Objectively Evaluating Anastomotic Perfusion in Colorectal Surgery - A Two Year Experience with Intraoperative Indocyanine Green Fluorescence Angiography

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Introduction

An anastomotic leak is a devastating complication for both the patient and the surgeon, leading to an increased length of stay,[1] higher local recurrence,[2] greater cost and increased mortality.[3] Leak rates in colorectal surgery range from 2.4% to 19%.[1] Several tenets must be followed to prevent an anastomotic leak: aseptic technique with gentle and careful dissection, tension-free anastomosis, precise placement of sutures, appropriate staple height, and brisk blood flow.[4] Proper blood supply is assured through various subjective measures, which include palpating mesenteric pulses, assessing cut edges for bleeding, and evaluating the color of the bowel. Other clinical adjuncts include Doppler signals, fluorescein injection, and indocyanine green fluorescence.

Indocyanine green (ICG) fluorescence angiography is a dynamic tool that assesses blood flow intraoperatively, thus accompanying the surgeon's clinical judgment of tissue perfusion. Its use has been demonstrated in numerous other fields, including ophthalmology, plastic and reconstructive surgery, as well as head and neck surgery.[5] Limited studies have only recently described its utilization in colon and rectal surgery.

The SPY Elite Intraoperative Perfusion Assessment System (Novadaq Technologies Inc., Bonita Springs, FL) is a tool that uses indocyanine green fluorescence angiography for visual assessment of blood flow. This system has been used in plastic, micro-, reconstructive, gastrointestinal and cardiovascular procedures to subjectively measure tissue perfusion. The SPY-Q software accompanied with this system, however, provides an absolute value and an objective measurement on a 0-256 gray scale. This number represents differences between ICG fluorescence intensity and in theory perfusion. This tool excels in its ability to provide an objective measurement to what was

once a subjective assessment. A segment of bowel may seem well vascularized to one surgeon while it may appear borderline or under-perfused to another. The SPY Elite's absolute numbers can potentially provide an objective cutoff value at which perfusion is deemed satisfactory.

The purpose of this study is to describe a 29-month experience at a single institution using the SPY technology and SPY-Q software to objectively assess bowel perfusion in colorectal anastomoses.

Materials and Methods

This study represents a single institution case series of 176 consecutive uses of the SPY Elite Imaging System (Novadaq Technologies Inc., Bonita Springs, FL) for colorectal anastomoses. All operations were done by two fellowship trained, board certified colorectal surgeons at Monmouth Medical Center in Long Branch, New Jersey. The SPY was utilized in all cases starting in June 2013 continuing through November 2015. The data was extracted from a prospective database of all cases. IRB approval was obtained and there was no funding involved.

The SPY imaging was used in an extracorporeal setting to assess the proximal and distal ends of the intestine for all procedures except low anterior resections (LAR). Since LAR anastomoses are performed intracorporeal, only the proximal ends of the anastomoses were assessed. After injection of the ICG by the anesthesiologist, the bowel was visualized with the SPY imaging system. Four random points near the terminal segment of intestine were analyzed for the absolute fluorescence number on a gray-scale from 0-256. The lowest absolute value was used in data analysis for each anastomosis as

this represents the theoretical least perfused or weakest anastomotic area. For each group of colon resections, the mean absolute value was calculated as shown in Table 1.

As the goal was to evaluate the use of the SPY for colorectal anastomoses and effect on patient care, the following data points were reviewed: patient demographics including age and sex, operation and indication for surgery. The ICG absolute numbers were recorded for each operation, along with any alteration to the location of the anastomosis during surgery and any complications. Complications included anastomotic leaks and strictures. One or more of the following diagnosed an anastomotic leak: clinical signs of sepsis and peritonitis, nature of drain fluid or wound discharge, and radiological findings of perianastomotic inflammation or free fluid. A stricture was diagnosed by obstructive symptoms and confirmed with endoscopic evaluation. Of note, the splenic flexure was mobilized in all LARs with ligation of the inferior mesenteric artery. Additionally, two leak tests (air and betadine) were performed in LARs to assess the anastomosis.

Results

Of the 176 cases, a total of 93 resections were done for malignant disease, while 83 were done for benign conditions. The various operations are detailed in Table 1, with the overwhelming majority of resections being LARs (60%).

Table 1.

Operation	#	Mean ICG Colon	Mean ICG Ileum	Alterations	Leak	Stenosis
Ileocolic	8	84	92	0	0	0
Transverse	2	52		0	0	0
Right	35	88	88	0	2	0

Extended Right	6	85	130	1	0	0
Left	10	90		0	0	0
Extended Left	1	78		0	0	0
Sigmoid	2	60		0	0	0
LAR	105	68		10	0	3
APR	1	74		0	0	0
Subtotal	2	73		0	0	0
Reversal ostomy	4	80	79	0	0	0

LAR, low anterior resection; APR, abdominoperineal resection

The lowest ICG reading documented was 20, which was for a patient who had a laparoscopic right colectomy done for an adenoma. Although the absolute number was low, the bowel appeared healthy and pink with bleeding cut edges. Decision was made to create the anastomosis at this site and the patient did well with no postoperative complications. The mean ICG absolute values for all of the colon resections was greater than 51.

As noted in Table 1, there were eleven (6.3%) alterations for low ICG readings at the anastomosis. Ten of these readings were from the proximal portion of an LAR while one was from the proximal portion of an extended right colectomy. The numbers ranged in the teens to 30s before alteration and increased to a range of 50s to 100s after additional proximal bowel was resected. There were no complications in any of these patients.

Two patients (1.1%) developed anastomotic leaks. The first was a laparoscopic right colectomy for adenocarcinoma in a patient with multiple comorbidities and

intraabdominal adhesions. SPY values ranged from 50-100. The patient was diagnosed with an anastomotic leak on return to the hospital 2.5 weeks later and died of sepsis despite operative intervention. The second case was also a laparoscopic right colectomy for adenocarcinoma. On postoperative day four the patient was found to have a leak on CT scan and underwent re-resection with creation of a new anastomosis. The remaining postoperative period was uneventful and the patient was discharged six days later. There were three cases (1.7%) of anastomotic strictures involving LARs with ICG readings of 55-75, 45-62 and 44-46.

Discussion

Kingham and Pachter report a colorectal anastomotic leak rate between 1% to 30% in the literature with an acceptable leak rate ranging from 3% to 6% among experienced colorectal surgeons.[1] The ensuing morbidity and mortality has multiple implications, including longer length of stay, higher costs and adverse effects on cancer recurrence.[1] In a prospective study of patients who underwent colorectal resection between 1996-2004, 25 out of 1417 patients (1.8%) had an anastomotic leak.[6] Comparing patients who leaked versus no leak, length of hospital stay was 28 days versus 10 days and mortality rate was 32% vs 4%, respectively.[6] It is evident that leaks have devastating consequences and prevention is the utmost importance among surgeons.

Clinical judgment is still the most important element utilized by surgeons to avoid anastomotic leaks. Prospective studies have shown that assessing active bleeding at cut edges, palpating pulses in the mesentery and evaluating the color of the bowel lack predictive accuracy and clinical risk assessment by the surgeon has

low predictive value for developing an anastomotic dehiscence.[7] Other adjuncts have been utilized including Doppler, fluorescein using UV Woods lamp and indocyanine green (ICG) fluorescence. ICG is an ideal molecule to use intraoperatively as it binds strongly to plasma proteins causing it to remain in the intravascular space. Its short half-life of three to five minutes allows for rapid clearance and repeated usage in the same surgery. Furthermore, this molecule has an excellent safety profile with reported anaphylactic reactions as very rare.[5]

Spy Elite System utilizes ICG fluorescence to enable visualization of arterial inflow, venous return and tissue perfusion intraoperatively. As an adjunctive tool, the Spy System is indicated for creating fluorescence images for visual assessment of blood flow in plastic, micro-, reconstructive and gastrointestinal and cardiovascular procedures.[5] In respect to colorectal surgery, there have been several studies examining the utility of ICG fluorescence angiography. Kudszus et al. used IC View (Pulsion Medical Systems AG, Munich, Germany), an intraoperative laser fluorescence angiography (LFA) system to assess bowel perfusion at anastomotic site. The authors conducted a matched control retrospective study (n = 402) comparing patients who underwent colorectal resections without laser fluorescence angiography to patients who underwent colectomies with LFA. The control group had an anastomotic leak rate of 7.5% compared to 3.5% in the LFA group. Moreoever, the study revealed a significantly reduced hospital stay in the LFA group.[8]

Near-infrared fluorescence angiography (PinPoint System, NOVADAQ, Canada) is another system that uses ICG during laparoscopic colorectal surgery and

has been proven to be feasible and reproducible in several studies. Ris et al. analyzed 30 consecutive colorectal resections using this system: a diverting ostomy was avoided in three out of six patients in part of because of the confidence imparted by the perfusion angiogram and no recorded anastomotic leaks.[9] The PILLAR II trial, a prospective, multi-centered clinical trial, evaluated the feasibility and utility of ICG fluorescence angiography (PinPoint) for intraoperative perfusion assessment as well. A total of 139 left colectomies and low anterior resections were analyzed with fluorescence angiography changing surgical plans in 11 of them. The anastomotic leak rate was 1.4% (n=2). There were no leaks in the 11 cases that had alterations. The authors concluded that PinPoint is a safe and feasible tool for intraoperative assessment of tissue perfusion during colorectal resection.[10]

In a case-matched retrospective study conducted by Kin et al., the authors sought to determine whether the use of intraoperative laser fluorescence angiography (SPY Imaging System, Novadaq Technologies Inc, Bonita Springs, FL) affected the anastomotic leak rate in colorectal resections. One hundred seventy three pairs were analyzed and the anastomotic leak rate was comparable in patients in whom intraoperative angiography had been used and those in whom it had not been used (7.5% versus 6.4%, p=0.67). Eight patients (4.6%) underwent additional colon resection secondary to the appearance of colon on angiography. One anastomotic leak was recorded in this subset of patients. The authors concluded that the benefit of intraoperative fluorescence angiography is equivocal as their data revealed no association with decreased rates of leaks; however, it did alter surgical management in several cases.[11]

Lastly, Boni et al. used fluorescence angiography (KARL STORZ GmbH & Co. KG, Tuttlingen, Germany) intraoperatively to assess colonic perfusion prior to and after completion of the anastomosis in colorectal resections. A total of 107 patients were included in the study with 4 cases having alterations in the transection point based on fluorescence intensity. None of these patients had a leak.[12]

The abovementioned studies all utilize ICG fluorescence in a qualitative manner. Although it is an adjunct to clinical judgment it still has a subjective component when assessing the intensity of fluorescence. The Spy Elite System includes Spy software that allows for quantification of perfusion by assigning numeric values of intensity of fluorescence. As stated in a previous study conducted at this institution the utility of these values remains to be determined and studies are scarce.[13] In colorectal surgery, Foppa et al. conducted a prospective study to describe the impact of intraoperative ICG angiography for small bowel ischemia and left colon resections. ICG angiography played a role in four out of 160 cases. The authors concluded that in cases of acute small bowel ischemia, resection is not warranted unless absolute values are below 19. In left colon resections, the recommended absolute unit for resection is less than 18.[14]

In this series, the authors utilized the absolute value to quantify bowel perfusion in 176 patients who underwent colorectal surgery. To the best of the authors' knowledge this is the largest study to date to examine the absolute value of the Spy Elite System in colorectal surgery. There were 93 resections done for malignant disease and 83 resections performed for benign disease. Complications included two anastomotic leaks (1.1%) and three stenoses (1.7%). One anastomotic

leak resulted in a mortality from sepsis. There were a total of eleven operations that required additional proximal resections due to low ICG readings (6.3%). Hypothetically, it is interesting to note that if these patients suffered leaks, the overall leak rate would have been 7.4%. The mean ICG absolute reading for all cases was greater than 51.

Although this study did not control for the use of the SPY, it may be another checkpoint to evaluate the anastomosis during surgery. Adding another metric to anastomotic perfusion has resulted in a very low leak rate of 1.1% over 176 cases in 29 months. Without controlling for only the spy versus other previously used factors, the authors cannot assign direct correlation to the absolute numbers themselves but this additional step seems to add benefit to an already low anastomotic leak rate.

There are several limitations in this study. First, the case size is small, albeit the largest available. Furthermore, although it is prospective in nature, it is not randomized and provides no control group. Lastly, the surgeons perform two leak tests (betadine and air) to assess the anastomosis in LARs, which may be confounding variables.

This study represents a 29-month experience at a single institution using the SPY technology in colorectal surgery. To date this the largest collection of data using SPY to objectively assess bowel perfusion in creating an anastomosis. The statistical significance of these values in relation to perfusion and anastomotic leaks has yet to be established in the literature. To determine these values randomized control trials are required.

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