

Original Article

Risk Factors of Post-operative Mortality in Patients Aged 80 Years or Older with Colorectal Cancer

Yih-Jong Chen¹
Jinn-Shiun Chen²
Reiping Tang²
Chung-Rong Changchien²
Jy-Ming Chiang²
Chien-Yuh Yeh²
Yau-Tong You²
Pao-Shiu Hsieh²
Wen-Sy Tsai²
Hsin-Yuan Hung²
Sum-Fu Chaing²
Cheng-Chou Lai²
Geng-Pin Lin²
Jeng-Fu You¹

¹Colorectal Section, Department of Surgery,
Chang Gung Memorial Hospital,
²School of Medicine, Chang Gung University,
Taoyuan, Taiwan.

Key Words

Colorectal cancer;
Old age over 80 year old;
Post-operative mortality;
Risk factors

Purpose. In Taiwan, there is an increasing trend in curative treatment for elderly patients with colorectal cancer. Since operation is the main treatment strategy for colorectal cancer, we analyzed the clinical information about the patients aged 80 years or older who had undergone operations for colorectal cancer to evaluate the risk factors of post-operative mortality.

Materials and Methods. All study participants, aged more than 80 years, were recruited from patients who had received major operations for colorectal cancer at Linkou Chang Gung Memorial Hospital between March 1996 and September 2009. The operation type was tumor resection either by colectomy or proctectomy. Clinical data, including comorbidity, pre-operative laboratory data, and cancer information, were collected to identify the significant risk factors associated with the post-operative mortality.

Results. A total of 929 patients were enrolled during the study period. The average age was 83.5 (± 3.5) years old. The post-operative mortality rate was 4.1%. Our result showed comorbidity with liver cirrhosis and pulmonary diseases, body mass index, pre-operative albumin level, laboratory examination for liver and renal function, emergent operation and metastatic status were significantly correlated with post-operative mortality.

Conclusions. Since the increasing proportion of patients older than 80-year-old receiving operations for colorectal cancer, evaluation of the patients' pre-operative clinical conditions is important to minimize the risk of post-operative mortality. This study showed that several risk factors, including comorbidity with liver cirrhosis and pulmonary diseases, pre-operative poor nutrition status, impaired renal function and liver function, emergent operation and metastatic status, should be put into consideration before operation for those patients with CRC aged over 80-year-old.

[J Soc Colon Rectal Surgeon (Taiwan) 2017;28:66-72]

For people who diagnosed colorectal cancer (CRC), the possibility of surgical intervention was the major consideration for treatment. It is well-known

that older age was associated with increasing co-morbidities, surgical morbidity and mortality. In Taiwan, the department of Household Registration Affairs in

Received: May 11, 2016.

Accepted: August 16, 2016.

Correspondence to: Dr. Jeng-Fu You, Colorectal Section, Department of Surgery, Chang Gung Memorial Hospital, No. 5, Fuxing St., Guishan Dist., Taoyuan City 33305, Taiwan. Tel: 0975365617; Fax: 886-3-328-5060; E-mail: jenodysey@gmail.com

2014 estimated that 3% of the country's population was over 80 years of age, and more than half of people live over 80 years old in lifetime. CRC has been the most prevalent malignancy in Taiwan lasting more than seven years,¹ and about 15.5% of all diagnosed patients whose ages were over 80 years old. For a surgeon, the increasing age, especially over 80 years old, the post-operative outcome and life quality were crucial for planning the operation for CRC.²⁻⁴ Several studies had shown that the rate of peri-operative morbidity and mortality was high in elderly patients with CRC.⁵⁻⁷ The post-operative mortality rate was about 5%-40% in old patients reported in studies and also higher than younger groups.⁸⁻¹⁴ The risk factors of surgery for CRC patients whose age over 80 years old have not yet been clearly defined in Taiwan. The aim of this study was to evaluate risk factors of post-operative mortality for CRC patients whose age over 80 years old.

Materials and Methods

We retrospectively analyzed a database containing the information about patients who underwent surgery for colorectal cancer from March 1996 to September 2009 at Linkou Chang Gung Memorial Hospital in Taiwan. All patients were over 80 years old and received major operation, including tumor resection and colectomy or proctectomy. Patients who only received local resection of tumor without bowel resection were excluded from the analysis.

Preoperative characteristics were obtained regarding age, gender, body mass index (BMI), and comorbidity. Laboratory data before operation, tumor location and whether emergent operation or not were recorded. Pathological differentiation and clinical stage by TNM system were also documented according to pathological results.

Postoperative mortality defined as mortality happened during operation or after operation within 30 days. This study is focused on analyzing the risk factors for post-operative mortality for the group of patients whose age over 80 years old.

Continuous variables are expressed as mean stan-

dard deviation and were analyzed with the Student *t* test, while categorical ones are expressed as a percentage value and were analyzed with Fischer's test or chi-square test. A *p*-value of 0.05 was considered statistically significant. All calculations were performed by using the SPSS v. 20.0 (SPSS Inc., Chicago, IL, USA) was used in the analysis.

Results

A total of 929 patients were enrolled and analyzed in this study. The mean age of these patients was 83.5 ± 3.5 year old and 465 (50.1%) were male. The rate of post-operative mortality was 4.1% (38 patients).

We divided these old patients who were post-operative survival or post-operative mortality into two groups. The clinical characteristics of the patients between two groups are shown in Table 1. There was no significant difference in age and sex ratio. The BMI in the post-op survival group was 22.6 ± 3.7 kg/m² and in the post-op mortality group was 20.9 ± 4.2 kg/m², and it was significantly lower in the post-op mortality group ($p < 0.05$). Comorbidity of these patients was analyzed. Patients who had liver cirrhosis and pulmonary disease showed increasing rate for the post-operative mortality group. The liver cirrhosis rates in survival and mortality group were 0.9% and 7.9% ($p < 0.001$), and the pulmonary disease rates were 4.8% and 13.2% ($p = 0.023$). In order to assess pre-op objective clinical information, the laboratory data before operation were merged. Higher hypoalbuminemia rate (survival: 29.9%, mortality: 60.0%, $p < 0.001$), higher AST level rate (survival: 6.4%, mortality: 25.7%, $p < 0.001$), higher hyperbilirubinemia rate (survival: 3.0%, mortality: 10.7%, $p = 0.024$), and increasing creatinine level rate (survival: 31.3%, mortality: 47.2%, $p = 0.044$) were significantly more frequently recorded among post-op mortality groups when compared with the post-op survival group. The rate of emergent operation was significantly higher for the post-operative mortality group compared with the survival group (survival: 4.2%, mortality: 13.2%, $p = 0.009$). There were no significant differences between the two groups for tumor location and histology

Table 1. Demographic data

	post-op survival (n = 891)	post-op mortality (n = 38)	<i>p</i>
	% (n)	% (n)	
Male ratio	50.1% (446)	50.0% (19)	NS
Comorbidity			
Hypertension	40.6% (362)	36.8% (14)	NS
Cardiac disease	14.6% (130)	15.8% (6)	NS
CVA	6.8% (61)	13.2% (5)	NS
Diabetes mellitus	15.8% (141)	23.7% (9)	NS
Liver cirrhosis	0.9% (8)	7.9% (3)	< 0.001
Hepatitis	1.3% (12)	0.0% (0)	NS
Pulmonary disease	4.8% (43)	13.2% (5)	0.023
UGI ulcer	8.1% (72)	13.2% (5)	NS
Laboratory examination			
Hemoglobin < 10 g/dL	27.7% (245)	39.5% (15)	NS
Albumin < 3.5 g/dL	29.9% (255)	60.0% (21)	< 0.001
AST > 34 U/L	6.4% (54)	25.7% (9)	< 0.001
CEA > 5 ng/mL	46.1% (389)	62.9% (22)	NS
Creatinine > 1.27 mg/dL	31.3% (270)	47.2% (17)	0.044
Total bilirubin > 1.3 mg/dL	3.0% (24)	10.7% (3)	0.024
Emergent operation	4.2% (37)	13.2% (5)	0.009

CVA: cerebral vascular accident, UGI: upper gastrointestinal tract, AST: aspartate aminotransferase, CEA: carcinoembryonic antigen, NS: non-specific.

type (Table 2). Regarding the TNM stage system, there were no significant differences between the two groups for T and N stage (Table 2). The distant metastasis rate in the post-op survival group was 13.9% and in the post-op mortality group was 28.9% ($p = 0.010$).

Discussion

Studies showed that older patients, especially more than 80-year-old diagnosed and treated for colorectal cancer due to the progressive increase in life expectancy.¹⁵ Considering the substantially increasing rate of post-operative mortality for elderly people, our studies wanted to assess the possible risk factors related to the major operation. The cause of post-operative mortality could be peritonitis due to an insufficiency of bowel anastomosis, post-operative cardiac or cerebral vascular thromboembolic events, pneumonia due to lung atelectasis, or others.

Our data showed that there was significant correlation between BMI and post-operative mortality. Our study also presented that the rates of overweight (BMI

≥ 25) in post-op mortality group (10.5%) showed much less than post-op survival group (22.7%) and the rates of underweight (BMI < 18.5) in post-op mortality group (13.2%) showed slightly more than post-op survival group (12.1%). Pre-operative serum albumin level was also significantly related to post-op mortality. Sixty percent of post-op mortality patients whose albumin levels were below 3.5 g/L, comparing to the post-op survival group (29.9%). For CRC surgery, pre-operative nutrition status was proved as an important factor for bowel anastomosis healing and wound healing, which were related to post-operative morbidity and mortality.¹⁶ Post-operative NPO status after colorectal surgery may influence the healing process, and pre-operative serum albumin level or body mass indicated the storage of protein or other components for tissue healing.^{17,18} As predicting factors of malnutrition status, less BMI and hypoalbuminemia could be risk factors for post-operative mortality in patients aged over 80.

Comorbidity was fairly common among old patients. In our study, 59.2% of all patients had one or more medical disease other than colorectal cancer,

Table 2. Pathological parameters

	Post-op survival (n = 891)	Post-op mortality (n = 38)	<i>p</i>
	% (n)	% (n)	
Tumor location			NS
Right side colon	23.2% (207)	36.8% (14)	
Left side colon	31.9% (284)	26.3% (10)	
Rectum	44.9% (400)	36.8% (14)	
Histology type			NS
Adenocarcinoma	91.8% (818)	84.2% (32)	
Mucinous adenocarcinoma	7.2% (64)	13.2% (5)	
Others	1.0% (9)	2.6% (1)	
TNM stage T			NS
Tis	2.0% (18)	0.0% (0)	
T1	3.5% (31)	2.6% (1)	
T2	10.8% (96)	5.3% (2)	
T3	45.5% (405)	36.8% (14)	
T4	38.3% (341)	55.3% (21)	
TNM stage N			NS
N0	55.3% (493)	55.3% (21)	
N1	25.7% (229)	23.7% (9)	
N2	18.9% (169)	21.0 (8)	
TNM stage M			0.010
M0	86.1% (767)	71.1% (27)	
M1	13.9% (124)	28.9% (11)	
TNM stage			NS
Is	2.0% (18)	0.0% (0)	
I	11.1% (99)	7.9% (3)	
II	38.5% (343)	34.2% (13)	
III	33.8% (301)	28.9% (11)	
IV	14.6% (130)	28.9% (11)	

and presence of liver cirrhosis and pulmonary disease correlated with post-op mortality significantly. Patients who had cirrhosis might have hypoalbuminemia or ascites, which may influence the healing process of bowel anastomosis. The complication due to cirrhosis like esophageal varices or compromise of immunity may also cause post-operative mortality. Pre-existing lung problem, including constrictive or restrictive lung disease, had widely proven as a risk factor for post-operative respiratory failure.¹⁹ Our study also confirmed patients who had pulmonary disease encountered more post-operative mortality. Some studies reported that diabetes mellitus, cardiac disease, history of cerebral vascular events or other diseases may cause increase rate of post-op mortality. However, our data do not show the same results.^{5,9,18}

For pre-operative laboratory examination to evaluate

the risk of colorectal surgery, this study revealed that abnormal data in serum level of albumin, aminotransferase (AST), total bilirubin and creatinine were the risk factors related to post-op mortality. These data indicated the importance of liver and kidney function, and nutrition status.^{9,20} If any kind of these abnormal data checked, the operation for these patients who aged over 80 should be carefully considered to the surgeons, patients, and their family. Emergent operation for CRC surgery likely caused higher mortality for these patients,¹² and the results were also presented in several studies. Patients visited hospital due to bowel obstruction or perforation due to CRC usually combined with multiple medical problems like unstable vital sign, sepsis or electrolyte imbalance, which may increase the risk for operation. Overviewing the pathologic characters, only whether metastatic

disease or not would influence post-operative mortality. The patients who had metastatic CRC may have much poor nutrition or immunity to encounter the operation.²⁰

Our study had some limitations. First, it is a retrospective study and not a randomized control trial. Second, the long-term survival rate after operation was not analyzed compared with non-operation treatment. In addition, the colon cancer and rectal cancer were different in pre-operative and post-operative treatment strategy through national guidelines, so that the operation may not be the first priority for cancer treatment.

Conclusions

In conclusion, we showed that aged over 80-year-old patients with CRC, many risk factors were observed. Comorbid disease including pulmonary disease and liver disease were risk factors for CRC surgery. With the condition of Poor pre-operative nutrition status and laboratory examination for liver and renal function, CRC surgery should be put into more consideration if indicated. If emergent operation encountered, the higher post-operative rate must be known by the patient and associated members. For old patients with metastatic disease of CRC, increasing mortality rate was observed after CRC surgery.

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原 著

對於患有大腸直腸癌之八十歲以上老年人接受手術後死亡的危險因子分析

陳繹中¹ 陳進勛² 唐瑞平² 張簡俊榮² 江支銘² 葉建裕² 游耀東²
謝寶秀² 蔡文司² 洪欣園² 蔣昇甫² 賴正洲² 林耕平² 游正府¹

¹林口長庚醫院 大腸直腸外科

²長庚大學

目的 在台灣，愈來愈多罹患大腸直腸癌的老年人接受大腸直腸切除的治療。在以手術為主的治療方針之下，我們針對八十歲以上並接受大腸直腸癌切除的病人，分析手術後死亡的危險因子。

方法 我們統計了從 1996 年 3 月到 2009 年 9 月共 929 位八十歲以上老年人在林口長庚紀念醫院接受腫瘤切除與大腸或直腸切除手術治療的大腸直腸癌患的資料，並分析包含共病、術前實驗室檢驗、癌症相關資料與術後死亡的關係。

結果 929 位病人的平均年齡為 83.5 (± 3.5) 歲且平均術後死亡率為 4.1 百分比。我們的研究顯示病人本身肝硬化、肺部疾病、身體質量指數、術前白蛋白濃度、術前腎功能與肝功能的實驗室檢查、是否為緊急手術與是否有遠端轉移均為術後死亡的危險因子。

結論 愈來愈多八十歲以上老年人接受大腸直腸癌症的手術。大腸直腸癌術後死亡的危險因子包括有肝硬化或肺部疾病病史、較差的營養狀況、較差的腎功能與肝功能、緊急手術與遠端轉移的患者。這些因素可以讓外科醫師做術前的評估以下降術後死亡的機率。

關鍵詞 大腸直腸癌、八十歲以上老年人、術後死亡、危險因子。