Title: Feasibility of multi-visceral resection in locally advanced colorectal cancer: Experience of a tertiary cancer centre in North-East India

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FEASIBILITY AND OUTCOMES OF MULTI-VISCERAL RESECTION IN LOCALLY ADVANCED COLORECTAL CANCER: EXPERIENCE OF A TERTIARY CANCER CENTRE IN NORTH-EAST INDIA

ABSTRACT:

PURPOSE

Locally advanced colorectal cancer may require an en bloc resection of surrounding organs or structures to achieve complete tumour removal. This decision must weigh the risk of complications of multi-visceral resection against the potential survival benefit.

The purpose of this study is to review a single centre experience of feasibility of en bloc multi-visceral resections for locally advanced colorectal carcinoma and to examine the effect of surgical experience on immediate outcome and rate of R0 resections.

METHOD

This is a study of twenty-seven patients who underwent multi-visceral resection for locally advanced colorectal carcinoma which was performed at our institute from January 2016 to December 2019. Among the twenty-seven patients, aged between 21 and 76 years (mean age: 48.67± 7.3 years), thirteen were males and fourteen were females. Overall eighteen patients had primary colon carcinoma and nine had primary rectal carcinoma. All rectal cancer patients received neoadjuvant chemoradiation. All patients underwent surgery with curative intent. All patients underwent open surgery of which 66.67% underwent colectomy, 14.81% underwent Anterior resection, 11.11% underwent Miles’ procedure and 7.40% patients underwent pelvic exenteration.
RESULTS

The mean operative time was 268.14 ± 72.2 min and the median amount of blood units transfused was 2.07 units. The mean hospital stay was 13.67 ± 3.4 days. Histologically, 44.44% patients had well differentiated adenocarcinoma and 55.56% patients had moderately differentiated adenocarcinoma. Final histopathological examination revealed malignant infiltration of the adjacent organs in 19/27 patients (70.37%). Pathological complete response was seen in 2 patients. R0 resection rate achieved was 96.29%. Lymph node metastasis was seen in 66.67% patients with colon cancer and 11.11% patients with rectal cancer with overall mean number of harvested lymph nodes being 12.44 ± 3.01. Postoperative complications were identified in seven patients (25.92%), while mortality was seen in two patients (7.40%).

CONCLUSION

Multi-visceral resection for advanced colorectal cancer invading into the adjacent organ may be performed with acceptable morbidity and mortality.

KEYWORDS: Advanced colorectal cancer, multi-visceral resection, surgical resection.

INTRODUCTION

Globally, colorectal cancer (CRC) accounts for approximately 10% of all new cancers\(^1\). Colorectal cancer invading into the adjacent organs/structures is detected in 5 to 20% of all surgical interventions performed for the management of colorectal cancer\(^2\). These adhesions may be either due to frank tumour infiltration or due to peritumoral inflammation. However, the nature of these adhesions cannot be ascertained intraoperatively. Therefore, the standard
management entails en bloc resection of the diseased organ along with adjacent organ infiltration. Neoadjuvant treatment with chemotherapy or radiation or a combination of both can significantly lead to downsizing of the disease thereby facilitating resection of the tumour with safe radial and circumferential margins.

We share our experience regarding the feasibility of en bloc multi-visceral resection for advanced CRC, the immediate surgical outcomes in regards to morbidity and mortality and the proportion of R0 resections.

**METHOD**

Twenty-seven patients underwent multi-visceral resection for locally advanced colorectal carcinoma at our institute from January 2016 to December 2019. Among the twenty-seven patients, aged between 21 and 76 years (mean age: 48.67± 7.3 years), thirteen were males and fourteen were females.

Pre-treatment staging was done by taking a detail history and conducting a physical examination in the outdoor office. Pre-treatment complete blood tests and carcinoembryonic antigen (CEA) levels were obtained. Full colonoscopy was performed in all patients. Patients with colonic and upper rectal primary underwent contrast enhanced computed tomography (CECT) of the abdomen and thorax. Those with disease in the mid rectum, lower rectum and anorectum underwent magnetic resonance imaging (MRI) of the pelvis and CECT of the abdomen and thorax. Patients in whom imaging suggested stomach infiltration, underwent esophago-gastro-duodenoscopy.

Four patients with obstructive symptoms underwent faecal diversion before commencing the treatment.

The rectal cancer patients received pre-operative chemoradiation with Capecitabine and 50.4 Gy in 28 fractions. They were re-evaluated with MRI 6-8 weeks later. One patient
who achieved significant symptomatic relief after chemoradiation defaulted for 2.5 years.

One patient with mid-rectal tumour received four cycles of chemotherapy (5-Fluorouracil + Oxaliplatin) after radiation when the radiological circumferential margin was deemed to be positive.

All patients with colonic primary were taken up for upfront surgery.

CEA levels were elevated (> 3ng/ml) in 77.77% patients (21/27). All patients underwent surgery with curative intent. All patients underwent open surgery of which 66.67% underwent colectomy, 14.81% underwent Anterior resection, 11.11% underwent Miles’ procedure and 7.40% patients underwent pelvic exenteration.

The criteria for multi-visceral resection was based on imaging features, mainly bulky disease in the primary with loss of fat planes with the adjacent or surrounding structures or organs or frank infiltration. Multi-visceral resection was pre planned in all patients.

Intra-operatively, multi-visceral resection was performed when the tumour bearing part could not separated from the surrounding structures or organs without compromising the oncologic outcomes.

Colectomy – Resection of the tumour bearing colon with longitudinal margins of at least 5 cm on either side, the corresponding mesocolic tissue along with a D3 lymphadenectomy i.e removing the nodal tissue along the lateral part of the superior mesenteric artery.

Anterior resection – For tumours of the recto-sigmoid junction, upper and middle rectum, removal of the rectum with at least a 5 cm margin proximally and 2 cm margin distally, total mesorectal excision, with high ligation of the inferior mesenteric artery.
Miles procedure (proctosigmoidectomy) – For low rectal and anorectal tumours when sphincter salvage is not possible, total mesorectal excision, high ligation of the inferior mesenteric artery and a permanent end sigmoid colostomy.

Pelvic exenteration – Removal of all the pelvic organs i.e anorectum, urinary bladder and uterus in females with permanent faecal and urinary diversions.

RESULTS

The mean operative time was 268.14 ± 72.2 min and the median amount of blood units transfused was 2.07 units. The mean hospital stay was 13.67 ± 3.4 days. Histologically, 44.44% patients had well differentiated adenocarcinoma and 55.56% patients had moderately differentiated adenocarcinoma. Final histopathological examination revealed malignant infiltration of the adjacent organs in 19/27 patients (70.37%). R0 resection rate achieved was 96.29%. Lymph node metastasis was seen in 66.67% patients with colon cancer and 11.11% patients with rectal cancer with overall mean number of harvested lymph nodes being 12.44 ± 3.01. Postoperative complications were identified in seven patients (25.92%), while mortality was seen in two patients (7.40%). The demographic details, location of tumour, pre-treatment CEA levels, ASA score, complications, post-operative hospital stay and post-operative histopathology information is shown in Table I.

The adjacent organs resected are shown in Table II.

We obtained pathologic complete response in two patients of rectal cancer post chemoradiation.

The first was a case of mid rectal tumour with urinary bladder infiltration. The patient received capecitabine based long course chemoradiation. Post chemoradiation and pre
surgery MRI showed dense adhesion of the disease site with urinary bladder and the uterus. She underwent pelvic exenteration, i.e removal of urinary bladder and uterus with bilateral adnexae in addition to proctectomy.

The second was also a mid rectal tumour in a post menopausal lady with infiltration into the uterus. The patient received capecitabine based long course chemoradiation. Post chemoradiation and pre surgery MRI showed persistent adhesion between the disease site and the uterus. She underwent hysterectomy and bilateral salpingo-oophorectomy in addition to proctectomy.

In both the cases it was difficult to ascertain on imaging and even intra-operatively whether the adhesion was due to persistent disease or radiation induced fibrosis.

Pre-operatively the patients were counselled accordingly and informed consent was obtained to go ahead with multi-visceral resection.

Since all the patients in our study were in stage III, they received Capecitabine and Oxaliplatin adjuvant chemotherapy (except the 2 mortalities). Adjuvant therapy was decided based on pre chemoradiation clinical staging.

The median follow up period is 17 months (range 2-61 months).

There were three recurrences in the follow up period, two local and one systemic. Local recurrences were seen in the pelvic side wall in a rectal cancer patient who underwent R1 resection, anastomotic site recurrence with kidney infiltration and encasement of upper ureter. Systemic recurrence was in the form of peritoneal disease.

**Summary of short term outcomes**

Peri-operative mortality seen in two patients. (7.40%)

R0 resection was performed in 26/27 patients. (96.29% cases)
Final histopathology revealed adjacent organ infiltration in 19 cases. (pT4b – 70.37%)

All surviving patients received adjuvant chemotherapy.

**DISCUSSION**

It may be difficult to differentiate intra-operatively malignant infiltration of colorectal tumour from inflammatory adhesion. Therefore, the standard management protocol mandates en bloc resection of the tumour along with the adjacent organ. In our study, malignant infiltration was histo-pathologically confirmed in 70.37% patients. Nishikawa et al\(^3\) in their study reported adjacent organ infiltration in 60.9% patients, Eveno C et al\(^4\) reported 64.5% adjacent organ infiltration and Gebhardt C et al\(^5\) had 55% adjacent organ infiltration. Few previous studies demonstrated adhesions between tumor and other organs harbor malignant cells in 25-40% of cases, which are lower rates compared with our study\(^2,6,7\).

Local recurrence rates are also reported to be higher when the adjacent organs were dissected from the the tumour than when en bloc resection is performed\(^8\). R0 resection is known to be one of the most important prognostic factors in the management of locally advanced colorectal cancer\(^9\). The rate of R0 resection, as reported in literature varies between 40-90\(^%\)\(^10\).

In our study, R0 resection was performed in 96.29% patients; 18/18 patients with colonic primary and 8/9 patients with rectal primary. Eveno et.al. reported there were 89.5% R0 resections in patients with clinical T4 colorectal cancer, but also reported R1 resections were due to invasion of the resection margin of an adjacent organ in 5.2% patients and due to invasion of the circumferential resection margin in 9.9% patients and one R2 resection due to a large rectal cancer\(^4\). Derici et al, in a retrospective study, reported there were 75.4% R0 resections in rectal cancer patients with macroscopically direct invasion to adjacent organs or structures and 82.8% R0 resection in patients who received neoadjuvant CRT\(^11\).
Three patients in our series developed recurrence. Circumferential resection margin was positive in one lower rectal cancer patient who developed recurrence in 11 months with pelvic side wall infiltration, colo-vaginal fistula and died 17 months after completing treatment.

One patient with splenic flexure growth who underwent curative treatment developed anastomotic site recurrence after 18 months with frank infiltration into the left kidney and encasement of the left upper ureter. The patient underwent curative surgery for recurrent disease with left nephro-ureterectomy.

One patient developed peritoneal recurrence after 14 months with a PCI index of 6 for which secondary cytoreduction was performed.

One patient was lost to follow up.

The oncologic outcomes of the multi-visceral resections are reported as overall survival rates of 30-53%\textsuperscript{2,4,11}. We could not demonstrate a distinct survival advantage due to limited number of patients and the relatively short follow up period. Kaplan-Meier curve of overall survival is shown in Graph I.

Graph I: Kaplan-Meier curve of overall survival
Multi-visceral resection has been shown to be an independent factor for post-operative complications and peri-operative mortality\textsuperscript{12}. Studies report postoperative morbidity and mortality rates after multi-visceral resection in the range from 28.0 to 43.7\%\textsuperscript{2,3,7,11,13-15} and \( \geq 13\%\textsuperscript{4,6,11,16} \), respectively. In our study post-operative complications were identified in 25.92\% patients. There were two mortalities (7.4\%) in our study.

Limitations of our study: First, it is a single centre study with a limited number of patients. Second, the follow up period is relatively short with proportionately more cases being done over the past 12 months.

**CONCLUSION**

Complete removal of all gross and microscopic disease remains the key to achieve long term outcomes in locally advanced colorectal cancer. Multi-visceral resection can be performed at high volume centres with acceptable morbidity and mortality rates. Most of the recurrences occur within 2 years of completing treatment. Hence, meticulous follow up is of paramount importance during this period. Longer follow up is needed for survival data to mature.

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Conflicts of Interest : None
Acknowledgements : None

**REFERENCES**


Table 1: Demographic details, location of tumour, pre treatment CEA levels, ASA score, complications, post-operative hospital stay and post-operative histopathology information

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>Sex</th>
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<th>ASA score</th>
<th>Complications</th>
<th>Post Op Stay</th>
<th>Clavein Dindo scale</th>
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<th>Nodes</th>
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<td>14 days</td>
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<tr>
<td>47</td>
<td>F</td>
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<td>218</td>
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**pT4b seen in 19/27 cases. (70.37%)**
Abbreviations in table

M – Male

F – Female

CEA – Carcinoembryonic antigen

ASA – American society of Anesthesiologists

‘P’ stage – Post operative histopathology stage
<table>
<thead>
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<tr>
<td>Kidney + ureter</td>
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</tr>
<tr>
<td>Liver segment</td>
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<tr>
<td>Spleen</td>
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<tr>
<td>Pancreas</td>
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<tr>
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<td>Small bowel</td>
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<tr>
<td>Large bowel</td>
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</tr>
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<td>Vagina</td>
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<td>Uterus + ovary</td>
<td>8</td>
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<td>Urinary bladder</td>
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Fig. 1.

Clockwise from top left: Pelvic exenteration, left hemicolecetomy with splenectomy and distal pancreatectomy, transverse colectomy with sleeve gastrectomy and segmental jejunal resection
Clockwise from top left: 
- Pelvic exenteration
- Left hemicolectomy with splenectomy and distal pancreatectomy
- Transverse colectomy with sleeve gastrectomy and segmental jejunal resection