Japanese Journal of Gastroenterology and Hepatology

Research Article

ISSN 2435-1210 | Volume 5

Impact of Surgical Staging for Aggressive Histology Rectal Cancers - A Retrospective Review

Kazi M[1], Nekkanti SS[1], Rohila J[1], Desouza A[1] and Saklani A [1*]

Department of Colorectal Surgical Oncology, Tata Memorial Hospital, Homi Bhabha National Institute (HBNI), Mumbai, Maharashtra 400012, India

***Corresponding author:**
Avanish Saklani,
Department of Colorectal Surgical Oncology,
Tata Memorial Centre,
Homi Bhabha National Institute (HBNI),
Dr Ernest Borges Marg,
Parel, Mumbai 400012,
Maharashtra, India,
E-mail: asaklani@hotmail.com

Received: 06 Oct 2020
Accepted: 10 Nov 2020
Published: 12 Nov 2020

Citation:

Saklani A. Impact of Surgical Staging for Aggressive Histology Rectal Cancers - A Retrospective Review. Japanese Journal of Gstroenterology and Hepatology. 2020; V5(2): 1-4.

1. Abstract

1.1. Introduction: Poorly Differentiated Adenocarcinomas (PDAC) and Signet ring adenocarcinomas (SRAC) are aggressive histologic subtypes of rectal cancer with high incidence of imaging occult peritoneal metastasis.

1.2. Methods: Retrospective review of aggressive histology, rectal cancer patients who underwent pre-treatment surgical staging as part of ovarian transposition or ostomy creation for diversion at a single tertiary cancer center between January 2014 and December 2019.

1.3. Results: 117 patients underwent surgical staging that were deemed non metastatic on imaging. Surgical staging led to detection of metastasis in 29.9% of patients. This led to modification in treatment protocol in 20.5% and change in intent of therapy in 15.4%. Majority (80%) were found to have peritoneal disease with PCI <17. Only T4 disease predicted presence of metastasis on surgical staging with an Odds ratio of 2.69 (p – 0.035).

1.4. Conclusions: Significant proportion of patients with aggressive histology advanced rectal cancer patients are upstaged after surgical staging. Further investigation of this tool for staging is warranted.

2. Abbreviations: CEA: Carcino-embryonic antigen; CT: Computerized tomography; HIPEC: Hyperthermic Intra-peritoneal chemotherapy; MDT: Multi-Disciplinary team; MRI: Magnetic resonance imaging; OR: Odds ratio;

PCI: Peritoneal carcinomatosis index; PDAC: Poorly differentiated adeno carcinoma; RT: Radiation therapy; SRAC: Signet ring adeno carcinoma

3. Introduction

Approximately 5% of the patients with colorectal cancer have synchronous peritoneal metastases at diagnosis of the primary tumor [1, 2] and the risk of peritoneal metastases is strongly influenced by the histological subtype [3]. Conventional staging modalities such as contrast-enhanced Computed Tomography (CT), and Magnetic Resonance Imaging (MRI), can miss occult peritoneal metastases in significant proportion of patients [4]. Staging laparoscopy is widely utilized in upper gastrointestinal malignancies however for its use is not routine in colorectal cancers. Limited reports have suggested over 20% upstaging of disease in advanced obstructing rectal cancers [5, 6] with surgical staging, notwithstanding which this modality has not been investigated further. This is a very significant proportion of patients where the intent and type of treatment offered changes drastically. Thus, the present study aimed to explore the utility of surgical staging in patients with aggressive histology rectal cancers viz. poorly differentiated adenocarcinomas (PDAC) and Signet ring cell adenocarcinomas (SRAC) who are at higher risk of peritoneal dissemination with the primary end point of disease upstaging with surgical staging.

4. Methods

A retrospective review of all rectal cancer patients treated at a single tertiary cancer center between January 2014 and December 2019 was

performed who had pre-treatment surgical staging. Study included patients with biopsy proven locally advanced PDAC or SRAC. All included patients had pelvic MRI and contrast CT scans of the thorax and the abdomen as part of clinical staging of the tumor and neoadjuvant therapy planned prior to surgery in the Multidisciplinary Team (MDT) meeting. Patients with distant metastasis detected on imaging prior to surgical staging were excluded from analysis. Since staging laparoscopy is not standard of care in rectal cancer, only patients requiring surgical interventions like divertingostomy for obstruction or ovarian transposition prior to starting neoadjuvant treatment underwent surgical staging. Patients with symptoms of obstruction and those with an impassable growth on colonoscopy were deemed near obstructed and considered for fecal diversion.

Rectal cancer was defined as tumors ≤15cm from anal verge. Staging included meticulous survey for peritoneal disease in all regions of the abdomen, small bowel and for deposits on the liver surface by laparoscopic or open methods as deemed feasible. Routine peritoneal washings were not performed but ascites if present was sent for cytological examination of malignant cells. Patients with equivocal peritoneal disease underwent biopsy of representative sites. Demographic, clinical and image-based staging was recorded. Operative findings recorded included site of abdominal metastasis and calculation of Peritoneal Carcinomatosis Index (PCI). Change in treatment was defined as modification of management plan as decided in the pre-surgical staging MDT meet that included both curative and palliative intent therapies.

Data was recorded in the IBM SPSS platform and analyzed using the SPSS version 25. For the continuous variables medians and range were calculated and comparisons were done using the Mann-Whitney U test. For the categorical variables, proportions were noted and compared using the Chi square test. The correlation of continuous and categorical variables to a categorical dependent variable was measured using Odds Ratio (OR) modeled from a logistic regression analysis. Statistical results were considered to be significant with p values of ≤0.05.

5. Results

In the study period, 597 patients with advanced rectal cancers were identified that had surgical staging. Of these 117 patients were non-metastatic, treatment naïve PDAC or SRAC (Figure 1). The subsequent analysis pertains to these 117 patients.

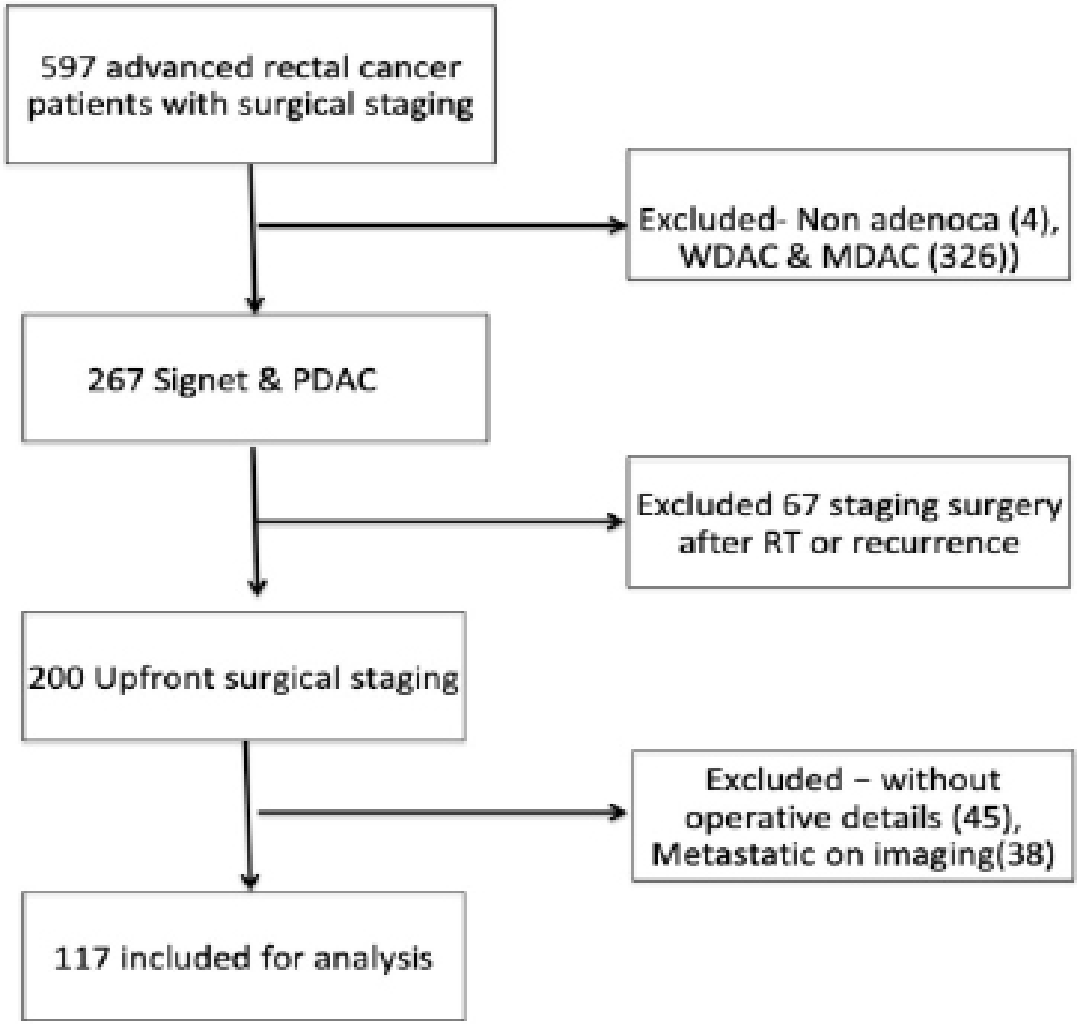

Figure 1: Patient selection

Clinical and imaging findings are detailed in (Table 1). Median age of our patients was 31 years and 68.4% were males. Signet ring cancers constituted 58.1% and majority (65.8%) were lower third rectal tumors. Large proportion (84.6%) of patients had tumors involving the mesorectal fascia and regional nodes on the MRI (88.9%).

The indication for surgical staging was obstruction or near obstructing rectal lesions in 105 patients (89.7%) and ovarian transposition to protect the ovaries from radiation in young women desirous of fertility in 12 patients (10.3%). 35 patients had intra-abdominal metastasis detected during the surgery (Table 2) and majority (60%) had low volume peritoneal disease (PCI <12). Thus 29.9% (35 patients) were upstaged by surgical staging. 24 patients (20.5%) required a change in the treatment plan decided in MDT before the intervention short course Radiation Therapy (RT) and chemotherapy or neoadjuvant chemotherapy or palliative chemotherapy alone. A change in intent of therapy from curative to palliative was found in 18 patients (15.4%).

Demographic and clinical factors were assessed for their correlation with detection of peritoneal disease on surgical staging and none were found to be significantly different except tumors in the upper rectum and those with higher T stage (Table 1). The possible factors were also analyzed in the multivariate model (Table 3) and a higher T stage alone predicted the presence of peritoneal disease with an OR of 2.7 (p – 0.035) for T4 tumors compared to T3 disease. Tumors in the upper rectum had an OR of 4.86 (p – 0.14) but missed statistical significance.

Table 1: Baseline characteristics

		All patients (117)	**Surgically staged M0 (82)**	**Surgically staged M1 (35)**	***p*value**
Age - median (range)		31 years (13-73)	31 years	31 years	0.79
Sex – n (%)	Male	80 (68.4%)	55 (67.1%)	25 (71.4%)	0.64
	Female	37 (31.6%)	27 (32.9%)	10 (28.6%)	
Histology – n (%)	Signet	68 (58.1%)	46 (56.1%)	22 (62.9%)	0.49
	PDAC	49 (41.9%)	36 (43.9%)	13 (37.1%)	
Distance from Anal Verge – n (%)	<5cm	77 (65.8%)	55 (67.1%)	22 (62.9%)	0.66
	5-10cm	30 (25.6%)	23 (28%)	7 (20%)	0.36
	10-15cm	10 (8.5%)	4 (4.9%)	6 (17.1%)	**0.03**
Clinical T stage – n (%)	T2	9 (7.7%)	8 (9.8%)	1 (2.9%)	0.2
	T3	62 (53%)	48 (58.5%)	14 (40%)	0.06
	T4	46 (39.3%)	26 (31.7%)	20 (57.1%)	**0.01**
Mesorectal Fascia – n (%)	Involved	99 (84.6%)	68 (82.9%)	31 (88.6%)	0.44
	Free	18 (15.4%)	14 (17.1%)	4 (11.4%)	
Clinical Nodal status – n (%)	N0	13 (11.1%)	7 (8.5%)	6 (17.1%)	0.89
	N+	104 (88.9%)	75 (91.5%)	29 (82.9%)	
CEA - median (range)		8.14ng/ml (1.3- 1352)	7.4 ng/ml	10.9 ng/ml	0.25

Table 2: Outcomes of surgical staging

		N	%
Indication for surgery	Obstruction	105	89.70%
	Ovarian transposition	12	10.30%
Intra-operative findings	Non metastatic	82	70.10%
	Ascites	9	7.70%
	Peritoneal disease	30	25.60%
	Krukenberg	1	0.90%
	Liver metastasis	1	0.90%
PCI for M1 patients (n=35)	<12	21	60%
	17-Dec	7	20%
	>17	7	20%
	Median	5	Jan-37
Change in Stage (M0àM1)		35	29.90%
Change in treatment		24	20.50%
Change in intent (curative to palliative)		18	15.40%

Table 3: Multivariate regression model – Factors predicting peritoneal disease on surgical staging.

		Odds Ratio (OR)	95% Confidence Interval (CI)	*p*value
Histology (Signet)		1.64	0.68 – 3.91	0.26
Distance from anal verge	< 5 cm	1.35	0.49 – 3.72	0.14
	5-10 cm	1	1 – 1	
	10-15cm	4.86	0.99 – 23.9	
Clinical T stage	T2	0.41	0.05 – 3.68	0.035
	T3	1	1 – 1	
	T4	2.69	1.14 – 6.36	

6. Discussion

PDAC and SRAC are aggressive histologic variants of rectal adenocarcinoma, afflicting younger individuals with higher incidence of synchronous peritoneal metastases and poorer prognosis [7]. Compared to the western population, there is a higher proportion of patients with signet ring cancers in Asian patients [8, 9]. Similarly, age at presentation is also younger in eastern population. In the present study, the median age was 31 years.

Preoperative imaging for detection of peritoneal disease is plagued with poor sensitivity and the identification depends on the size and location of nodules. For small lesions (<0.5cm), CT has a sensitivity of 11% that increases to 94% for nodules larger than 5cm [4]. MRI has better ability to predict peritoneal disease but is not routinely performed unless there is clinical suspicion of peritoneal metastasis due to cost, long imaging times, special preparation and need for expert radiological interpretation.

Staging laparoscopy is part of routine pre-treatment investigation in advanced upper gastrointestinal cancers, especially gastric cancers. Its utility, however, for colorectal cancers is under-studied. Our review shows disease upstaging in nearly 30%. These figures are nearly similar to those for advanced gastric cancer where staging laparoscopy

upstages a third of patients [10] and hence calls for considering surgical staging for select rectal cancer patients.

For the present study we chose patients with aggressive histology and advanced cancers planned for neoadjuvant radiation that had an incidental surgical staging. Not all tumors impassable on colonoscopy are symptomatic for obstruction and RT can shrink some of these. However in our setup, many patients come from remote areas and have limited access to healthcare hence diversion is preferred for most patients with impassable growths.

Even though treatment intent was changed for only 15% of our patients since low and moderate volume peritoneal disease are considered for curative intent cytoreduction and Hyperthermic intraperitoneal chemotherapy (HIPEC), treatment protocol changed in 20% where it was deemed more appropriate to instate systemic chemotherapy early by delivering short course RT as opposed to long course concurrent chemo-RT. For those with high volume disease, palliative chemotherapy could be administered without delay thus eluding the time lost due to long course RT.

Amongst the factors we studied; age, sex, nodal status, CEA levels and MRF involvement were not significantly different for those with or without metastatic disease. Only T4 stage and tumors higher than 10cm from anal verge could predict peritoneal disease on surgical staging. Rectal cancers above the peritoneal reflection have higher incidences of peritoneal metastasis and in our cohort; these had nearly 5 times higher risk of metastasis detected on surgical staging. This factor, other than T stage and histology can also be used to choose patients for staging laparoscopy.

80% of metastatic disease detected on surgical staging had low to moderate volume disease and could thus be prognosticated early, offered curative therapy with timely initiation of systemic treatment and avoid on table surprises with unprepared performance of peritonectomy or HIPEC. The clinically overt peritoneal disease patients can seldom be offered curative therapies and with upcoming role of neo-adjuvant intraperitoneal chemotherapy, there is a further increase in the need to detect peritoneal disease early before commencement of treatment.

6.1. Short Comings and Future Perspective

Since synchronous peritoneal metastasis are seen in only 5% of rectal cancer patients [1, 2], routine surgical staging cannot be advocated. A comparative analysis with incidental surgical staging performed for other histologies would have been worthwhile and is a drawback of our study. Large proportion of surgically staged patients was obstructed, suggestive of advanced pathology thus introducing a selection bias. However, at least in aggressive histology, locally advanced rectal cancers, a significant proporton benefitted from surgical staging. A matched analysis of similar locally staged patients with and without surgical staging with an end point of survival would be of greater significance in understanding the role of staging laparoscopy.

7. Conclusion

Surgical staging in aggressive histology, advanced rectal cancer leads to significant upstaging of disease with change in intent and therapy. There is a great scope for exploration of this modality of pre-treatment staging to select patients with limited peritoneal disease for curative treatments and early identification of high volume disease for palliative therapies.

References

1. Segelman J, Granath F, Holm T, Machado M, Mahteme H, Martling A et al. Incidence, prevalence and risk factors for peritoneal carcinomatosis from colorectal cancer. Br J Surg 2012; 99: 699-705.
2. Patil PS, Saklani A, Gambhire P, Mehta S, Engineer R, De'Souza A et al. Colorectal Cancer in India: An Audit from a Tertiary Center in a Low Prevalence Area. Indian J SurgOncol. 2017; 8: 484-90.
3. Razenberg LGEM, van Gestel YRBM, Lemmens VEPP, de Wilt JHW, Creemers G-J, de Hingh IHJT et al. The Prognostic Relevance of Histological Subtype in Patients with Peritoneal Metastases from Colorectal Cancer: A Nationwide Population-Based Study. Clinical Colorectal Cancer. 2015; 14: e13–9.
4. Koh J-L, Yan TD, Glenn D, Morris DL. Evaluation of preoperative computed tomography in estimating peritoneal cancer index in colorectal peritoneal carcinomatosis. Ann SurgOncol. 2009; 16: 327–33.
5. Saklani A, Sugoor P, Chaturvedi A, Bhamre R, Jatal S, Ostwal V et al. Clinical Utility of Staging Laparoscopy for Advanced Obstructing Rectal Adenocarcinoma: Emerging Tool. Indian J SurgOncol. 2018; 9: 488-94.
6. Koea JB, Guillem JG, Conlon KC, Minsky B, Saltz L, Cohen A et al. Role of laparoscopy in the initial multimodality management of patients with near-obstructing rectal cancer. J GastrointestSurg. 2000; 4: 105–8.
7. Wu X, Lin H, Li S. Prognoses of different pathological subtypes of colorectal cancer at different stages: A population-based retrospective cohort study. BMC Gastroenterology. 2019; 19: 164.
8. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018; 68: 394-424.
9. Tamhankar AS, Ingle P, Engineer R, Bal M, Ostwal V, Saklani A. Signet ring colorectal carcinoma: Do we need to improve the treatment algorithm? World J GastrointestOncol. 2016; 8: 819–25.
10. Machairas N, Charalampoudis P, Molmenti EP, Kykalos S, Tsaparas P, Stamopoulos P et al. The value of staging laparoscopy in gastric cancer. Ann Gastroenterol. 2017; 30: 287–94.