### **Original** Article

# En bloc Resection in Multivisceral Resection to Treat Adenocarcinoma of the Colon

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#### Key Words

Locally advanced adenocarcinoma of the colon; En bloc resection; Prognosis *Purpose.* The aim of this study was to determine the outcome of en bloc resection in patients with adenocarcinoma of the colon.

*Methods.* Patients with locally advanced colon cancer who underwent surgery at Kaohsiung Veterans General Hospital between January 2004 and December 2012 were included. The records of all patients who underwent en bloc resection or non-en bloc resection were analyzed, retrospectively. The overall and disease-free survival (OS and DFS, respectively) rates were evaluated using the Kaplan-Meier method.

**Results.** In total, 1638 patients had colorectal adenocarcinoma; of these, 138 patients had locally advanced adenocarcinoma of the colon, including 83 men and 55 women, with a mean age of 64 years. Of these, 108 patients underwent en bloc resection and 30 did not (non-en bloc). The 5-year OS rate in the en bloc group was 22%, whereas in the non-en bloc group, it was 19% (p = 0.012). The 5-year DFS in the en bloc group was 70.9%, whereas in the non-en bloc group, it was 52.5% (p = 0.015).

*Conclusions.* En bloc resection could provide good prognosis in patients with locally advanced colon cancers. However, if en bloc resection is considered difficult, to ensure a good DFS rate, wide excision should be performed.

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Colorectal cancer is the most common cancer and the third leading cause of cancer-related death in Taiwan.<sup>1</sup> In the United States, of the estimated 100,000 colon cancer cases that present each year, 10-20% represent locally advanced disease, with tumors extending through the colon wall with perforation and/or invasion to adjacent organs or structures.<sup>2</sup> According to the American Joint Committee on Cancer staging such lesions are classified as T4 tumors.<sup>3</sup> Overall ~5-22% of locally advanced colon cancers present contiguous involvement of adjacent structures without distant metastases.<sup>4-10</sup> There is no standard definition for

locally advanced colorectal cancer, and the term has been used frequently as a synonym for tumors that invade adjacent structures. An alternative definition could be of a cancer with high fixation or adherence to a local site that cannot be resected easily because of the high risk of microscopic remnants or gross residual disease.<sup>11</sup> In 2006, Kapoor et al. demonstrated that en bloc resection of a right-sided invasive colonic adenocarcinoma was possible and resulted in low mortality and morbidity rates, and extended survival.<sup>12</sup> Histological infiltration has been observed in 55-70% of cases with viscera-adherent tumors (T4a).<sup>7,9,13,14</sup>

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While this does not represent invasion per se, it might reflect severe adhesion to the colon. Because inflammatory and neoplastic adhesions can only be distinguished through pathological assessment, separation of the affected organs is not advised because it could lead to tumor perforation and dissemination of malignant cells.<sup>15</sup> Until 60 years ago, infiltrative colorectal carcinoma was considered nonresectable.<sup>16</sup> However, since then, extensive surgical procedures aimed at complete resection of locally advanced primary colorectal carcinoma have been conducted. However, resection of such tumors, especially adherent tumors, can present a challenge, even for skilled surgeons. The proportion of adjacent structure involvement tends to be the highest in patients with T2-T3 colorectal cancers. These patients might require complex surgical intervention, involving en bloc organ resection plus colectomy. For locally advanced primary colorectal cancer, multivisceral resection provided the best longterm survival outcome, without affecting morbidity or 30-day mortality; however, it might increase operative duration, intraoperative bleeding, and perioperative transfusion requirements.<sup>17,18</sup> Patients who underwent adherent organ separation had a lower 5-year survival rate (0-23%) compared with those who underwent en bloc resection (40-61%).<sup>6,7,14</sup>

In the present study, we report our experience of en bloc resection to treat invasive or adhesive colon cancer. In addition, we compared the outcome of patients who underwent en bloc resection to that in patients who underwent non-en bloc resection.

## **Materials and Methods**

## Patients

The clinicopathological data of patients treated for a primary colon tumor, entered in the prospective database of Kaohsiung Veterans General Hospital between 2004 and 2012, were reviewed, retrospectively. Of the 1658 patients who underwent surgical resection, 138 had tumor adhesion or infiltration to adjacent organs. Patients who had undergone previous attempts at resection, who had carcinomatosis, tumor perforation, or distant metastases were excluded. Patients' demographics, resection procedures, perioperative complications, operative duration, and pathological characteristics were collected. All patients were followed until death or tumor recurrence. Due to the retrospective nature of the present study, the need for informed consent was waived.

The definition of en bloc resection here was mean take down the main tumor and adhesive organs in one specimen without dissection. Non-en bloc resection was making separated. Both them were all reach free margin of resection in pathologically. If the main tumor was detached from adjacent organs during dissection, the operator need to make a piece of tissue from margin of the main tumor and rapid examination with frozen technique by pathologist. If the surgical margin is residual cancer, wide excision of adjacent organ should be done. Even there was no tissue look like as malignancy in adjacent organ.

#### Statistical analyses

Relationships between various parameters were analyzed with the Chi-square or Mann-Whitney U test. The Fisher's exact test was used when the number of examined parameters was low. Kaplan-Meier estimates were used to calculate survival rates. The 3and 5-year overall survival (OS) and disease-free survival (DFS) rates were analyzed. OS was calculated from the time of surgery to death from any cause. DFS was calculated from the time of surgery to tumor recurrence or colon cancer-related death. All data were analyzed using SPSS Statistics, version 22 (IBM, Armonk, NY). A *p* value of < 0.05 was considered statistically significant.

## Results

### **Patient characteristics**

Patient clinicopathological characteristics are shown in Table 1. Of the 138 patients, 108 underwent en bloc resection, and 30 underwent non-en bloc resection. All patients underwent preoperative colonoscopy to determine tumor location and for histological confirmation of colon cancer. The mean follow-up intervals were 58 months (range, 10-92 months) and 35 months (range, 4-61 months) for the en bloc and non-en bloc groups, respectively. The most common location for locally advanced colon cancer in all patients was the sigmoid colon.

#### Invasion site characteristics

A comparison of organ involvement sites between the two groups is shown in Table 2. Overall, the most frequently invaded organs were the visceral peritoneum (n = 79), small intestine (n = 25), and urinary bladder (n = 20). The majority of patients who underwent en bloc resection had tumors with peritoneal invasion. Whereas, in the non-en bloc group, the most frequently invaded adjacent organs were the duode-

 
 Table 1. Characteristics of patients with colorectal cancer undergoing resection

	Ν	Non-en bloc N (%)	En bloc N (%)	<i>p</i> value
No. of patients	138	30	108	
Sex				
Female	55 (40)	13 (46)	42 (39)	0.660
Male	83 (60)	17 (54)	66 (61)	0.983
Mean age	64	64.84	63.82	
Location				0.351
Cecum	7	5	2	
Ascending colon	34	2	32	
Transverse colon	21	2	19	
Descending colon	7	5	2	
Sigmoid colon	40	17	23	
Rectosigmoid junction	23	2	21	
Pathology stage				0.912
Stage II (T4N0)	54	12	42	
Stage III	84	18	66	
T4aN1		4	32	
T4aN2/T4bN1-2		11/3	21/13	
Cell differentiation grade				0.005
Moderate	108	18 (60)	92 (83)	
Poor	30	12 (40)	18 (17)	
Tumor size (mean, mm)	61.85	71.37	59.20	0.011
Operative duration (min)	93-366	107-302 <sup>a</sup>	93-366 <sup>a</sup>	0.520
(Mean, min)	(208)	(235)	(201)	

<sup>&</sup>lt;sup>a</sup> The longest operative duration was for right-side

hemicolectomy + Whipple procedure.

num, urinary bladder, and uterus. All pathology had the free margin and no cancer cell seen microscopically.

#### **Postoperative outcomes**

The 3- and 5-year DFS rates for the entire cohort were 70.1% and 66.3%, respectively (Fig. 1). The 3and 5-year OS rates for the entire cohort were 51.8% and 21.4%, respectively (Fig. 2). The 5-year OS rates for the en bloc and non-en bloc groups were 22.2% and 19.1%, respectively (p = 0.012; Fig. 3). The 5year DFS rates for the en bloc and non-en bloc groups were 70.9% and 52.5%, respectively (p = 0.015; Fig. 4). The median times to recurrence for the en bloc and non-en bloc groups were 25 and 11 months, respectively. There were no significant differences in operative duration between the groups, although the longest operative duration was 366 minutes, which was for a right-side hemicolectomy with the Whipple procedure.

## Discussion

Previous series have demonstrated that in patients with advanced colon cancer, extended resection is the most consistent independent factor correlated with

Table 2. Involved structures

Organ or structure	Non-en bloc N = $30$	En-bloc N = 108
Visceral peritoneum <sup>a</sup>	13	66
Abdominal wall and small bowel	2	2
Duodenum	3	2
Jejunum	0	6
Liver and duodenum	0	2
Ovary	3	0
Pancreas head and duodenum	0	2
Small bowel	0	6
Stomach	0	2
Ureters and uterus	2	0
Urinary bladder	5	13
Urinary bladder and ileum	0	2
Uterus	2	5

<sup>a</sup> All of the patients were received multivisceral resection as the excision or resection of at least one further organ.





Fig. 1. Kaplan-Meier survival curve analysis of the 3 and 5-year disease-free survival of the entire cohort. The 3- and 5-year DFS rates for the entire cohort were 70.1% and 66.3%, respectively.



Fig. 2. Kaplan-Meier survival curve analysis of the 3 and 5-year overall survival of the entire cohort. The 3- and 5-year OS rates for the entire cohort were 51.8% and 21.4%, respectively.

survival benefit.<sup>5,6,14,22,23</sup> Therefore, complete resection is considered the gold standard treatment for locally advanced colon cancer.<sup>7,9,14</sup> Previous studies have indicated that, compared with non-en bloc resection, radical en bloc resection resulted in superior survival in patients with advanced colon cancer. They suggested that improved survival might be explained by the relatively low incidence of regional lymph node metastases in these patients.<sup>12,13,19,20</sup> High recurrence rates have been noted in patients who were not treated with en bloc resection.<sup>21</sup> Conversely, a high re-



Fig. 3. Kaplan-Meier survival curve analysis of the 3 and 5-year overall survival of patients undergoing en bloc resection vs. those undergoing non-en bloc resection (p = 0.012).



Fig. 4. Kaplan-Meier survival curve analysis of the 3 and 5-year disease-free survival of patients undergoing en bloc resection vs. those undergoing non-en bloc resection (p = 0.015).

currence rate (46%) has been reported in patients who were treated with en bloc resection.<sup>22</sup> In the present study, there was a clear survival advantages in patients who underwent en bloc resection compared with those who did not. Patients undergoing en bloc resection had significantly improved 3- and 5-year OS and DFS rates compared with patients who underwent non-en bloc resection. However, both groups showed good DFS rates (70.9% vs. 52.5%); this is probably because those in the non-en bloc group underwent extended excision of the primary tumor. Furthermore, the 5-year OS rate in the en bloc group was markedly superior to that in the non-en bloc group (22% vs. 19%). However, this might indicate that some adhesions that were easily separated were not truly invasive. Although operative duration tended to be longer in the non-en bloc group compared with the en bloc group, the difference was not significant.

It is worth bearing in mind that the same surgeon did not perform all operations, and that in some patients, en bloc resection was not performed because of the specialty of the surgeon involved. In addition, en bloc resection was contraindicated in some patients such as those with huge masses, in whom en bloc resection would result in serious physical injury. For these reasons, in the present study, some patients underwent non-en bloc resection but pathology should get free margin of the main tumor (R0 resection). If the surgical margin has residual cancer, wide excision of more adjacent organs should be done. Even there was no tissue look like as malignancy in adjacent organs.

The present study had several limitations. We focused on local recurrences rates but did not evaluate lymph node invasion, comorbidities, surgical complications, organ invasion status because the differences in these parameters between the groups were not significant.

Cellular differentiation grades in non enbloc resection group had more proportion in poor differentiated type may a factor of poor prognosis. The max numbers of involved organs were two in the study. The difference about the number of organs involved was not discussed due to the number of patients who had same organs involved in the study is too small to make a definitive recommendation.

In addition, although we assessed a large number of patients with colon cancer, only a small percentage of them had locally advanced colon cancer; therefore, the sample size included in the final analysis was small. Otherwise, some patients became lost to follow-up during a clinical research trial result in negative effects on the outcome and put a bias on the result of the study.

The numbers of organ involved were different between two groups, that may affecting the patient survival and recurrent rate. But the pathology stage had no significant difference between two groups.

In conclusion, en bloc resection resulted in superior survival rates compared with non-en bloc resection. Future studies investigating differences in factors such as lymph node invasion, complications, and intraoperative stage between en bloc and non-en bloc resection are warranted.

## Conclusions

In patients with locally advanced colon cancer, en bloc resection resulted in significantly superior survival rates compared with non-en bloc resection. We highly recommend en bloc resection in such patients, whenever possible. However, if en bloc resection is not feasible, patients should at least undergo wide excision and get free margin of the tumor to minimize recurrence.

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<u>原 著</u>

# 探討完整切除對於大腸癌併多器官切除 之重要性

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**目的** 手術時發現有局部侵犯及發炎的大腸癌建議做同時完整切除沾黏鄰近器官會有較 好的預後,但過去醫學文獻報導發表個案數少,且有時因手術複雜需實施分段切除,比 較本院過去病例找出可能影響的因素以及兩者預後的差別。

**方法** 從 2004 年 1 月至 2012 年 12 月間,收集高雄榮民總醫院外科部大腸直腸外科有 接受手術發現局部侵犯的大腸癌病例。回朔性地回顧完整切除腫瘤及鄰近器官和分段切 除的病例,比較這兩組病人的病理切片,治療和癒後,將資料統計分析並比較其中的差 異加以呈現。

**結果** 共 1638 位大腸直腸癌病患在期間內接受手術,138 位病患 (83 位男性、55 位女性) 有局部侵犯的大腸腫瘤被收錄於研究中。108 位接受完整切除腫瘤及鄰近器官,30 位接受分段切除。兩組間年齡、性別、腫瘤分期和部位無明顯差異。五年存活率分別為22% (完整手術切除) 和 19% (分段手術切除) (*p* = 0.012)。五年無復發率為 70.9% (完整 手術切除) 和 52.5% (分段手術切除) (*p* = 0.015)。

結論 依本研究的解果,完整切除局部侵犯的大腸癌和所沾黏的鄰近器官有較好的預後。此外,如無法實施同時切除也應盡量以分段切除沾黏器官,令邊緣達到安全範圍,降低復發率。

關鍵詞 大腸癌局部侵犯、完整切除、存活率。

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