Clinical Utility of Staging Laparoscopy for Advanced Obstructing Rectal Adenocarcinoma: Emerging Tool

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Abstract

The multimodal treatment for advanced rectal adenocarcinoma mandates accurate preoperative staging with contrast-enhanced computed tomography (CECT) of the thorax, abdomen, and pelvis, and magnetic resonance imaging (MRI) of the pelvis. Unlike gastric cancer, the role of staging laparoscopy (SL) in advanced colorectal cancer has not been evaluated. This study aims to evaluate the clinical value of SL in treatment decision-making for advanced rectal cancer (RC) with near or complete obstructing tumors. Observational review of colorectal database at Tata Memorial Hospital from January 2013 to December 2016 identified 562 patients diagnosed and treated for advanced RC. Of the 562 cases, 48.7% (274) were clinically and radiologically diagnosed of near or complete obstructing advanced RC. Medical records of 34% (94/274) who underwent SL with diversion stoma (DS) were analyzed. In the absence of ascites, extensive peritoneal deposits, and unresectable liver metastases on SL, a curative treatment was offered, which entailed neoadjuvant chemoradiation (NACTRT), whereas the cohort of patients with extensive peritoneal disease received palliative therapy. Of the 94 patients with advanced RC, conventional imaging studies staged 73.5% (69/94) cohort as non-metastatic locally advanced and 26.5% (25/94) had potentially resectable metastatic RC. Pre-therapeutic SL upstaged the disease by 26% (18/69) and 8% (2/25) in locally advanced and potentially resectable metastatic RC cohorts, respectively. Treatment decision changed in 21.2% (20/94) of the patients, and midline laparotomy was thus avoided. In our observational study, SL was found to be a safe and effective staging modality in RC; it detected occult peritoneal disease and prevented midline laparotomy in 21.2% of the cohort, which was of value to determine treatment strategy in patients with advanced RC before initiating NACTRT. SL and laparoscopic-assisted de-functioning stoma were associated with minimal morbidity and led to early initiation of NACTRT.

Keywords Rectal cancer · Staging laparoscopy · Peritoneal deposits · Neoadjuvant chemoradiation · Diversion stoma

Introduction

A total of 40,340 new cases of rectal cancer (RC) were diagnosed in the USA in 2013, and RC is a major cause of cancer-related mortality in the developed world [1]. The prognosis of patients with RC depends on the disease stage at the time of diagnosis [2–4]. Accurate tumor staging facilitates the

formulation of a structured multidisciplinary approach to manage the disease and to assess a patient's prognosis over the course of treatment. Oncological outcomes of accurately staged advanced RC are superior and have been improved by adapting evidence-based multimodal treatment protocol with neoadjuvant chemoradiation (NACTRT) and total mesorectal excision over the last decades [5, 6].

Although preoperative tumor staging has improved significantly by sophisticated modern imaging techniques such as endorectal ultrasound, contrast-enhanced computed tomography (CT), and magnetic resonance imaging (MRI), occult peritoneal metastases are detected only during surgery in many patients. Five percent of the patients with RC will have near or incomplete obstruction at presentation and they have a high propensity for liver or peritoneal metastases [7, 8]. Unlike in the developed world, incidence of obstructing RC in Indian continent is high. NACTRT in these patients carries a time lag of 3 months before

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surgery is contemplated; subset of patients may develop obstruction which may interrupt NACTRT; with this in mind, preemptive laparoscopic stoma was performed for all near and complete obstructing tumors. Interestingly, a high incidence of change in management was noticed when staging laparoscopy (SL)—a day care procedure—was adapted; hence, a retrospective analysis was performed.

Laparoscopy has been proposed as an accurate staging modality in a variety of upper gastrointestinal malignancies. SL may aid in the more accurate staging of digestive cancers, thus offering guidelines for the most appropriate treatment and avoiding the morbidity associated with non-therapeutic laparotomy. The procedure enables direct inspection of intra-abdominal organs and facilitates obtaining biopsy specimens and aspiration cytology. In gastric cancer (GC), SL can avoid surgical exploration in the presence of peritoneal metastases or liver metastases undetected by the conventional staging [9, 10]. SL has been included in the diagnostic algorithm for GC [11, 12]. The role of laparoscopic staging of RC is unclear [13].

This study aimed to evaluate the importance of SL to predict occult peritoneal and hepatic metastases in advanced RC and its impact on decision strategy for treatment.

Method

Preoperatively, all patients were optimally investigated with routine blood investigations, including blood counts, liver and renal functions, carcinoembryonic antigen (CEA), and a colonoscopy to map the location of the disease and to obtain tissue diagnosis. Pre-therapeutic staging included MRI of the pelvis to delineate and locally stage RC, and contrast-enhanced computed tomography (CECT) of the thorax, abdomen, and pelvis for distant metastatic evaluation.

Planning of Treatment Modality

Imaging studies of every patient diagnosed with advanced RC were reviewed at the joint meeting of the Gastrointestinal Disease Management Group (GI-DMG) as per routine policy. Indications for directing patients toward NACTRT were biopsy-proven rectal adenocarcinoma, MRI scans indicative of tumor stage $\geq T3$, threatened or positive mesorectal fascia (MRF), positive pelvic lymph nodes, and resectable liver metastases.

Diversion stoma was performed to relieve the obstruction and depending on the SL findings patient was considered for definitive NACTRT in the absence of intra-abdominal metastasis and was considered for chemotherapy with short-course radiotherapy in the presence of visceral metastasis with or without low peritoneal carcinomatosis index (PCI < 10 – 12) and was offered palliative chemotherapy in the presence of ascitis, PCI index > 12 .

Planning of SL with Diversion Stoma

SL and diversion stoma (DS) were indicated in patients who had near or complete obstructing RC, which was defined as advanced rectal tumors with altered bowel habits, spurious diarrhea, constipation, inability to map the proximal limit of the tumor by digital rectal examination and impassable colonoscope, and dilated bowel loops on imaging.

Patients who present with near obstructing T3 or T4 RC benefited from NACTRT, but the edema resulting from pelvic radiation can convert an impending obstruction to a total obstruction and interrupt treatment. A DS was recommended to be used in lesions where the lumen was less than 1 cm in diameter. An arbitrary cutoff 1 cm was used as the Olympus PCF-PH190L/I, an ultra-slim colonoscope diameter, is of only 9.7 mm, and if the scope was impassable, patients were considered to have an obstructing growth.

All patients received detailed information on SL with DS. Procedure was performed under general anesthesia with a single-dose antibiotic cover immediately before the scheduled procedure.

A supra-umbilical, 10-mm trocar was introduced into the abdomen by open Hasson's approach, and 5-mm working ports were inserted in the right and the left iliac fossae. Peritoneal surfaces were thoroughly evaluated. Before any manipulation, ascites when present was suctioned and sent for cytological examination. Routine peritoneal washings were not done. The paracolic gutters, pelvic cavity, surface of the bowel, root of the transverse mesocolon and small bowel, ligament of Treitz, and liver surface were systematically evaluated for metastatic deposits.

A laparoscopy-assisted diverting loop ileostomy or a transverse stoma was performed when sphincter preservation surgery was contemplated after NACTRT, and for tumors where sphincter preservation was not achievable, laparoscopy-assisted sigmoid stoma was performed.

Individuals with documented ascites, extensive PD, and unresectable liver metastases on SL underwent laparoscopy-assisted DS, thus avoiding midline laparotomy and received palliative chemotherapy or best supportive care depending on performance status.

Ethics

Data of this study were collected in the course of common clinical practice and, accordingly, the signed informed consent was obtained from each patient for any surgical and clinical procedure. The study protocol conforms to the ethical guidelines of the "World Medical Association Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subjects" adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, as revised in Tokyo 2004. No approval of the institutional review committee was needed.

Statistical Analysis

All statistical analyses were carried out with the statistical software package SPSS 20.0 (SPSS Inc., Chicago, IL). The Cox proportional hazards regression model was used for univariate analysis. A *P* value of less than 0.05 was considered to be statistically significant.

Results

Medical records of 562 patients diagnosed and treated for advanced RC between January 2013 and December 2016 at the Division of Gastrointestinal and Colorectal Surgical Oncology, Tata Memorial Hospital, Mumbai, Maharashtra, India, were evaluated from a prospectively maintained database. Of these 562 patients, 48.7% (274/562) were clinically–radiologically and on colonoscopy diagnosed of near or complete obstructing advanced RC. Of 274 patients, 34% (94/274) underwent SL with DS to relieve the obstruction and also to facilitate planning of treatment depending on the intraoperative findings, whose outcomes are analyzed (Fig. 1).

Clinical and Pathological Characteristics

The median age of 94 patients was 40 years (range 15–81 years). Male:female distribution was 72%:28%. Majority of the tumors were cT3 (58 cases, 62%), whereas cT4 amounted to 36 cases (38%). A total of 28 cases (29.8%) had middle third tumors extending to lower third. MRF was involved in 43 cases (46%) and was threatened in 10 cases (11%). A total of 47 cases (50%) had poorly differentiated adenocarcinoma on biopsy. Radiologically, 82 cases (87.2%) were node positive (Table 1).

Perioperative Outcomes

The mean operative time of the SL was 45 min (range 30–90 min). Dense adhesions impaired a thorough abdominal inspection in three patients, in whom only a limited examination was possible. Mean blood loss ranged from 25 to 200 mL. Of 94 cases, 3 (3.1%) had conversion to open in view of the presence of significantly distended short sigmoid colon, which was technically challenging. Minor morbidity, wound infection, and parastomal hernia were observed in 3.1% cases. Average length of hospital stay was 2.7 days (range 1–15 days).

Of 94 cases, preoperative conventional imaging staged 69 (73.5%) and 25 (26.5%) patients as locally advanced and potentially resectable metastatic obstructive RC, respectively. As per the decision of the GI-DMG, SL and DS were planned in 94 cases before initiating definitive NACTRT. Pre-therapeutic SL upstaged the disease by 26% (18/69) and 8% (2/25) in locally advanced and potentially resectable metastatic RC cohorts, respectively. SL revealed unsuspected intra-abdominal metastases in 21.2% (20/94) cases, which changed the treatment decision from NACTRT to palliation, and thus midline laparotomy was avoided (Tables 2, 3, and 4).

Outcomes Following SL and NACTRT and Short-Course Radiotherapy with Chemotherapy

Of the 94 individuals with extensive occult peritoneal disease who received palliative chemotherapy, 14 were excluded of definitive surgical treatment in view of PCI >12. Nine patients while on NACTRT had progression of disease for which leucovorin, 5-fluorouracil, and oxaliplatin (FOLFOX)-based chemotherapy was initiated; 18 individuals were awaiting surgery post-NACTRT. Curative resections were offered in 47 individuals following NACTRT; of these, 27 underwent open resection whereas minimally invasive rectal surgery was

Fig. 1 Breakdown of the entire cohort of 564 cases who were treated for rectal cancer

Table 1 Clinical and pathological characteristics

S no.	Variables	Results
1	Median age (range)	40 years (15–81 years)
2	Gender	
	Male	68 (72%)
	Female	26 (28%)
3	Clinical T stage	
	T3	58 (62%)
	T4	36 (38%)
4	MRI epicenter of primary	
	Middle third to lower third	28 (29.8%)
	Upper third to middle third	21 (22.3%)
	Lower third	20 (21.3%)
	Upper third to lower third	15 (16%)
	Upper third	6 (6.4%)
	Middle third	4 (4.3%)
5	MRI: Circumferential resection margin status	
	Free	41 (43.6%)
	Threatened	10 (10.6%)
	Involved	43 (45.7%)
6	Tumor differentiation	
	Well differentiated	08 (8.5%)
	Moderately differentiated	37 (41.5%)
	Poorly differentiated	49 (50%)
7	Clinical nodal status	
	Node negative	12 (12.8%)
	Node positive	82 (87.2%)
	Perirectal and mesorectal nodes	45 (47.9%)
	Lateral pelvic node	27 (28.7%)
	Para-aortic nodes	08 (8.5%)
	Inguinal nodes	02 (2.1%)

performed in 20 individuals. Complete cytoreductive surgery with hyperthermic intraperitoneal chemotherapy was performed in two. Six patients were treated with short-course

Table 3 SL findings of unsuspected intra-abdominal metastases

Sites	n = 20/94
Ascites	1 (1%)
Liver	1 (1%)
Peritoneal deposits	13 (13.8%)
Ascites and peritoneal deposits	3 (3.1%)
Liver and peritoneal deposits	2 (2.1%)

SL, staging laparoscopy

radiotherapy (SCRT) with chemotherapy (FOLFOX): two underwent definitive surgical resection whereas four had progression of the disease (Tables 5 and 6).

Upfront peritoneal surgery was not offered in any, because of poor nutritional reserve and suboptimal preparation for a complex and specialized cytoreductive surgery and HIPEC which could have hindered post-operative recovery.

Discussion

In this era of personalized cancer care, imaging plays a critical role in the management of patients with cancer. Challenges still exist for the application of imaging technologies in staging, stratification of treatment, and monitoring [14, 15]. Complete history and physical examination; digital rectal examination; biopsy; colonoscopy; CECT of the thorax, abdomen, and pelvis; and MRI of the pelvis are required for the diagnosis and optimal staging of RC [16]. Approximately 15% patients with colorectal cancer (CRC) present with large bowel obstruction. Conventional colonoscopy fails to map the entire colon in approximately 6–26% of the cases, mainly because of occlusive CRC [17–20]. In this situation, CT colonography (CTC) might be the next choice for complete evaluation of the proximal colon; however, the yield of CTC in stenosing

Table 2 Perioperative outcomes of staging laparoscopy and diversion stoma

S no.	Variables	Results
1	Mean operative time	45 min (range 30–90 min)
2	Mean blood loss range	25–200 mL
3	Conversion to open (exploratory laparotomy)	3 (3.1%)
4	Minor morbidity	3 (3.1%)
	Wound infection	2 (2.1%)
	Parastomal hernia	1 (1%)
5	Mean duration of hospital stay	2.7 days (range 1–15 days)
6	Type of diversion stoma	
	Loop ileostomy	25 (26.8%)
	Transverse stoma	18 (19%)
	Sigmoid stoma	51 (54.3%)

Table 4 Change in treatment decision

Treatment plan	<i>n</i> = 20/94
Palliative chemotherapy	14 (14.9%)
SCRT + chemotherapy	06 (6.3%)
<i>SCRT</i> , short-course radiation	

CRC appears to be limited and relatively low and less than 1.9% [21]. Up to 25% patients with locally advanced RC will have extra-pelvic disease [22]. Metastases of > 1-cm diameter are detected by CT scan with sensitivity and specificity of 90% and 95%, respectively [23]. Staging by conventional imaging techniques has its own limitations and often results in under-staging and unnecessary laparotomy. Compared with other invasive diagnostic procedures, SL should be performed only when there are no available non-invasive staging methods with similar or equivalent information and diagnostic yield, and when the information provided by SL is necessary and capable of changing the treatment plan [24–26].

The role of SL in GC is well established [27–31]. The data on the role of SL in RC are sparse. This study is perhaps the largest series, and to the best of our knowledge, this is the first study from the Indian subcontinent to evaluate the clinical utility of SL in advanced obstructive RC.

Many authors reported a high incidence of CRC affecting young (< 40 years) Indian population with a majority of them having poorly differentiated histology and locally advanced disease affecting long segment of the rectum [32–35]. Koea et al. [36] reported 28.5% upstaging of the disease when SL was performed for near obstructing RC. In this study, median age at presentation was 40 years and 50% had poorly differentiated histology, and with SL, we found unsuspected distant metastases in 20 cases (21.2%) of which 13 (13.8%) had unexpected PD, 3 (3.1%) had PD with ascites, and 2 (2.1%) had PD with liver metastases. On univariate analysis, it was found that

Table 6 Outcomes following staging laparoscopy and SCRT and chemotherapy

<i>n</i> = 2			
Surgery	Open approach	Robotic approach	Total
AR + liver resection	01	01	02

age, carcinoembryonic antigen (CEA) levels, MRI epicenter of tumor, clinical T stage, MRF involvement, tumor histology, and lymph node involvement did not influence the intra-abdominal metastases.

The CREST trial [37] reported self-expanding metallic stents as a reasonable alternative to emergency surgery with acceptable procedure-related complications. However, it is not a widely accepted procedure as yet and has a limited role in lower third RC.

Our series demonstrates the diagnostic and therapeutic role of laparoscopy in the initial management of the near or complete obstructing advanced RC; it identified unsuspected intra-abdominal metastases in 21.2% of the cases (20/94), which facilitated in personalizing appropriate treatment regimens.

NACTRT involved 6 weeks of chemoradiation followed by definitive surgical resection after 8–12 weeks, depending on the response to therapy. In low-resource developing countries, sub-optimal RC staging will overburden health resources and will have a negative impact on the health care service system, which can be curtailed by optimal staging and triaging to various available treatment modalities depending on SL findings.

In metastatic CRC to avoid progression, upfront chemotherapy and SCRT with delayed surgery is an effective alternative treatment [38]. In our study, following SCRT with chemotherapy, two of the six metastatic RC patients underwent salvage curative resection. Furthermore, DS was accomplished in all cases with minimal morbidity, early hospital discharge, and early initiation of NACTRT.

Table 5 Outcomes following staging laparoscopy and NACTRT

Surgery	Open approach	Laparoscopic approach	Robotic approach	Awaiting surgery	Total
AR	08	03	01	02	14
ISR	01	02	00	02	05
APR	07	08	02	05	22
ELAPR	04	03	00	03	10
Exenteration	05	00	01	03	09
Exenteration + CRS + HIPEC	02	00	00	03	05
Total	27	16	4	18	65

AR, anterior resection; ISR, intersphincteric resection; APR, abdominopelvic resection; ELAPR, extralevator APR; CRS, cytoreductive surgery; HIPEC, hyperthermic intraperitoneal chemotherapy; NACTRT, neoadjuvant chemoradiation therapy; SCRT, short-course radiotherapy

n = 74 (14 patients who received palliative chemotherapy, 6 patients who received SCRT with chemotherapy and 9 patients with progression while on NACTRT were excluded)

The future role of SL in the treatment decision and multidisciplinary therapy of RC is emerging. In comparison to laparotomy, SL permits a more thorough and systematic examination of all parts of the abdominal cavity. Its major advantage is in detecting occult intra-abdominal metastases and in preventing unnecessary laparotomies, and its good safety profile is more than encouraging for future studies.

Conclusion

In conclusion, our study demonstrated that laparoscopy is a safe and effective staging tool in advanced obstructing RC. It is able to detect occult peritoneal and liver metastases missed by conventional imaging techniques. SL improves the accuracy of disease staging and is helpful in predicting prognosis and assisting in patient selection for neoadjuvant treatment in resource-limited economies with high proportion of poorly differentiated tumors.

Compliance with Ethical Standards

Data of this study were collected in the course of common clinical practice and, accordingly, the signed informed consent was obtained from each patient for any surgical and clinical procedure. The study protocol conforms to the ethical guidelines of the “World Medical Association Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subjects” adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, as revised in Tokyo 2004. No approval of the institutional review committee was needed.

Conflict of Interest The authors declare that they have no conflict of interest.

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