

Original Research Article

Emergency resection for stage II colon cancer: patterns of recurrence and prognostic factors

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ABSTRACT

Background: The prognosis in colon cancer patients who undergo emergency curative resection remains uncertain. This study aimed to analyze the oncological outcomes in stage II colon cancer patients who underwent emergency or elective colon resection and identify the prognostic factors for recurrence following emergency resection.

Methods: Patients in this study underwent curative resection for stage II colon cancer between March 2008 and December 2020. Based on surgical condition, patients were divided into two groups: emergency and elective. The two groups were compared regarding clinicopathological features and postoperative recurrence. Prognostic factors for recurrence were analyzed in the emergency resection group.

Results: Among 161 patients, 60 and 101 patients were emergency group and elective group, respectively. The emergency group had significantly lower adequately harvested lymph nodes than the elective group ($p=0.02$). The emergency group had significantly poorer disease-free survival compared to the elective group ($p=0.019$). The most common recurrence site was local recurrence. No statistically significant difference was observed between the two groups in recurrence site. The presence of lymphovascular invasion and clinical perforation were prognostic factors for recurrence in the emergency resection group.

Conclusion: Emergency resection for stage II colon cancer is associated with poor disease-free survival compared to elective resection. The prognosis may improve by performing appropriate radical surgery including extensive lymph node dissection. Adjuvant chemotherapy should be performed following emergency surgery for stage II colon cancer, especially when lymphovascular invasion or colonic perforation is identified.

Keywords: Colon cancer, Stage II, Emergency resection, Disease-free survival

INTRODUCTION

Colon cancer is the third most common cancer worldwide and the second leading cause of cancer-related death.¹ The incidence of colon cancer has been increasing rapidly. The goal of treatment consists of removal of the primary tumor together with complete mesocolic dissection of the lymphatic drainage region. Current recommendations require retrieval of at least 12 lymph nodes for proper postoperative staging. Up to 40% of colon cancer patients present as emergencies due to

obstruction or perforation. Emergency surgical intervention is necessary in those patients. The prognosis of colon cancer patients who undergo emergency curative resection remains uncertain. Many studies report that emergency patients are more likely to have more postoperative complications and decreased overall survival including worse oncological outcome.²⁻⁴ The results can be explained by advanced stage of the disease at presentation, technical difficulties, and the critically ill state of the patients. Also, the patients who require emergency colon resection might not undergo a radical

operation, unlike patients with elective resection. However, some studies claim that emergency curative resection of colon cancer has survival outcomes similar to elective resection.^{5,6}

Stage II colon cancer (T3N0M0, T4N0M0) is diagnosed in approximately one-third of patients with colon cancer. Although patients with stage II colon cancer are generally considered to have a good prognosis, approximately 5-30% of these patients may develop recurrence after surgery. The role of adjuvant chemotherapy for stage II colon cancer is controversial. Currently, guidelines recommend that adjuvant chemotherapy for stage II disease should be targeted to patients who are at high risk of recurrence. However, the identification of high-risk factors vary among different research studies. Previous studies have reported that emergency surgery was a risk factor for recurrence in colon cancer.^{7,8} However, relatively few studies have examined the prognostic risk and recurrence of emergency surgery in only stage II colon cancer. The aim of this retrospective study was to analyze the oncological outcomes after emergency curative colon resection compared to elective resection of stage II colon cancer. The secondary aim was to identify prognostic factors that influence postoperative recurrence after emergency resection.

METHODS

This was a retrospective study. All patients who underwent curative resection for stage II colon cancer at Trang Hospital between March 2008 and December 2020 were enrolled. Data were collected from the medical records and pathological reports. After surgery, patients were followed for at least 3 years. The inclusion criteria were a diagnosis of pathologically confirmed stage II colon cancer and a history of curative surgical colon resection. The exclusion criteria were rectal cancer, death within 30 days after surgery, and patients who underwent only colostomy without resection. A total of 161 patients were included in our analysis. The patients were divided into two groups according to their surgical condition: emergency and elective. Patients who presented as an emergency and underwent emergency surgery within 24 hours after the diagnosis were classified as emergency. All other patients were considered as elective. Emergency resection was performed in 60 patients, and elective resection was performed in 101 patients. The two groups were analyzed and compared on the following variables: age; sex; body mass index (BMI); primary tumor location; size of tumor; T stage; presence of lymphovascular invasion; histologic differentiation; number of harvested lymph nodes; surgical procedure; postoperative adjuvant chemotherapy; and the presence or absence of recurrence. In addition, prognostic factors toward survival were also analyzed. The patients were followed every 3-4 months for the first 2 years, then every 6 months for the next 3 years and then once yearly. The follow-up included clinical assessment, serum carcinoembryonic antigen, and imaging evaluations

included chest radiography and abdominal computed tomography. Colonoscopy was performed annually. Both groups were compared regarding tumor recurrence and disease-free survival in correlation with clinicopathological characteristics. Local recurrence was defined as recurrent tumors in the original tumor bed, peritoneal recurrence was defined as the occurrence of a disseminated lesion in a part of the peritoneum away from the original tumor site, and distant recurrence was defined as a recurrent tumor at an organ far from the original tumor site. Disease-free survival was defined as the time from initial surgical resection to recurrence or metastasis of colon cancer.

Statistical analysis

The chi-square test was used to compare qualitative variables. Disease-free survival was calculated using the Kaplan-Meier method and statistical significance was determined by the log-rank test. The associations between clinical factors and recurrence were assessed using the Cox proportional hazard regression model. The level of significance was set at $p < 0.05$. All statistical analyses were performed using the IBM SPSS software (version 23).

RESULTS

Between March 2008 and December 2020, 161 patients with a median follow-up time of 68.8 months (range 2-192 months) were eligible for the present analysis. Sixty patients (37.3%) were in the emergency resection group and 101 patients (62.7%) were in the elective resection group. The characteristics of patients between the two groups were compared. The clinicopathological characteristics of the patients are summarized in (Table 1).

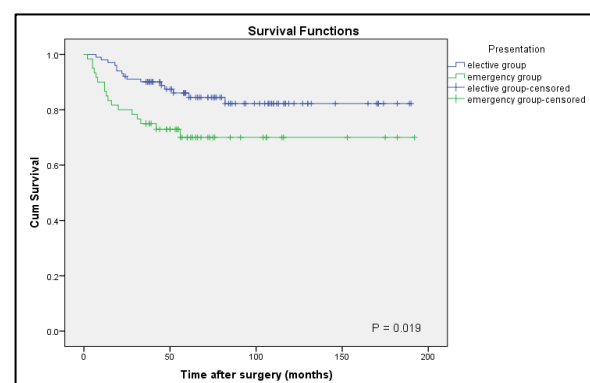


Figure 1: Disease-free survival of patients in the emergency and elective groups.

A significant difference was observed in the number of harvested lymph nodes and surgical procedure. The adequate number of harvested lymph nodes (≥ 12 nodes) was lower in the emergency group compared to the elective group (46.7% vs. 71.3%, $p=0.02$).

Table 1: Clinicopathological characteristics in stage II colon cancer patients.

Variables	Total (n=161) Frequency (%)	Emergency (n=60) Frequency (%)	Elective (n=101) Frequency (%)	P value
Age (years)				
<60	70 (43.5)	24 (40.0)	46 (45.5)	0.443
≥60	91 (56.5)	36 (60.0)	55 (54.5)	
Sex				
Male	87 (54.0)	32 (53.3)	55 (54.5)	0.890
Female	74 (46.0)	28 (46.7)	46 (45.5)	
BMI (kg/m²)				
<25	98 (60.9)	41 (68.3)	57 (56.4)	0.136
≥25	63 (39.1)	19 (31.7)	44 (43.6)	
Tumor location				
Right sides	47 (29.2)	18 (30.0)	29 (28.7)	0.862
Left sides	114 (70.8)	42 (70.0)	72 (71.3)	
Size of tumor (cm)				
<5	53 (32.9)	16 (26.7)	37 (36.6)	0.195
≥5	108 (67.1)	44 (73.3)	64 (63.4)	
T stage				
3	145 (90.1)	55 (91.7)	90 (89.1)	0.601
4	16 (9.9)	5 (8.3)	11 (10.9)	
Lymphovascular invasion				
No	138 (85.7)	49 (81.7)	89 (88.1)	0.261
Yes	23 (14.3)	11 (18.3)	12 (11.9)	
Histological differentiation				
Well	116 (72.1)	47 (78.3)	69 (68.3)	-
Moderate	40 (24.8)	12 (20.0)	28 (27.7)	0.239
Poor	5 (3.1)	1 (1.7)	4 (4.0)	0.377
Number of harvested nodes				
<12	61 (37.9)	32 (53.3)	29 (28.7)	0.002
≥12	100 (62.1)	28 (46.7)	72 (71.3)	
Surgical procedure				
Resection with anastomosis	136 (84.5)	37 (61.7)	99 (98.0)	<0.001
Resection with colostomy	25 (15.5)	23 (38.3)	2 (2.0)	
Adjuvant chemotherapy				
No	80 (49.7)	24 (40.0)	56 (55.4)	0.059
Yes	81 (50.3)	36 (60.0)	45 (44.6)	

Table 2: Recurrence patterns following colon resection.

Site of recurrence	Total (n=161) Frequency (%)	Emergency (n=60) Frequency (%)	Elective (n=101) Frequency (%)	P value
Local recurrence	16 (9.9)	8 (13.3)	8 (7.9)	0.402
Distant recurrence				
Liver	7 (4.3)	4 (6.7)	3 (3)	0.476
Lung	5 (3.1)	2 (3.3)	3 (3)	1.000
Peritoneum	4 (2.5)	3 (5.0)	1 (0.9)	0.291

Primary resection with colostomy was more common surgical procedure in the emergency group (38.3% vs 2.0%, $p<0.001$). No statistically significant differences were found between the two groups in terms of age, gender, BMI, primary tumor location, size of tumor, T stage, presence of lymphovascular invasion, histologic differentiation, and postoperative adjuvant chemotherapy.

A total 32 patients (19.8%) experienced recurrence during the study follow-up period. The recurrence rate was higher in the emergency group ($n=17$, 28.3%) compared to the elective group ($n=15$, 14.9%). The most common site of recurrence was local recurrence ($n=16$, 9.9%), followed by the liver ($n=7$, 4.3%), lung ($n=5$, 3.1%), and peritoneum ($n=4$, 2.5%). In both groups, the most frequent type of recurrence was local recurrence.

Table 3: Univariate and multivariate analysis factors associated with recurrence.

Variables	Total (n=60)	Univariate		Multivariate	
		HR (95% CI)	P value	HR (95% CI)	P value
Age (years)					
<60	24	0.74 (0.28-1.91)	0.532	-	-
≥60	36				
Sex					
Male	32	0.55 (0.21-1.45)	0.226	-	-
Female	28				
BMI (kg/m²)					
<25	41	0.84 (0.30-2.39)	0.746	-	-
≥25	19				
Tumor location					
Right sides	18	1.34 (0.5-3.63)	0.564	-	-
Left sides	42				
Size of tumor (cm)					
<5	16	0.47 (0.18-1.23)	0.125	-	-
≥5	44				
T stage					
3	55	1.89 (0.43-8.31)	0.397	-	-
4	5				
Lymphovascular invasion					
No	44	3.48 (1.28-9.48)	0.015	4.02 (1.43-11.27)	0.008
Yes	16				
Histological differentiation					
Well	47	-	-	-	-
Moderate	12	0.78 (0.22-2.71)	0.695	-	-
Poor	1	0.00 (0.00-0.00)	0.986	-	-
Number of harvested nodes					
<12	32	0.87 (0.33-2.29)	0.779	-	-
≥12	28				
Clinical presentation					
Obstruction	42	3.56 (1.37-9.27)	0.009	3.98 (1.50-10.58)	0.006
Perforation	18				
Surgical procedure					
Resection with anastomosis	37	1.16 (0.44-3.04)	0.766	-	-
Resection with colostomy	23				
Adjuvant chemotherapy					
No	24	0.94 (0.36-2.47)	0.898	-	-
Yes	36				

BMI, body mass index; HR, hazard ratio; CI, confidence interval

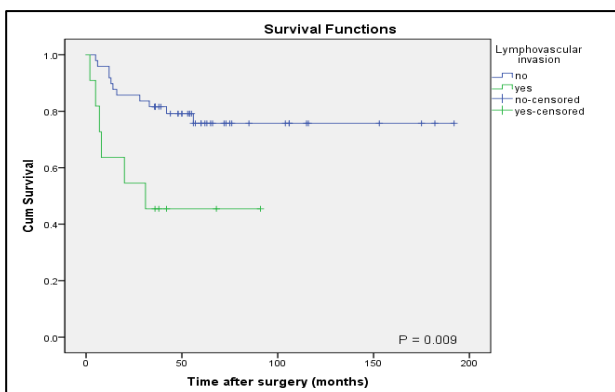


Figure 2: Disease-free survival in emergency resection for lymphovascular invasion.

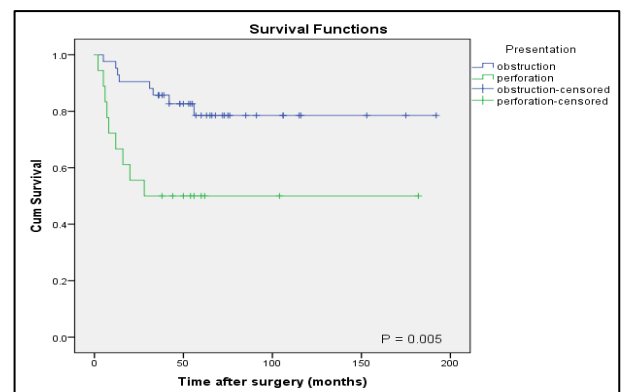


Figure 3: Disease-free survival in emergency resection for clinical presentations.

No statistically significant difference was found between the two groups in the site of recurrence (Table 2). The 3-year disease-free survival rate for all patients was 83.9%. The 3-year disease-free survival rates of patients in the emergency and elective groups were 75% and 89.1%, respectively. The emergency group had a significantly poorer disease-free survival compared to the elective group ($p=0.019$). The Kaplan-Meier survival curves for disease-free survival are shown in (Figure 1).

The risk factors for recurrence in the emergency resection patients are shown in (Table 3). According to univariate analysis, the factors associated with recurrence were presence of lymphovascular invasion (HR 3.48, $p=0.015$) and clinical presentation with colonic perforation (HR 3.56, $p=0.009$). From a multivariate analysis of these factors, both the presence of lymphovascular invasion (HR 4.02, $p=0.008$) and clinical presentation with colonic perforation (HR 3.98, $p=0.006$) were significantly poor prognostic factors for disease-free survival. The Kaplan-Meier survival curves for disease-free survival for lymphovascular invasion and clinical presentation are shown in (Figure 2 and 3).

DISCUSSION

Oncological outcomes of colon cancer patients who underwent emergency resection remain unclear. Many studies have shown that emergency colon resection was associated with higher recurrence and poorer disease-free survival. Factors that adversely affect the outcomes of patients who undergo emergency colon resection are advanced stage at the time of diagnosis, the fear of causing further physiological deterioration from the instability of patients, technical difficulty from a distended colon, and severe contamination in cases of bowel perforation.⁹⁻¹¹ Oncologic control for colon resection includes complete resection of the involved segment of colon, as well as proximal vascular ligation at the origin of the primary feeding vessel to optimize lymphadenectomy. However, in the emergency setting, the primary goal of surgery may not be oncologic. Surgeons usually focus on the acute life-threatening problem of the patients. In that case, incomplete oncologic resection and inadequate lymph node dissection may occur that result in pathological understaging of the tumor. Furthermore, in emergency settings, there could be a lack of colorectal specialist surgeons; therefore, the surgical treatment might be associated with increased mortality and poor surgical outcomes. The results of the present study concluded similarly that a lower disease-free survival rate was found among patients who underwent emergency resection compared to elective resection. In our study, emergency surgery for colon cancer was treated by general surgeons who may perform a resection intended only to address the urgency of the situation without respecting oncologic principles. However, previous studies showed no statistical differences in long-term survival when the two groups were compared.^{5,12,13} Arnarson et al reported that

specialist surgeons did not significantly affect postoperative complication rates of either short- or long-term survival after emergency operation for colon cancer.¹⁴

A recent systemic review and meta-analysis showed that tumor location, differentiation, stage, and ASA grade differed significantly between the elective and emergency resection groups.¹⁵ Our results, however, showed differences between the two groups in terms of the number of harvested lymph nodes and surgical procedure. In this study, resection with colostomy was done in 38.3% of patients who underwent emergency resection. This procedure was in the absence of intestinal anastomosis that eliminated potential anastomotic leakage from an unprepared colon. In our study, the adequate number of harvested lymph nodes (≥ 12) was significantly lower in the emergency group compared to the elective group. Similarly, Elmessiry et al reported that inadequate lymphadenectomy was more frequent in emergency surgery.¹¹ The number of harvested lymph nodes is the strongest prognostic factor for staging of colon cancer patients. A small number of harvested lymph nodes results in pathological understaging, which suggests that some patients may potentially have had stage III disease. Consequently, these patients may not receive the survival benefit of adjuvant chemotherapy. However, other studies reported that the quality of lymphadenectomy in emergency resection was similar to elective resection.^{16,17} Most studies reported emergency surgery compared to elective surgery in patients with stages II, III, and IV. Tumor stage was the strongest predictor of survival with significantly lower overall survival observed in higher stages compared to an early stage. Advanced stage was found in the emergency group to be higher than the elective group; therefore, overall survival and disease-free survival were poor in the emergency group.¹⁸⁻²⁰ Our study directly compared emergency and elective colon resection only in stage II disease, which has a good prognosis but the risk factors for recurrence remain unclear. The administration of adjuvant chemotherapy in patients with stage II colon cancer is controversial. At present, adjuvant chemotherapy is only recommended for stage II disease when high-risk factors are present. Previous studies reported that emergency surgery was confirmed to be a high-risk factor for recurrent colon cancer, and adjuvant chemotherapy may improve the outcome in emergency surgery patients.^{21,22}

In our study, overall recurrence occurred in 19.9% of the patient population. The recurrence rate was higher in the emergency group compared to the elective group (28.3% vs. 14.8%). Most studies reported that the liver was the most common site for recurrent colon cancer because the majority of intestinal mesenteric drainage enters the hepatic portal venous system. This was in contrast to our study where the most common site was local recurrence in both groups. Recurrence was seen at the anastomotic site, rectal stump, and pelvic nodes. The cause of local

recurrence may be due to insufficient resection, inadequate nodal dissection, and intraoperative implantation of cancer cells around the anastomotic site. Emergency resection reduced the extent of lymph node dissection to prioritize life-saving surgery. Furthermore, colon perforation as the emergency presentation was associated with the dispersal of cancer cells into the peritoneal cavity. The prognostic factors for recurrence in emergency surgery found in our results were the presence of lymphovascular invasion and the clinical presentation of perforation. Lymphovascular invasion is a micropathological tumor factor believed to increase the risk of tumor metastasis and the spreading of a tumor. Several studies have shown that lymphovascular invasion is an unfavorable prognostic factor for survival in patients with stage II colon cancer.²³⁻²⁵

In a systematic review, lymphovascular invasion was significantly associated with a poor prognosis in terms of overall survival and disease-free survival.²⁶ Perforated colon cancer was a risk factor for stage II colon cancer recurrence. The spillage of tumor cells into the peritoneal cavity through the perforation site allowed the tumor to spread widely.²⁷ Chen et al reported that colon cancer with perforation had a poorer progressive-free survival rate and higher recurrence rate compared with colon cancer with obstruction.¹⁸ Similar to our results, perforated colon cancer had a poorer disease-free survival rate compared with obstructed colon cancer. Kim et al concluded that perforated colon cancer patients should be recommended for treatment with aggressive surgical procedures and adjuvant chemotherapy based on oncologic principles.²⁸

Limitations

The limitation of this study included the single-center retrospective study, the relatively small sample size, and some patients did not have sufficient follow-up time. Therefore, further investigations with larger cohorts are required to confirm the data from this study.

CONCLUSION

Our data indicated that patients who underwent emergency resection for stage II colon cancer experienced decreased disease-free survival compared to patients who underwent elective resection. Adequately harvested lymph nodes was significantly lower in the emergency group. Prognostic factors for recurrence in emergency surgery were the presence of lymphovascular invasion and clinical presentation with perforation. Emergency resection should be recommended for treatment with appropriate radical surgery including extensive lymph node dissection to achieve oncological control. Adjuvant chemotherapy should be performed following emergency surgery for stage II colon cancer, especially when lymphovascular invasion or colonic perforation is identified.

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