

Original Article

# Diagnosis of Adjacent Organ Invasion and Results from En Bloc Extended Resection for Locally Advanced Colorectal Cancer

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**Key Words**

Adjacent organ;

Direct invasion;

Colorectal cancer;

En bloc resection

**Purpose.** Surgical treatment remains as the only hope of cure for the patient with colorectal cancer. Not infrequently the adjacent organs are invaded by the primary tumor. Resection of organs involved might not only relieve patient's symptoms, but also increase the patient's hope for cure. The study is the retrospective analysis of the diagnosis and treatment of such kind of invasion.

**Materials and Methods.** From January 2000 to December 2009, 1583 cases of primary colorectal cancer were treated surgically by a single surgeon. Thirty-six patients (2.27%) had en bloc resection of locally advanced colorectal cancer with adjacent organ invasion. There were 17 men and 19 women. Age ranged from 28 to 84 years old, with an average of 60.9 years old. Enteral invasion occurred in 19 patients, urinary system involvement in fourteen patients and genital organ invasion in eight patients. Primary colorectal cancer were ten for rectal cancer, 20 for sigmoid cancer, four for descending colon cancer, one each for transverse colon and ascending colon cancer. Less than half of cases were diagnosed with image studies prior to surgery.

**Results.** Complications included three cases of urinary tract infection, two cases of wound infection and one case each for anastomotic leakage, intestinal obstruction, wound dehiscence and duodenal ulcer with perforation. Operative mortality was 2.8% (1/36).

**Conclusion.** This experience suggests that although direct invasion of the adjacent organ by primary colorectal cancer is not common, en bloc resection of the primary tumor with organ involved could be carried out with reasonable morbidity. Appropriate preoperative work up might detect some of the involvement, however, adequate exploration of the abdominal cavity during laparotomy is necessary to determine the extent of involvement. With help of multidisciplinary specialist, en bloc resection of involved organ offers the best interest for the patients.

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become the number one cancer in Taiwan. Although it is ranked number three in mortality, next to lung cancer and hepatic malignancy, improvement of prognosis still depends on early detection and effective treatment. Even with advancement of radiotherapy and chemotherapy, surgical treatment remains as the only hope of cure for the patient with colorectal cancer. Not infrequently the adjacent organs are invaded by the primary colorectal tumor. Resection of organs involved might not only relieve patient's symptoms, but also increase the patient's hope for cure.<sup>1-8</sup> The study is the retrospective analysis of the diagnosis of adjacent organ invasion and results from en bloc resection for locally advanced colorectal cancer by a single surgeon in a 10 year period. The hospital of the senior author has several specialists in different specialities, and the senior author himself has over 30 years' experience of colorectal surgery, he is capable of performing major resection for cure if needed and the disease is localized.

## Materials and Methods

From January 2000 to December 2009, 1583 cases of primary colorectal cancer were treated surgically by a single surgeon in a single institute. There were 958 colon cancers and 625 rectal cancers. There were 822 males and 761 females. Age ranged from 19 to 95 years, with an average of 64.4 years. There were 226 patients with Dukes' A tumors, 499 patients with Dukes' B tumors, 615 patients with Dukes' C tumors and 243 patients with Dukes' D tumors. (Table 1) All the patients who received elective surgery received appropriate work up, which included colon series or colonoscopy, ultrasound of abdomen, or CT scan of abdomen. Upper gastrointestinal endoscopy, upper gastrointestinal series, small bowel series and intravenous pyelography were reserved for the patients who were considered to be appropriate for their condition. RBC labeled technetium nuclear scan and angiogram were standard work up for the patients who presented with gastrointestinal bleedings. We agree that some of the above mentioned examinations are not the usual way of practice for the preoperative evaluation for

colorectal cancer; however, those studies are necessary and frequently indicated when upper GI pathology is suspected.

Some emergent cases were patients who were admitted through the emergency room and were explored by general surgical colleagues and then referred to the colon and rectal specialists for handling of colorectal problems. Exploration of the entire peritoneal cavity was possible for all cases and was performed for all cases in the series.

Thirty-six patients (2.27%) had en bloc resection of locally advanced colorectal cancer with adjacent organ invasion. Excluded were the patients who were not having primary colorectal cancer, who did not have surgical resections, who only had palliative resections and who had wide spread cancers. Wide spread carcinoma included the patients who had unresectable distant metastases like liver metastasis and peritoneal carcinomatosis. Less than half of cases were diagnosed with image studies prior to surgery. The other half patients were diagnosed during surgery by inspection, palpation and intra-operative ultrasound, including some patients who were having emergent surgery.

There were 17 males and 19 females fulfill the inclusions. Age ranged from 28 to 84 years old, with an average of 60.9 years old. Primary colorectal cancer were ten for rectal cancers, 20 for sigmoid cancers, four for descending colon cancers, one each for transverse colon and ascending colon cancer (Table 2). Single organ invasions occurred in 23 patients and multiple organ involvements occurred in 13 patients. Common invasion included enteral invasions in 19 patients, urinary system involvements in 14 patients and genital organ invasions in eight patients. Twenty-three patients with organ infiltration are node negative in this series.

**Table 1.** Stage in patients with colorectal cancer seen in 10 years

Dukes stage	Number of patients
A	226
B	449
C	615
D	243
Total	1,583

**Table 2.** Location of primary cancer in patients with adjacent organ invasion

Location	Number of patients
Rectum	10
Sigmoid colon	20
Descending colon	4
Transverse colon	1
Ascending colon	1
Total	36

The primary end points were progression-free survival and overall survival. Progression-free survival was defined as the length of time from surgery to disease progression or to death from disease progression or unknown causes. The overall survival was defined as the time from the surgery to death. Survival was evaluated using Kaplan-Meier survival test with the log-rank test. Survival curves were computed according to the Kaplan-Meier method and compared using log-rank test.

## Results

Colectomies for colorectal cancer included 20 sigmoidectomies, nine anterior resections, one abdominoperineal resection, four left hemicolectomies and two right hemicolectomies (Table 3). All the patient had R0 resection in this series. Most common procedures other than colectomies included 14 cystectomies, with 13 partial cystectomies and one total cystectomies; followed by resection of ileum in 13 patients, salpingoophorectomies in six patients and hysterectomies in five patients. Only 19 patients had true invasion of the adjacent organ resected. Four patients were suspected to have adjacent organ invasions with image studies prior to surgery. Eight patients were diagnosed as having adjacent organ invasion prior to surgery following preoperative image studies, one of them was found without true invasion following surgery. Complications included three cases of urinary tract infections, two cases of wound infections and one case each for anastomotic leakage, intestinal obstruction, wound dehiscence and duodenal ulcer with perforation (Table 4). Operative mortality was 2.8%

**Table 3.** Operative procedure other than colectomy in patients with adjacent organ invasion

Operative procedure	Number of patients
Cystectomy	14
Partial	13
Total	1
Ureterectomy	1
Partial nephrectomy	1
Salpingoophorectomy	6
Hysterectomy	5
Partial	1
Total	4
Resection of ileum	11
Resection of jejunum	3
Resection of duodenum	1
Resection of cecum	2
Resection of sigmoid colon	1
Appendectomy	1
Partial pancreatectomy	2
Splenectomy	2

**Table 4.** Complications following surgery in patients with adjacent organ invasion

Complication	Number of patients	%
Urinary tract infection	3	8.3
Wound infection	2	5.6
Anastomotic leakage	1	2.8
Intestinal obstruction	1	2.8
Wound dehiscence	1	2.8
Duodenal ulcer with perforation	1	2.8

(1/36). Operative mortality was defined as the patient who died within one month following surgery. The 82 year-old male was known to have multiple associated disease included hypertension, old CVA, chronic renal insufficiency and gastrointestinal bleeding. Operation was initially delayed for two months due to malnutrition and unwillingness of families to agree to have surgery. He had right hemicolectomy with ileocolic anastomosis and resection of jejunum with anastomosis. He eventually died of respiratory and renal failure. None of the patient received preoperative radiotherapy because preoperative radiotherapy was not the standard treatment during the study period in the hospital. However, radiotherapy was offered to the patient following surgery if indicated. It appeared that preoperative radiotherapy was not definitely going to

change the results in this series.

Subsequent follow up revealed two patients had resection of recurrent or metastatic lesions, both of them were surviving and healthy 8 years later. Three patients received radiotherapy, complicated by radiation enterocolitis, but still alive after second operation. One patient had second operation of lysis of adhesions and closure of colostomy three months later, he died of tuberculosis related respiratory failure and urinary tract infection seven months following initial surgery for cancer.

Four patients were excluded from survival analysis: a patient was lost in follow up, a patient died of postoperative complications, a patient died of respiratory failure following second operation, and a patient with Dukes' D lesion and pathology proven liver metastasis.

The overall survival and disease free survival for all patients with adjacent organ invasion is shown in Fig. 1. The disease free survival in the Dukes' B and C patients with adjacent organ invasion was shown in Fig. 2. The overall survival in the Dukes' B and C patients with adjacent organ invasion was shown in Fig. 3. Although most series suggested emergent surgery has worse prognosis, there is no definite trend suggested so in the series.

## Discussion

Locally advanced colorectal cancers represent 5-22% of all colorectal carcinomas.<sup>1-8</sup> Failure for local control, especially in locally advanced colorectal cancer, will result in devastating conditions such as intestinal or urinary obstruction, lower gastrointestinal bleeding, and adjacent organ failure. Therefore, the successful local eradication of locally advanced colorectal cancer will provide better quality of life as well as survival benefit. However, en bloc resection, which has been regarded as one of the important principles in surgical oncology, is not always feasible. This series only includes the patients who could have en bloc resection for cure, so the patients with incurable wide spread metastatic disease were not included in the series. It is not surprising that the curative

resection of this series is relatively low.

There was an argument of how a colon cancer with invasion to the adjacent organ but without lymph node or distant metastasis should be classified. It is widely accepted that the depth of invasion is a prognostic factor in colon cancer, especially in stage II, or Dukes' B cancer. The UICC staging system separated T3N0 from T4N0 colon cancer, categorizing T3 stage into group a (T3N0), whereas T4 stage into group b (T4N0). The Erlangen group analyzed a group of stage II colonic cancer patients and identified T4 stage

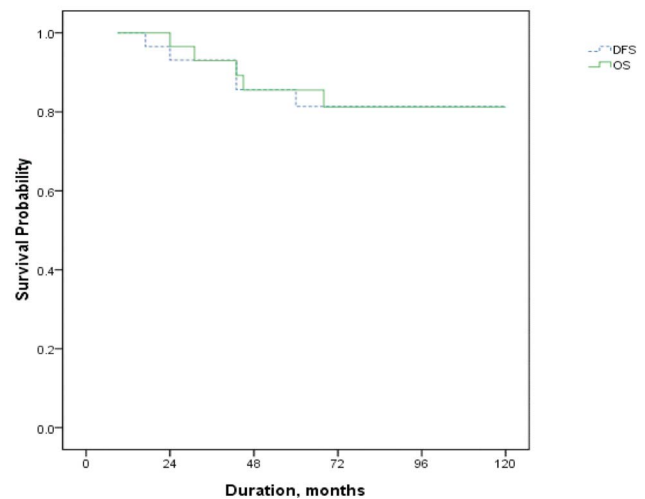


Fig. 1. Overall survival and disease free survival in all patients with adjacent organ invasion.

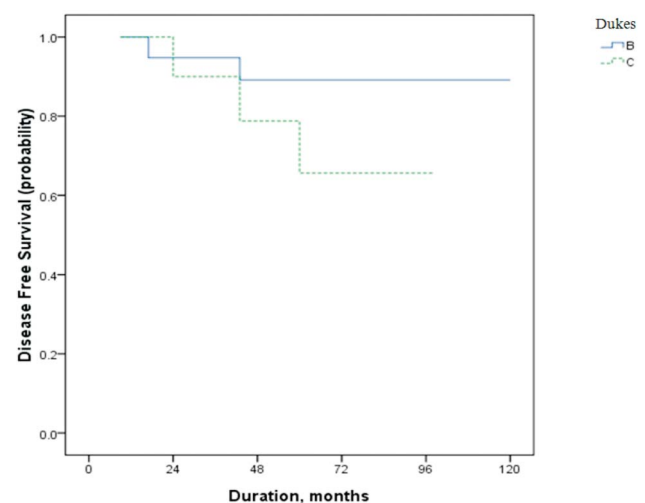
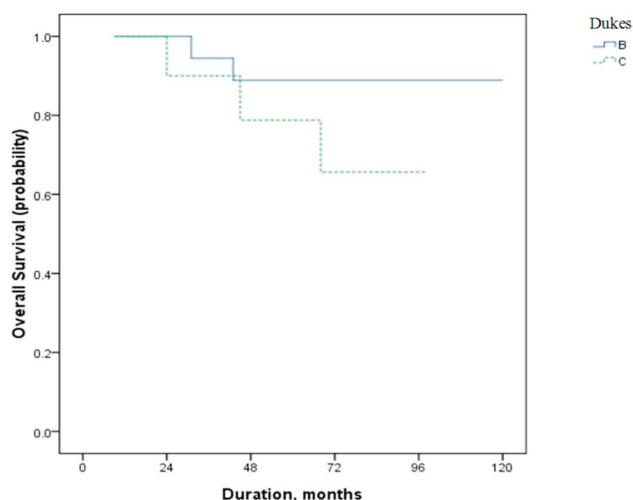


Fig. 2. Disease free survival in the Dukes' B and C patients with adjacent organ invasion.



**Fig. 3.** Overall survival in the Dukes' B and C patients with adjacent organ invasion.

as a predictor of poor prognosis.<sup>9</sup> Recent study confirmed that T4 stage is an important independent prognostic factor.<sup>10</sup> On the contrary, many investigators have reported the feasibility of the en bloc resection and some have shown a fairly good long-term prognosis.<sup>11,12</sup> Most experts would believe this group of patients should be classified as Dukes' B or stage II instead of Dukes' D or stage IV.

In the present study, we analyzed the surgical outcomes of patients with locally advanced colon cancer who had undergone en bloc combined resection to examine the feasibility of the procedure and to find out the prognostic significance of contiguous invasion.

Locally advanced colorectal cancer is characterized by tumor infiltration or adherence to adjacent organs in the absence of distant metastases.<sup>1-8</sup> The rationale for en bloc combined resection is that microscopic tumor infiltration into adjacent organs cannot be ascertained preoperatively or even intraoperatively. If the tumor involve major organ like pancreas, a surgeon specialized in pancreatic surgery would be consulted to decide whether en-bloc resection for cure is possible. If the patient cannot be cured, then a stoma or gastroenterostomy would be performed. However, in this series, only patients with en-bloc resection were included. In our cases, final pathology supported that there were only 19 patients truly had invasion of the adjacent organ resected.

Since the preoperative staging modalities such as CT scan are unreliable in demonstrating local tumor infiltration, contiguous invasion to adjacent organs is often encountered at laparotomy. It is also impossible in most cases to differentiate true tumor infiltration macroscopically from peritumorous inflammatory adhesion. Although CT scan has been used for most of patients for staging prior to surgery, however, the accuracy is not as high as it expected to be. In our study, CT scan predicted the possibility of true tumor invasion in only 12 (33.3%) patients. However, one patient was found not to have true invasion following surgery. The rate of correct diagnosis of direct invasion by CT scan is also similar to other report series. Reportedly, histologic tumor infiltration is demonstrated in 39-84% of cases in which the tumor is found to be adherent to the adjacent viscera whereas the rest represent inflammatory adherence.<sup>3,5,7,8,10-17</sup> It is also found that there is no difference in survival data between cases with true tumor invasion to those cases with only inflammation adhesion in this series, which might be due to small size of population.

Any attempt to separate the carcinoma from adherent organs may lead to tearing or transection of the tumor with the risk of intraoperative dissemination of tumor cells, resulting in early local recurrence.<sup>1,3,5,13</sup> Therefore, en bloc combined resections are obligatory in these cases to avoid tumor cell spillage by cutting into the tumorous mass. Intraoperative assessment of tumor involvement using biopsy or frozen section is also unwise because they are associated with high rates of false-negative results and the risk of tumor spillage and dissemination, which results in high local recurrence rate.<sup>3-5</sup> Therefore, if adherence is encountered during exploration, it is rationale to assume that it is true tumor invasion and then to proceed with en bloc resection whenever technically feasible.

En bloc resection can be justified if it provides a reasonable benefit accompanied with acceptable mortality and morbidity. Benefits of the procedure include not only good survival rate but also relief from symptoms. Authors have shown that en bloc resection of adjacent involved organs in locally advanced colon cancer can achieve good local control and produce a

5-year survival of 50-77%.<sup>10,11,18</sup> Without en-bloc-resection, the patient would have continuous symptoms like pressure sensation, tenesmus, urinary frequency and intestinal obstruction etc. En-bloc-resection would certainly exempt patients from having above symptoms. It was difficult to use quality score to apply in such kind of setting; however, en-bloc-resection certainly can affect patient's quality of life.

Despite survival benefits and better quality of life, literatures demonstrated that patients undergoing extended resections experience higher postoperative morbidity and mortality.<sup>11,18</sup> The overall morbidity rates were 49.1% in multivisceral resection group versus 17.8% in standard operation group ( $p < 0.0001$ ) in Nakafusa's report.<sup>11</sup> Others have reported that extended resection for colorectal cancer has been achieved with acceptable morbidity and mortality rates.<sup>7,13,14,18</sup> However, postoperative morbidity rate was shown to be high in most of their reports.<sup>7,13,14</sup> With the improvement of postoperative care and surgical techniques, postoperative mortality and morbidity rates have decreased and are comparable to the rates achieved with standard or nonextended resection. In our series, there was only one operative mortality, however, some significant morbidity other than minor wound problems still encountered. This result would make this procedure a far more feasible and safe approach in modern times.

Adjacent organ invasion is most frequently observed in sigmoid colon and rectal cancer, representing 66-89% of the cases.<sup>1,4,5</sup> This may be due to cancer predilection and redundancy of sigmoid colon. In our series, the predilection site was also the sigmoid colon. Locally advanced tumors of the left colon may directly involve the left kidney, spleen, abdominal wall, stomach, and distal pancreas. Sigmoid cancer may invade the bladder, ovaries, and uterus. It is not going to say that total cystectomy is unnecessary in all patient with bladder invasion, however, we believe that partial cystectomy, not total cystectomy offers patients good oncology outcome without much sacrifice of the life quality.<sup>19-21</sup> Similarly, we also felt that totally hysterectomy is not routinely necessary while facing the tumor with direct invasion of the cancer to the uterus. Partial hysterectomy is probably all needed. Locally

advanced carcinoma of the right colon adherent to adjacent organs is relatively rare. In author's opinion, if it is R0 resection which is the case in this series that all patients had R0 resection, there is no difference in cure between partial hysterectomy and total hysterectomy. Moreover, the patterns of infiltrated organ are quite different. Right-sided colon cancers may compromise the liver, pancreas, duodenum, and right kidney. The management of advanced right colon cancer with adherence to the duodenum or pancreas or both represents a dilemma for the colorectal surgeon. Pre-operative imaging does not provide proper information about duodenopancreatic invasion. Upper gastrointestinal endoscopy may also fail to identify duodenal infiltration, because tumor infiltration may be limited to the muscle layer without invasion of the duodenal mucosa. A large mass invading the duodenum or pancreas was present in 3 patients with pathologic examination showing infiltration of the duodenum and pancreas. It has been suggested that in this particular situation, intraoperative decision making to perform pancreatoduodenectomy is difficult. Tumorous mass is usually too bulky to measure adequate margins. Patients found to have limited duodenal wall adherence may be safely treated by a local resection and duodenal repair whereas those with involvement of larger parts of the duodenal wall or pancreas require a pancraticoduodenectomy.<sup>22-24</sup> We have not encountered patients underwent pancreatoduodenectomy in the present series.

All the patients who received elective surgery in this series received appropriate work up, which included colon series or colonoscopy, ultrasound of abdomen, or CT scan of abdomen. Upper gastrointestinal endoscopy, upper gastrointestinal series, small bowel series and intravenous pyelography, RBC labeled technetium nuclear scan and angiogram was reserved for the patients who were considered to be appropriate for their condition. Despite appropriate work up, only a portion of the patients were suspected or even diagnosed to have direct invasion of the adjacent organ by colorectal cancer. Some emergent cases were patients who were admitted through the emergency room and were explored by general surgical colleagues and then referred to the colon and rectal spe-

cialists for handling of colorectal problems. Exploration of the entire peritoneal cavity was possible for all cases and was performed for all cases in the series. Adequate exploration of the abdominal cavity during laparotomy is necessary to detect the involvement and determine the extent of resection.<sup>25</sup>

## Conclusion

This experience suggests that although direct invasion of the adjacent organ by primary colorectal cancer is not common, en bloc resection of the primary tumor with organ involved could be carried out with reasonable morbidity. Appropriate preoperative work up might detect some of the involvement, however, adequate exploration of the abdominal cavity during laparotomy is necessary to determine the extent of involvement. With help of multidisciplinary specialist, en bloc resection of involved organ offers the best interest for the patients.

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原 著

## 大腸直腸癌併周邊器官侵犯之手術治療

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**目的** 手術治療目前仍是治癒大腸直腸癌的唯一希望。然而，有時大腸直腸癌會併發周邊器官侵犯。切除周邊受侵犯器官，不僅能解除病人症狀，對於疾病根治也有很大的幫助。本研究為回溯分析手術切除大腸直腸癌併周邊器官侵犯之經驗。

**方法** 自 2000 年 1 月至 2009 年 12 月，共 1583 位病患接受單一外科醫師手術治療大腸直腸癌。其中 36 位病人 (2.27%) 因癌症侵犯周邊器官，同時接受周邊器官切除。共有 17 位男性及 19 位女性，年齡介於 28 至 84 歲之間 (平均年齡 60.9 歲)。其中 19 位病人癌症侵犯小腸，14 位侵犯泌尿系統，8 位侵犯生殖系統。而原發腫瘤有 10 位為直腸癌，20 位為乙狀結腸癌，4 位為降結腸癌，1 位為升結腸癌，1 位為橫結腸癌。這些病人中，不到一半的病人術前能依據影像作出周邊器官侵犯的診斷。

**結果** 3 位病人術後發生泌尿道感染，2 位發生傷口感染，腸道吻合處滲漏，腸道阻塞，傷口癒合不良，十二指腸潰瘍與穿孔各有一位。手術後死亡率為 2.8% (1/36)。

**結論** 大腸直腸癌侵犯周邊器官也許不是很常發生的案例，但此研究分析顯示完整切除受侵犯周邊器官的手術併發症與死亡率是可被接受的。術前完整的腫瘤分析對於腫瘤局部侵犯範圍的掌握有所幫助，但術中良好的手術視野與腫瘤範圍分析更是重要。而各專科醫師的共同努力，合作也更顯重要。

**關鍵詞** 大腸直腸癌、周邊器官侵犯。