



SURGICAL OUTCOMES OF RIGHT AND LEFT COLON CANCERS AND STATUS OF LAPAROSCOPIC ASSISTED COLON SURGERIES

Oncology

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ABSTRACT

BACKGROUND: Stage-wise differences do exist in right and left colon cancers in highly prevalent countries, whether these differences do really exist in our population where there is reportedly low incidence of colon cancers and what differences do they exhibit in terms of prognosis and treatment outcomes are the main backbone of this study.

AIM: The principle aim of this retrospective study is to evaluate the clinico-pathological data of our colon cancer patients along with surgical procedures offered for right-sided and left-sided colon cancers.

METHODS: All colon cancer patients admitted to this institution from 2012-2018 were collected and relevant clinico-pathological data were retrieved & recorded. Head to head comparison done between right and left colon cancer patients and differences were recorded. Stage-wise distribution was confirmed by final histopathological examination. Surgical procedure done, intra-operative timing, metastases, nodal retrieval, blood loss and creation of anastomosis were studied. Detection of reasons for conversion from laparoscopy to open method were recorded from operative notes and recorded videos. Recovery in post-operative period until the start of adjuvant treatment was followed. Recurrences pattern in both groups were noted.

Both MIS/Laparotomy for RCC/LCC were compared and multivariate analysis was done using Student's t test, Wilcoxon Rank-sum and Chi-square test. The Kaplan-Meier method and log-rank test were used for univariate analysis of RFS and CSS. Cox Proportional Hazards Regression was used for univariate analysis as well.

RESULTS: In our study there was no significant difference of open surgery versus MIS in RCC whereas MIS is superior over open surgery in LCC.

CONCLUSIONS: In our study as most of our cases were by open laparotomy method than laparoscopically assisted, not only there existed significant differences in RCC and LCC, also recurrences differed in site-wise.

KEYWORDS

RCC - Right Colon Cancer, LCC - Left Colon Cancer, MIS - Minimally Invasive Surgery

INTRODUCTION

In the areas of high incidence of colonic cancer like Hungary 51.2, South Korea 44.5, Slovakia 43.8 per 100,000 population there exists a significant difference in epidemiology, clinical and pathological factors along with treatment aspects and access to tests that detect genetic mutations. Although India does not figure in top 25 countries worldwide for incidence in colorectal cancer, its incidence in Southern part is quite high and is underreported probably due to limitations in registry and data collection. The recent MMTR crude incidence rate of colo-rectal cancer was 3.4 in females and 4.8 in males in Tamil Nadu, and constitutes among the top six cancers in India.

In such areas of high demographic population with limited access to tertiary cancer centres coupled with advanced stage presentations constitute a significant challenge to treating physicians who have a limited option to offer for cure.

Whether there exists a real difference between right-sided and left-sided colon cancers and any difference they exhibit in treatment options are a subject matter of debate even in highly-prevalent countries. There were concerns about the involvement of minimally invasive techniques in oncology in general that it may compromise survival and in particular to colon cancer that it may lead to increased port site recurrences.

Previously Ishihara from Japan reported that RCC had a significantly worse prognosis than LCC. Later Waedchow et al reported stage wise differences between RCC and LCC, that stage I RCC is better than stage I LCC but stage II-III RCC is worse than stage II-III LCC. Whether these stage-wise differences do really matter in our demographic population is subject matter of this study. By evaluating site-specific outcomes and subjecting it to primary systemic therapy before surgery can be a future guiding research study.

The principle aim of this retrospective study is to evaluate the clinico-pathological data of our patients along with surgical procedures for right-sided and left-sided colon cancers. We have also included transverse colon cancer into this study with first 2/3 rd into RCC and distal 1/3rd into LCC. We excluded all rectal cancers from our study as also the tumours which were treated by Neo-adjuvant therapy. Only upfront colon cancers treated by surgery either by Minimally invasive

method or Laparotomy depending on the availability of resources in elective/emergency mode were selected. We sought to determine whether there exists any prognostic difference in RCC and LCC with respect to surgical modes of treatment.

METHODS

A single centre retrospective study included patients with colon cancer (all stages) treated by upfront surgery in elective and emergency mode from January 2012-December 2018 were selected. Patients were followed up on a monthly basis with regular guidelines as per institutional protocol. All surgeries were performed by senior most surgeon and his dedicated team. Guidelines as per the institution for the colon surgeries were included and followed. Harmonic diathermy along with Hemolock clips were as a part of standard requirement and laparoscopy settings were standardized. All surgeries were recorded and intra-operative parameters were noted. Right-sided colon surgeries especially right hemicolectomy were not followed by proximal diversion enterostomy while left-sided colon surgeries especially anterior resection were followed by proximal enterostomy. Conversion from laparoscopy to laparotomy reasons were also noted and ease of laparoscopy in such difficult situations were also analysed. Specimen retrieval and extra corporeal anastomosis is not considered as conversion to open procedure instead group has MIS only. All steps were standardized and head to head comparison between MIS and open procedures was attempted. All patients were post-operatively followed on return of bowel function and start of adjuvant chemotherapy along with other morbidity patterns.

ANALYSIS

Age, gender, colonoscopy findings with morphology of the lesion, presence of abdominal symptoms with or without obstruction, lower GI bleed, any altered bowel habits and any abdominal mass and CT/PET-CT as indicated for evaluating metastatic disease, CEA levels were analysed and entered respectively for RCC and LCC. The location of primary tumour is included as right-sided if arising from caecum, ascending colon, hepatic flexure and proximal 2/3rd transverse colon. Similarly LCC were distal 1/3rd transverse colon, splenic flexure, descending colon, sigmoid colon only. Rectal cancers were excluded. Surgical effectiveness was measured in terms of time to laparotomy findings, evaluation of metastatic disease, total time duration, blood loss, oncological principles were followed in both MIS

and laparotomy types, pedicle first ligation (SMA/IMA), bowel handling, nodal retrieval, anastomosis creating, any untoward events for conversion to laparotomy, colostomy creation and recovery period were all evaluated. Postoperatively RCC/LCC treated by MIS/laparotomy methods were monitored in ICU for 72 hours and bowel restoration time was calculated along with other morbidity patterns. Adjuvant chemotherapy if required was administered (FOLOFOX-4) as a institution protocol depending on histopathology. KRAS/MSI genetic testing were not done due to non-availability.

Follow-up protocol included monthly visits for clinical examination along with 3 monthly CEA levels and annual CT abdomen/pelvis in addition to symptomatic evaluation.

Clinic-pathological parameter for RCC and LCC were tabulated and univariate/multivariate analysis was done. Both MIS/Laparotomy for RCC/LCC were compared and multivariate analysis was done using Students t test, Wilcoxon Rank-sum and Chi-square test. The Kaplan-Meier method and log-rank test were used for univariate analysis of RFS and CSS. Cox Proportional Hazards Regression was used for univariate analysis as well. P values of <0.01 Were considered statistically significant. Statistical analysis was done using latest version SPSS software.

RESULTS

The total number of patients analysed were 41, 13 excluded for poor data collection. RCC were 16, LCC were 12. Nine of patients were operated upon by MIS rest by Conventional Laparotomy route. Mean age for RCC was 49.18 years, while for LCC it was 54.12 years. Elderly population (>50 years) were more seen with LCC (8/12) than RCC (6/16). Abdominal pain was more seen with RCC group (16/16) than LCC (6/12), although lower GI bleed was seen in more patients with LCC (77%) than RCC (23%). Even with significant lower GI bleed cancer colon patients Hemoglobin was greater than 10% in our patient population uniformly, stating it hardly causes anemia. Altered bowel habits were more seen in LCC (55%) than RCC (45%). Stage wise distribution for RCC is I/II/III/IV were 1/5/9/0 and LCC was 0/4/6/1. Abdominal mass was palpable in (60%) of RCC and (40%) of LCC. CEA levels were more elevated in metastatic disease. LCC were more associated with colonic polyps.

MIS and laparotomy methods on comparison for RCC shows no difficulty in superior dissection upto duodenum and careful dissection of ureters/gonadal vessels with SMA branches clipping. Most of the cases operated were laparoscopic assisted due to application of hand staplers in later stages of surgery. But the advantages of MIS was clearly seen in LCC cases particularly anterior resection surgeries. Caecal dissection was best done by MIS, ascending colon was also better in MIS but in hepatic flexure growth MIS scored inferior to open laparotomy methods. Similarly as we go down from splenic flexure towards recto-sigmoid junction MIS scores over open laparotomy route.

RECURRENCE FREE SURVIVAL RATES IN MIS AND OPEN LAPAROTOMY IN RCC/LCC.

As MIS was started in 2015 in our institution and only a few cases have been done since then, to conclude about merits and demerits would be premature.

DISCUSSION

Prognostic data on site-specific colon cancer is currently unsettled. The reason being whether such attempts make an attempt towards any systemic therapy based on certain high-risk features remains a debated research. Based on embryology the colon segment extending from caecum to proximal two-thirds transverse colon, supplied by superior mesenteric artery is defined as RCC and distal one-third transverse colon to upper anal canal derived from inferior mesenteric artery is taken as LCC, we followed these principles. Site-specific survival data were initially published in highly prevalent countries, whether these are relevant and does really make an impact in prognosis in low-prevalent countries remains the bone of contention of this study.

According to Chapuis et al., as with recurrence, the factors which were independently associated with CC death were: urgent resection (HR 2.81, CI 1.32-5.98, $p = 0.007$) and right colon tumour (HR 2.05 CI 1.33-3.16, $p = 0.001$), and the pathology variables: infiltration of an adjacent structure (HR 3.28 CI 1.43-7.50, $p = 0.005$), $> 30\%$ of nodes involved (HR 1.65, CI 1.03-2.64, $p = 0.036$) and high grade (HR 1.60 CI 1.02-2.50, $p = 0.004$). In our study there were two patients with

obstruction of its patient with RCC had good prognosis than LCC. RCC per se had no poor prognostic value. Of course signet ring adenocarcinoma LCC succumbed to death.

In research published to date, diabetes is consistently associated with colorectal cancer incidence, and, in some studies, with colorectal cancer fatality. Thus, diabetes could plausibly increase the risk of colon cancer recurrence. In our study, we did not observe an association between diabetes and colon cancer recurrence.

Location of the primary tumor has become an increasingly recognized prognostic factor in metastatic colorectal cancer (mCRC). Analysis of recent respective trials in patients with mCRC treated with palliative chemotherapy have demonstrated prolonged PFS and OS associated with left-sided primary tumors. Patients with left-sided primary tumors had a significantly improved median OS compared with right-sided tumors, and improved OS was observed among the subgroup of patients that had recurred. Overall, patients with left-sided primary tumors displayed a more prolonged and indolent clinical course without any difference in the ultimate rates of death. In their study, after adjusting for known clinical confounders, patients with right-sided primary tumors were at increased risk of all cause mortality than left-sided tumors.⁶

The authors hypothesized that malignant cell shedding occurs with obstruction-related perforations that predispose to locoregional (peritoneal) recurrences, representing an additional mechanism of future failure in obstructive tumors. Right-sided obstructions are believed to occur with more bulky tumors capable of overcoming a larger circumference, which are linked to worse oncologic outcomes. In our study RCC tumor presenting with obstruction had no worse outcomes.⁷

Conversion was also associated with worse survival outcomes when patients were stratified by pathological stages II and III. Other series did not find differences in oncologic outcomes between conversion and laparoscopy. Martinek et al.,⁹ showed a tendency toward a longer survival (OS and DFS) period in the laparoscopic group compared to conversion, but no statistically significant difference was confirmed. In multivariate analysis, pT3e4 cancer and poor differentiation were independent predictors of both lower OS and lower DFS, whereas leakage and lack of adjuvant chemotherapy were independent risk factors only of lower DFS.⁸

Conversion has been previously associated with demographic and perioperative factors such as gender, comorbidities, tumor size and location, patient selection, intraoperative complications, and surgeon experience. Many factors could be associated with worse survival in converted patients. This includes tumor stage, more inflammatory response due to conversion and possibly more postoperative complications. In our study, we could not identify any of those factors.

One reason for the poor survival of elderly patients could be attributed to the increased rates of cancer-unrelated death; however, 90.7% of deaths in the training cohort of our study were related to primary cancer progression, and 85.4% of those in the validation cohort were also cancer related. We found that patient survival times after recurrence in the right side of the colon were shorter than for those after recurrence in the left side. Recent studies showed poorer prognoses in patients with right-side colon tumors even after background adjustment, which is possibly because of the difference in malignant potential.⁹

Our study showed that the poorer prognoses in patients with cancers located on the right side of the colon were also true for recurrent tumors. These findings might be explained by the reported differences in the molecular and cellular features of right-side tumors, such as microsatellite instability or CpG island methylation. Interestingly, a history of adjuvant chemotherapy after primary surgery showed no effect on survival once a patient developed recurrence, although the benefit of adjuvant chemotherapy on overall survival has been well established.⁹

According to Klaver et al., in this large multicentre cohort of pT4 colon cancer patients treated with curative intent, it is shown that SSIs, both deep incisional and organ/space SSIs, increase the risk of intraabdominal recurrence, also translating into worse DFS and OS.¹⁰ In our study four patients had SSI in open wound and there were no reports of recurrence or worse survival.

According to Lee et al., colon cancer with sealed-off perforation showed no difference in prognosis compared with free perforation even after propensity score matching was performed. One of our patient had sealed and adherent perforation of sigmoid colon, at laparotomy it was deemed in operable and the patient is PFS for one year with FOLFIRI chemotherapy.

According to Liu et al., confirmed the feasibility and compared the advantages and disadvantages of two techniques. SILS had some advantages, such as shorter hospital stay, smaller incision length, more rapid time to return to bowel function, slighter pain score, and a lower complication rate. SILS and CLS had several similar clinical outcomes, such as blood loss, rate of conversion to open surgery, anastomotic fistula rate, readmission, local recurrence, and distal metastases.

COST trial(clinical trials of surgical therapy) suggest that it is safe to proceed with laparoscopically assisted colectomy in patients with cancer. Patients prefer to undergo minimally invasive procedures even if the benefits are limited, possibly because aesthetic results are considered to be better. The absence of oncologic risk and the resulting marginal short-term benefits counterbalance the longer operative times and provide support for plans to conduct comprehensive analyses of the quality of life, cost, and cost effectiveness of laparoscopically assisted colectomy.

Overall, there were no statistically significant differences in overall survival or DFS between surgical techniques when analysed by TNM stage. A trend favouring survival following laparoscopic resection of stage III colonic cancer has been reported previously, although these findings have since been explained as an outlier effect owing to underpowered subgroup analysis. The long-term follow-up of CLASICC has shown a converse trend, favouring open surgery in patients with stage III colonic cancer. Although this appears to suggest worse oncological outcomes associated with laparoscopic surgery, the numbers at risk are small and no confirmatory reports have been found. Any real effect therefore remains speculative, and it is evident that caution should be employed pending further research in this group of patients.

COLOR (Colon carcinoma Laparoscopic or Open Resection) is a European multicenter randomized trial which has started in September 1997. In 24 hospitals in Sweden, The Netherlands, Germany, France, Italy and Spain, 1,200 patients will be included. The primary end point of the study is cancer-free survival after 3 years and results are MIS not inferior to open method.

Laparoscopic colectomy for cancer has now been extensively compared with traditional open surgery in the context of randomized studies. From this review of the best available literature, we conclude that laparoscopic resection for colon cancer is associated with numerous short-term benefits, including decreased postoperative pain and analgesia requirements, speedier recovery of bowel function, shorter length of stay in hospital, and potentially a decreased rate of wound infection. As well, patients undergoing laparoscopic colectomy may demonstrate benefits in quality of life, particularly in terms of social functioning.

Patients undergoing MIS have less release of tissue factor and inflammatory cytokines that compromise recovery. Hence although MIS is equal to open method in RCC it is preferable over open method.

CONCLUSION

However stage wise recurrence patterns hardly differ in RCC and LCC. Also laparoscopic versus open methods also do not significantly contribute to recurrence patterns among RCC and LCC. Laparoscopy is favorable LCC than RCC.

FIGURE : 1
FLOW-CHART.

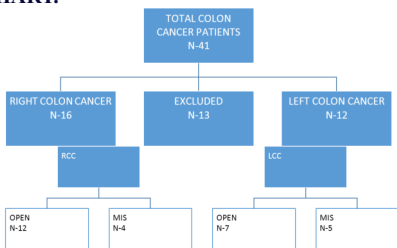


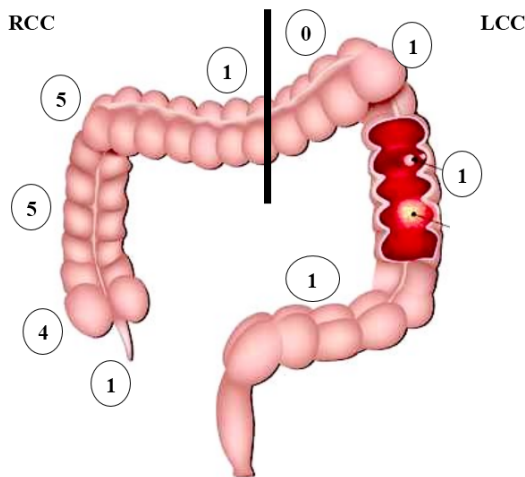
TABLE : 1

	n	OPEN	MIS
APPENDIX	1	1	0
CAECUM	4	2	2
ASCENDING COLON	5	4	1
HEPATIC FLEXURE	5	5	0
PROXIMAL2/3 TRANSVERSE COLON	1	0	1
DISTAL1/3 TRANSVERSE COLON	0	0	0
SPLENIC FLEXURE	1	1	0
DESCENDING COLON	1	0	1
SIGMOID COLON	10	7	3
	28	20	8
RCC/LCC	16/12	12/8	4/4

TABLE : 2

S.NO	PARAMETER	RCC n:16	LCC n:12
1	AGE <50;>50	10:6	4:8
2	GENDER M:F	12:4	9:3
3	ABDOMINAL PAIN	16/16 (100%)	6/12 (50%)
4	LOWER GI BLEED	3/13 (23%)	10/13 (77%)
5	HEMOGLOBIN		
6	ALTERED BOWEL HABBITS	9/20 (45%)	11/20 (55%)
7	ABDOMINAL MASS	12/20 (60%)	8/20 (40%)
8	METASTATIC DISEASE	0	1
9	COLONOSCOPY	13/20 3/7	7/20 4/7
10	CEA		
11	COMORBIDS	4/7	3/7
12	PATHOLOGY I:II:III	5:9:1	1:9:2
13	STAGE I:II:III:IV	1:5:9:0	0:4:6:1

FIGURE : 2



RCC	LCC
M>F 3:1	M>F 3:1
Pain 100%	Pain 50%
Mass 60%	Mass 40%
LGI 23%	LGI 77%
Altered Bowel habits 45%	Altered Bowel habits 55%
Low +	Low ++
	Obstruction +

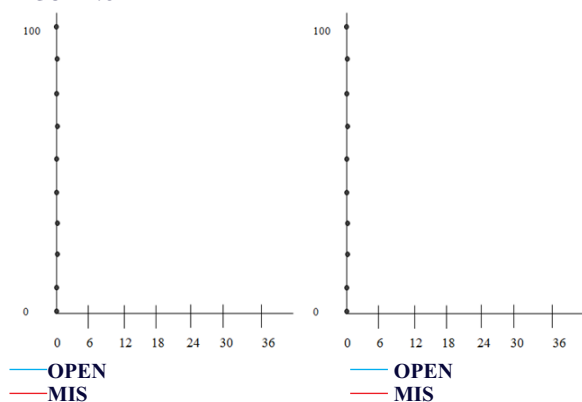
TABLE : 3 Recurrences

	OPEN	MIS
RCC	2/12 (16.6%)	Nil
LCC	2/8 (25%)	Nil

TABLE : 4 Mortality

	OPEN	MIS
RCC	Nil	Nil
LCC	3/8 (37.5%)	Nil

FIGURE : 3



No.	Surgical Step	RCC		LCC	
		OPEN	MIS	OPEN	MIS
	Time to intraperitoneal manipulation		Fast		Fast
	Evaluation of metastatic disease		Better		Better
	Peritoneal Metastatic disease		Better		Better
	Multi organ involvement	Better		Better	
	Intraperitoneal adhesions	Better		Better	
	Bowel handling	Better		Better	
	Vascular pedicle ligation	Better		Better	
	Lymph node retrieval	Equal		Equal	
	Specimen Retrieval	Easy		Easy	
	Bowel anastomosis	Easy		Easy	
	Colostomy	Easy		Easy	
	Postoperative analgesia		Less		Less
	Parenteral Antibiotics		Less		Less
	Time to Bowel Movement		Quick		Quick
	Adjuvant chemotherapy starting		Early		Early
	Total Time of Surgery				
	Average blood loss	equal	equal		<200ml
	Length of Incision		less		less
	Margins Proximal	Equal	equal		good
	Margins Distal	Equal	equal		good
	30 day mortality	Equal	equal		least
	Complication (Intra operative)	Equal	equal		less
	Conversion to open procedure – Reason				
	Port site/Incision site recurrence		1 case		2 cases

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