Surg*. 2010;395:1025–30.
13. Degett TH, Andersen HS, Gögenur I. Indocyanine green fluorescence angiography for intraoperative assessment of gastrointestinal anastomotic perfusion: a systematic review of clinical trials. *Langenbecks Arch Surg*. 2016;401:767–75.
14. 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;22:15–23.
15. De Nardi P, Elmore U, Maggi G, et al. 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;34:53–60.
16. Watanabe J, Takemasa I, Kotake M, et al. Blood perfusion assessment by indocyanine green fluorescence imaging for minimally invasive rectal cancer surgery (Essential Trial): a randomized clinical trial. *Ann Surg*. 2023;278:e688–94.
17. Son GM, Kwon MS, Kim Y, et al. Quantitative analysis of colon perfusion pattern using indocyanine green (ICG) angiography in laparoscopic colorectal surgery. *Surg Endosc*. 2019;33:1640–49.
18. Seeliger B, Barberio M, D'Urso A, et al. Fluorescence in rectal cancer surgery. *Ann Laparosc Endosc Surg*. 2018;3:4.
19. Cahill RA, Anderson M, Wang LM, et al. Near-infrared (NIR) laparoscopy for intraoperative lymphatic road-mapping and sentinel node identification during definitive surgical resection of early-stage colorectal neoplasia. *Surg Endosc*. 2012;26:197–204.
20. Park JH, Moon HS, Kwon IS, et al. Usefulness of colonic tattooing using indocyanine green in patients with colorectal tumors. *World J Clin Cases*. 2018;6:632–40.
21. Nagata J, Fukunaga Y, Akiyoshi T, et al. colonic marking with near-infrared, light-emitting, diode-activated indocyanine green for laparoscopic colorectal surgery. *Dis Colon Rectum*. 2016;59:e14–8.
22. Chand M, Keller DS, Joshi HM, et al. Feasibility of fluorescence lymph node imaging in colon cancer: FLICC. *Tech Coloproctol*. 2018;22:271–77.
23. Currie AC, Brigic A, Thomas-Gibson S, et al. A pilot study to assess near infrared laparoscopy with indocyanine green (ICG) for intraoperative sentinel lymph node mapping in early colon cancer. *Eur J Surg Oncol*. 2017;43:2044–51.
24. Watanabe J, Ota M, Suwa Y, et al. Evaluation of lymph flow patterns in splenic flexural colon cancers using laparoscopic real-time indocyanine green fluorescence imaging. *Int J Colorectal Dis*. 2017;32:201–7.
25. Watanabe J, Ota M, Suwa Y, et al. Real-Time indocyanine green fluorescence imaging-guided complete mesocolic excision in laparoscopic flexural colon cancer surgery. *Dis Colon Rectum*. 2016;59:701–5.
26. Emile SH, Elfeki H, Shalaby M, et al. Sensitivity and specificity of indocyanine green near-infrared fluorescence imaging in detection of metastatic lymph nodes in colorectal cancer: Systematic review and meta-analysis. *J Surg Oncol*. 2017;116:730–40.
27. Ismael G, Al Furajji H, Cahill RA. Near-infrared laparoscopic fluorescence to guide fascial plane identification in total mesorectal excision for rectal cancer: A Video Vignette. *Colorectal Dis*. 2015;17 Suppl 3:36.
28. Dip FD, Moreira Grecco AD, Nguyen D, et al. Ureter identification using methylene blue and fluorescein In: Fluorescence Imaging for Surgeons. Springer International Publishing, Cham, 2015, pp 327–32.
29. Schols RM, Bouvy ND, van Dam RM, et al. Advanced intraoperative imaging methods for laparoscopic anatomy navigation: an overview. *Surg Endosc*. 2013;27:1851–59.
30. Soriano CR, Cheng RR, Corman JM, et al. Feasibility of injected indocyanine green for ureteral identification during robotic left-sided colorectal resections. *Am J Surg*. 2022;223:14–20.