Mesenteric Vascular Evaluation with Pre-operative Multidetector Computed Tomographic Angiography and Intraoperative Indocyanine Green Angiography to Reduce Anastomotic Leaks after Minimally Invasive Surgery for Colorectal Cancer

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ABSTRACT

Background: The aim of this prospective study was to determine the effect of mesenteric vascular evaluation using pre-operative multidetector computed tomography angiography (MDCTA) and intraoperative indocyanine green (ICG) angiography on reducing the anastomotic leak rate of colorectal cancer patients undergoing minimally invasive resection.

Methods: Twenty-seven consecutive patients with colorectal cancer were studied, 18 males and 9 females, average age 69.1 ± 3.9 years. All patients underwent pre-operative mesenteric vascular evaluation using MDCTA with three-dimensional (3D) reconstruction and intraoperative evaluation of perfusion using ICG angiography.

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Twelve patients underwent laparoscopic resection (Olympus Visera Elite II OTV-S200) and 15 patients underwent robotic resection (DaVinci Si). Colorectal resection lines and anastomoses were guided by intraoperative ICG perfusion. Postoperative anastomotic leaks were assessed.

Results: Pre-operative MDCTA 3D reconstructions defined the left colic and sigmoid artery anatomy and guided operative planning. The intraoperative ICG angiography resulted in a change of the planned lines of resection in seven patients (26%). The rate of postoperative anastomotic leaks in this study was 0% (0/27), compared to a leak rate of 6.8% at our institution in the preceding two years.

Conclusion: Pre-operative evaluation of mesenteric vascular anatomy using MDCTA with 3D reconstruction and intraoperative evaluation of perfusion using ICG angiography were found to be technically feasible and safe. An appropriately designed study should be undertaken to prove whether it was truly effective at reducing the postoperative anastomotic leak rate in colorectal cancer patients undergoing minimally invasive resection at our institution.

Key Words: Colorectal cancer, Colorectal surgery, Minimally invasive surgical procedures, Anastomotic leak, Computed tomography angiography, Fluorescein angiography.

INTRODUCTION

Colorectal cancer is the third most common malignancy and the second most common cause of cancer mortality, responsible for about 9.2% of all cancer related deaths.[1] Laparoscopic surgery for colorectal cancer was established in the late 1990s and early 2000s, with several randomized controlled trials finding that laparoscopic colorectal surgery had similar oncologic outcomes to open surgery, and

patients benefitted from reduced trauma and experienced quicker recovery.[2–6] Robotic surgery for colorectal cancer followed shortly thereafter, with reports demonstrating that robotic surgery was technically feasible, safe, and had similar outcomes compared to laparoscopic approaches.[7–9] Yet, neither laparoscopic nor robotic approaches to colorectal cancer significantly improved the rate of postoperative anastomotic leakage (AL), one of the most devastating complications of colorectal surgery. AL is associated with significantly increased morbidity, mortality, and cost of treatment.[10,11] One technical factor known to contribute to AL is insufficient blood supply at the anastomosis.[12] Pre-operative mesenteric vascular evaluation using multidetector computed tomography angiography (MDCTA) and intraoperative fluorescent angiography using indocyanine green (ICG) are being studied for their ability to improve perfusion at the anastomosis and reduce AL rates. Cutting of the marginal vessel and perfusion status assessment by a visual grading system, visible light spectroscopy for serosal oxygen saturation, and multispectral imaging for tissue oxygen saturation are other methods that have been used throughout the years.[13–15]

At our institution over the past two years, anastomotic leak rates following minimally invasive colorectal surgery for cancer have been 6.8%. The purpose of this study was to determine the effect of introducing routine use of pre-operative vascular anatomy evaluation using MDCTA and intraoperative vascular evaluation using ICG angiography on the anastomotic leak rate of colorectal cancer patients undergoing minimally invasive resection.

MATERIALS AND METHODS

Consecutive adults (aged >18 years) undergoing curative-intent surgery for colorectal cancer through a laparoscopic or robotic approach were included in this study. All patients that underwent laparoscopic/robotic surgery, even the converted ones, were included. There were no excluded cases. Allergy to iodine water-soluble contrast and hyperthyroidism were considered exclusion criteria. Informed consent was obtained from all patients as ICG is not on the list of approved drugs in our country.

For pre-operative evaluation of mesenteric vascular anatomy, MDCTA was performed on all patients using a 128 slice CT (Siemens Somatom Perspective CT Scanner, Siemens Medical Solutions USA) with 50 ml Iomeron (400 mg/ml, Bracco Imaging S.p.A., Italy) as contrast agent. The data from the MDCTA was loaded onto a SECTRA 3D table for virtual dissections, and mesenteric arterial anatomy was studied using 3D models. This protocol was introduced in our routine work up more than four years ago.

For intraoperative ICG angiography, 25 mg powdered Verdye (Renew Pharmaceuticals Ltd, Germany) was dissolved in 10 ml sterile water. During surgery, this was injected intravenously in three divided doses, with 10 ml of saline injected after each dose. The first dose (4 ml) was injected at the start of surgery to visualize the vascular pedicles. After dissection and bowel resection, the second dose (4 ml) was injected to assess the perfusion of the remaining bowel. If insufficient perfusion was noted at a transection line, then the transection line was modified accordingly. The third dose of ICG (2 ml) was given after creation of the anastomosis to look for potential ischemic zones at the anastomosis. After the first five cases, it was determined that the third dose of ICG was unnecessary, and it was omitted from subsequent cases. We used the Olympus Visera Elite II OTV-S200 system for the laparoscopic procedures (n = 12) and the DaVinci Si robotic system equipped with Firefly for the robotic procedures (n = 15).

The following data were collected prospectively: patient age and sex, tumor characteristics, use of pre-operative chemoradiotherapy, pre-operative mesenteric vascular anatomy based on MDCTA 3D reconstructions, surgical approach (laparoscopic/robotic), mesorectal excision, total mesorectal excision (TME), transanal total mesorectal excision (TaTME), or partial mesorectal excision (PME), conversion from laparoscopic/robotic to open surgery, anatomic resection performed (right colectomy, left colectomy, sigmoid colectomy, total colectomy, or proximal/middle/distal rectal resections), high or low tie of inferior mesenteric artery (IMA) branches, modification of the transection line based on intraoperative ICG angiography, quality of TME/PME/TaTME, positive pathologic resection margins, postoperative anastomotic leaks, and hospital length of stay.

This is a pilot study for routine ICG use to test the feasibility and outcomes in our setting.

RESULTS

Twenty-seven consecutive patients were studied, 18 males and 9 females, average age 69.1 ± 3.9 years (43 – 84 years). Seven patients had colon cancer (two right colon, one descending colon, four sigmoid colon). Twenty patients had rectal cancer (8 proximal rectum, >12 cm from anus; 8 mid rectum, 6 – 12 cm from anus; and 4 distal rectum, < 6 cm from anus).[16] Eight of the 20 patients with

rectal cancer underwent pre-operative chemoradiotherapy. Patient characteristics are summarized in **Table 1**.

Pre-operative MDCTA 3D reconstructions in the 24 patients undergoing resection of the sigmoid colon or rectum revealed the following IMA variants: type A, left colic artery (LCA) and sigmoid artery (SA) branch from the IMA at a single point, n = 7; type B, LCA and SA branch from a common trunk, n = 5; and type C, LCA and SA branch from independent points on the IMA, n = 12.[17] (See

Figure 1) We performed high tie of the IMA in the cases with type A and B anatomy (12 patients).

Fifteen of the operations were performed robotically and 12 laparoscopically. There were three conversions to open procedures – two obese males with bulky tumors in the middle/distal rectum, and one patient undergoing total colectomy due to inadequate exposure of the transverse mesocolon and middle colic vessels. In the seven patients with colon carcinoma, there were two right hemicolectomies,

Table 1.
Patient Characteristics

№	Age	Sex	Localization	Pre-O ChRT	Tlc	Procedure	Type of surgery	Stoma	TME/PME/ TaTME/CME	High/ Low Tie	Type of IMA
1	69	M	Proximal rectum	No	No	ARR	R	No	PME	Low	C
2	64	F	Middle rectum	Yes	No	ARR	R	No	TME	High	A
3	83	M	Proximal rectum	No	Yes	ARR	R	No	PME	Low	C
4	80	M	Middle rectum	Yes	No	ARR	R	Yes	TME	High	A
5	71	M	Distal rectum	Yes	Yes	ARR	R	Yes	TME	High	B
6	59	M	Proximal rectum	No	No	ARR	R	No	PME	Low	C
7	76	M	Sigmoid colon	No	No	ARR	R	No	PME	Low	C
8	71	F	Proximal rectum	No	No	ARR	R	No	PME	Low	C
9	57	M	Middle rectum	No	No	ARR	R	No	TME	High	A
10	43	F	Middle rectum	Yes	No	ARR	R	Yes	TME	High	B
11	63	M	Middle rectum	Yes	No	ARR	R	Yes	TME	High	B
12	75	M	Middle rectum	No	No	ARR	R	Yes	TME	High	A
13	66	M	Proximal rectum	No	No	ARR	R	No	PME	Low	C
14	45	M	Middle rectum	Yes	No	ARR	L	Yes	TaTME	High	A
15	78	M	Sigmoid colon	No	No	SE	L	No	CME	Low	C
16	71	M	Sigmoid colon	No	Yes	SE	R	No	CME	Low	C
17	84	F	Proximal rectum	No	Yes	ARR	L	No	PME	Low	C
18	68	M	Ascending colon	No	No	RH	L	No	CME	High	-
19	81	M	Ascending colon	No	No	RH	L	No	CME	Low	-
20	62	M	Middle rectum	Yes	No	ARR	L	Yes	TME	High	B
21	72	F	Descending colon	No	No	ELH	L	No	CME	Low	C
22	68	F	Proximal rectum	No	Yes	ARR	R	No	PME	Low	C
23	75	F	Distal rectum	No	Yes	ARR	L	Yes	TaTME	High	A
24	68	M	Distal rectum	Yes	No	ARR	L	Yes	TaTME	High	A
25	73	F	Sigmoid colon	No	No	SE	L	No	CME	Low	C
26	68	M	Proximal rectum	No	No	TC	L	Yes	TME	High	-
27	76	F	Distal rectum	No	Yes	ARR	L	Yes	TaTME	High	B

Abbreviations: Pre-O ChRT, pre-operative chemoradiotherapy; TLC, transection line change; ARR, anterior rectal resection; RH, right hemicolectomy; SE, sigmoidectomy; ELH, extended left colectomy; TC, total colectomy; R, robotic operation; L, laparoscopic operation; AL, anastomotic leak; TME, total mesorectal excision; PME, partial mesorectal excision; TaTME, transanal TME; CME, complete mesocolic excision.
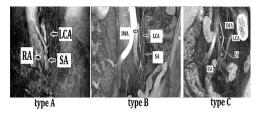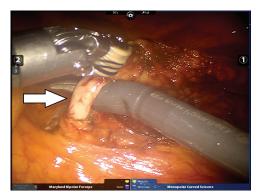
Figure 1. Images from SECTRA 3D reconstruction of types of inferior mesenteric artery.

one left hemicolectomy, three sigmoid colectomies, and one total colectomy. The total colectomy was performed in a patient with a proximal rectum malignancy and multiple polyps with high grade dysplasia in the ascending and transverse colon. There were 20 rectal resections, 16 with TME/PME and four with TaTME. When a difficult rectal mobilization was expected (narrow pelvis, male patient, high body mass index, bulky tumor), TaTME was preferred. There were 19 stapled anastomoses and one hand-sewn anastomosis. All cases had bubble leak test. It was positive in 1 patient only and we sutured on top of the site. Protective stoma was created in 11 patients.

During the intraoperative ICG angiography, fluorescence appeared 17 ± 8 seconds after the first dose. Perfusion assessment of the resection lines was completed 34 ± 11 seconds after the second dose. This added less than 2 min of intraoperative time. Intensity of color and time to appear were taken into consideration. We looked for fluorescence in the area of the colon where the resection margin was marked. A clear demarcation line was seen by fluorescence in all cases. In seven of the 27 cases (26%), it was judged by ICG that perfusion of a resection line was inadequate, and the resection line was modified accordingly. In the cases where perfusion of resection lines was judged to be poor, they appeared healthy and nonischemic to the naked eye. Inadequately perfused transection lines were detected in patients with all three types of IMA anatomy (3 type A/B and 4 type C). All cases of type C that needed transection line change had low tie of IMA, whereas all cases of types A and B had high tie. (See **Figure 2**) Even in low tie patients, ischemia of the transection line was detected with ICG angiography. (See **Figure 3**)

On pathological evaluation, there were no positive margins. The quality of the mesorectal resection was graded using the Quirke criteria, and all surgical specimens were graded high quality.[18] There were no postoperative anastomotic leaks assessed by digital rectal examination and contrast enhanced CT of the pelvis. Median postoperative length of stay was six days.
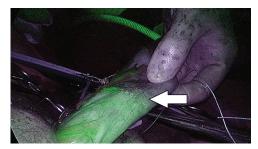

Figure 2. Dissection of inferior mesenteric artery (*arrow*) during robotic surgery.

DISCUSSION

Colorectal carcinoma accounts for about 10% of all cancers and cancer mortalities worldwide. Multidisciplinary team care and precise surgical technique are necessary for optimal outcomes. Yet, even with precise surgical technique, anastomotic leaks remain a refractory complication, resulting in increased morbidity and costs, and reduced cancer-specific survival and overall survival.[19] This study was undertaken to determine if the implementation of pre-operative mesenteric vascular evaluation with MDCTA and intraoperative evaluation of perfusion with ICG angiography could reduce the anastomotic leak rate of colorectal cancer patients undergoing minimally invasive resection at our institution.

Pre-operative MDCTA with 3D reconstructions was implemented to evaluate the mesenteric arterial anatomy and plan the sites of vascular ligation to optimize both the quality of lymph node sampling and the preservation of arterial supply to the remaining bowel. Studies by Kanamoto, Mari, and others have shown that prior knowledge of the mesenteric vascular anatomy, including vascular variants, represents an advantage when performing laparoscopic colorectal resection.[20,21] We utilized the classification of IMA anatomy

Figure 3. Indocyanine green angiography and transection line (*arrow*) marked.

described by Ke, Kobayashi, and others.[22,23] Understanding the IMA variants preoperatively may help guide the division of IMA branches.[24]

Intraoperative ICG angiography to assess perfusion at the resection lines and the anastomosis during minimally invasive surgery yielded encouraging early results as reported by multiple institutions.[25,26] Current limitations of ICG angiography include methods that are incompletely standardized and assessment of perfusion that is inherently qualitative, not quantitative. Recent reviews have in fact concluded that more reliable scoring and grading tools are needed.[27] A recent study by Sang-Ho Park et al.[28] suggested that artificial intelligence based real-time microcirculatory analysis may improve the consistency and accuracy of ICG assessment.

Using common techniques for ICG assessment in their studies of 107 and 30 patients respectively, Boni et al. and Ris et al.[25,26] reported encouraging early results, with AL rates of 0% with the use of ICG. In a subsequent, larger study of 420 patients, Hasegawa et al.[29] reported AL rates of 2.8% with ICG vs. 13.6% without ICG. In two meta-analyses by Zhang et al.[30] and Li et al.,[31] a statistically significant reduction in AL rates was reported with ICG angiography. In the Zhang study, the pooled data revealed an AL rate of 3.22% with ICG vs. 9.17% without ICG. Several randomized clinical trials (RCT) have now been completed evaluating intraoperative ICG in colorectal surgery, including PILLAR II,[32] PILLAR III,[33] and FLAG.[34] These RCTs have reported results that are not in agreement. The PILLAR III study, the only RCT that evaluated low anterior resection (mean anastomotic level 5.2 cm) in cancer patients exclusively (n = 347) found that the routine use of ICG did not improve outcomes in the hands of experienced surgeons (AL rates of 9% vs 90.6%).

At our institution, in the two years prior to this study, our AL rate was 6.8%, including all elective >18 years old patients operated through open, laparoscopic, robotic, and TaTME approaches. After the implementation of the above-described protocol of pre-operative mesenteric vascular evaluation with MDCTA and 3D reconstruction, and intraoperative evaluation of perfusion with ICG angiography, our AL rate was 0% in this initial experience of 27 patients. Though these results are encouraging, the limitations of this study include the small cohort size and the single institution experience.

CONCLUSION

Pre-operative evaluation of mesenteric vascular anatomy using MDCTA with 3D reconstruction and intraoperative evaluation of perfusion using ICG angiography were found to be technically feasible and safe. An appropriately designed study should be undertaken to prove whether it was truly effective at reducing the postoperative anastomotic leak rate in colorectal cancer patients undergoing minimally invasive resection at our institution.

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