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REVIEW ARTICLE

Colon cancer with perforation

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Abstract
Perforation of the colon is a rare complication for patients with colon cancer and usually requires emergent surgery. The characteristics of perforation differ based on the site of perforation, presenting as either perforation at the cancer site or perforation proximal to the cancer site. Peritonitis due to perforation tends to be more severe in cases of perforation proximal to the cancer site; however, the difference in the outcome between the two types remains unclear. Surgical treatment of colon cancer with perforation has changed over time. Recently, many reports have shown the safety and effectiveness of single-stage operation consisting of resection and primary anastomosis with intraoperative colonic lavage. Under certain conditions, laparoscopic surgery can be feasible and help minimize the invasion. However, emergent surgery for colon cancer with perforation is associated with a high rate of mortality and morbidity. The long-term prognosis seems to have no association with the existence of perforation. Oncologically curative resection may be warranted for perforated colon cancer. In this report, we perform a literature review and investigate the characteristics and surgical strategy for colon cancer with perforation.

Keywords Colon cancer · Perforation · Laparoscopic surgery

1. Introduction

Perforation of the colon is rare and usually requires emergent surgery. It is associated with a high mortality and high morbidity. The causes of perforation include malignancy (36%), spontaneous perforation (20%), iatrogenic perforation (20%) and diverticulum (19%) among others [1]. For patients with colon cancer, colonic perforation is not a common complication, and the incidence ranges from 2.6 to 10% [2–7].

Perforation of the colon tends to occur in older patients, and the most frequent perforation site is the sigmoid colon. Tan et al. [8] reviewed 129 patients who underwent surgery for colonic perforation in their institute. Among them, diverticulitis and cancer were the diagnoses in 51.9% and 34.9%, respectively. The sigmoid colon (47.3%) was the most common site of perforation, followed by the cecum (24.8%). Patients with malignant perforation tended to be older and have a higher American Society of Anesthesiologists (ASA) grade than those with perforated diverticulitis.

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Patients with perforated cancers face double life-threatening conditions of a malignant disease and sepsis attributed to peritonitis. The rate of operative mortality from perforated colon cancer has been reported to range from 5 to 52% [5, 9–14] despite advances in perioperative intensive-care treatment. Several authors have reported that the stages of perforated colon cancers are higher than those of uncomplicated colon cancers [9–11, 15], although such findings are controversial [6, 16].

As shown above, the presenting features of perforation and the prognosis of colon cancer with perforation remain unclear. In this report, we performed a literature review and investigated the characteristics and surgical strategy for colon cancer with perforation.

Site of perforation

There are two mechanisms underlying colorectal cancer perforation; perforation at the cancer site because of tumor necrosis, and perforation induced by blowing out of the distended proximal colon due to tumor obstruction. Perforation has generally been thought to have a worsening effect on local recurrence and the long-term survival, but the

influences of these different types of colonic perforation on the prognosis remain unclear.

A number of studies have shown that perforation proximal to the cancer site carries a poorer prognosis than cancer site perforation [6, 7, 17–19]. When perforation occurs proximal to the obstructing tumor, it tends to be severe due to intestinal distension, and peritoneal contamination is diffuse and fecal. Such a condition leads to severe septic shock, resulting in an increased risk of perioperative mortality. In contrast, when perforation occurs at the cancer site, the contamination is usually localized, typically leading to purulent collection and resulting in a lower risk of severe peritonitis. However, several studies have ruled out this association [5, 7, 20]. To confirm the relationship between the site of perforation and the outcome of the patients, larger-scale studies are necessary. However, the rarity of this condition and its associated high perioperative mortality rate make such studies difficult (Table 1).

Surgical treatment

Perforation of colon cancer usually requires emergent surgery. The patients are predominantly aged, and their condition may be poor due to sepsis and accompanying diseases. The optimum surgical treatment of colonic perforation with cancer remains controversial. There is no standardized protocol for the management of patients with colonic perforation, and the treatment strategy depends on the patient's general condition and the experience of the primary surgeon. As these patients usually present emergently, prospective studies are difficult to perform, and most reports are small single-institutional series.

Emergent surgeries of the colon have traditionally been performed in stages. Goliger et al. [21] reported a series of 115 patients with colorectal perforation in 1957, and only 22 patients (19%) underwent resection. Glenn et al. [22] reported that the resection rate of colon cancer perforation rose from 47% in 1938–1942 to 81% in 1966–1970. The outcomes of initial surgery with a colostomy were often unsatisfactory due to difficulty in performing colostomy for frail, aged patients, in addition, many of them did not undergo second-stage surgery. In 1988, Mealy et al. [23] reported that single-stage surgery consisting of resection and primary anastomosis of the colon without a colostomy was not associated with increased morbidity or mortality over traditional staged management.

Emergency resection followed by primary ileocolic anastomosis is a generally accepted strategy for perforated cancers of the right-sided colon, even in the presence of peritonitis [5, 24, 25]. Discontinuity resection, such as Hartmann's procedure, is performed in most patients with perforation of left-sided colon cancers [5, 26]. However, Hartmann's operation carries a disadvantage of morbidity associated with the stoma and the need for a second operation to close the stoma and perform reconstruction, which may not be easy. Many investigators have found that resection and primary anastomosis may be performed in selected patients. An abscess or fecal peritonitis is not a contraindication for anastomosis, but the presence of a major comorbidity, such as diabetes, renal failure, cardiovascular disease, compromised immunity, malnutrition or a high ASA score, is associated with a risk of leakage [27–34]. Breitenstein et al. [35] compared the effectiveness and safety of primary anastomosis versus Haetmann's operation in a case-matched study in 2007.

Table 1 The incidence and operative mortality of cancer site perforation and proximal perforation

				Perforation site			Operative mortality		Long-term survival
Author	Ref	Year	n	Cancer (%)	Proximal (%)	(Distal)	Cancer[a]	Proximal[B]	
Welch	20	1974	118	82	18		62%	18%	–
Mandava	5	1996	51	82	18		–	–	Equal
Kriwanek	11	1996	35	91	3		–	–	–
Carraro	17	1998	83	65	35		17%	48%	Better in proximal to cancer perforation
Chen	6	2000	48	73	27		9%	31%	Equal
Khan	18	2001	48	75	23	(2%)	---	---	Better in cancer site perforation
Alvarez	19	2005	24	75	25		22%	50%	Equal
Anwar	16	2006	42	74	24	(2%)	–	–	–
Lee	44	2007	26	73	27		–	–	Equal
Biondo	51	2008	38	92	8		–	–	–
Tan	7	2010	45	76	24		–	–	Equal

Ref. reference number

[a]cancer site perforation

[b]proximal to cancer perforation

They concluded that primary anastomosis and protective ileostomy is a superior treatment to Hartmann's operation in acute left-sided colon perforation. Furthermore, many reports have shown that single-stage resection with primary anastomosis and intraoperative colonic lavage carry almost the same rates of morbidity and mortality as multistage procedures [36–43].

The surgical approach for perforated colon cancer should be an oncologically curative operation for uncomplicated colon cancer. Lee et al. [44] showed that the pathway of complicated cancer is similar to that of uncomplicated cancer and concluded that an aggressive surgical approach based on oncologic criteria should be performed in the presence of perforated colonic cancers.

Laparoscopic surgery

Laparoscopy can be a useful approach for diagnosing the cause of an acute abdomen and help determine whether the laparotomy incision should be made at the upper or lower abdomen. In some cases, treatment can be completely performed laparoscopically without laparotomy.

In cases of colonic perforation after colonoscopy, several authors have reported that early laparoscopic management is safe and reduces the surgical and physiological stress for the patient because of its low morbidity and mortality rates and shorter hospital stay than with the open approach [43, 45, 46]. Anania et al. [47] evaluated the outcome of laparoscopic colon resection in patients with complicated diverticulitis and revealed its safety and effectiveness.

There are few reports of laparoscopic surgical treatment for colon cancer perforation. In 2005, Gonzalez et al. [34] reviewed 21 cases of laparoscopic palliative surgery for complicated colorectal cancer, including perforation (10 patients), bleeding (7 patients) and obstruction (4 patients). Three patients (14%) required conversion to an open procedure due to adhesions and inadequate visibility. There was one intraoperative complication (4.8%) and seven postoperative complications (33%) without perioperative death. Although the rates of conversion and complication in that study were comparable with previously reported results for elective laparoscopic resections of uncomplicated colorectal cancer, detailed data of the ten patients with perforation were not shown. A laparoscopic approach to perforated colon cancer may be difficult due to poor visibility and frail inflamed tissue. Regarding sigmoidectomy for perforated diverticulitis, some studies have reported that a laparoscopic procedure was safe and feasible [48–50]. Although the safety and efficacy are still controversial, laparoscopic surgery for perforated colon cancer can be attempted by trained surgeons.

Prognosis

The morbidity and mortality rates after emergent surgery to treat perforation of colorectal cancer remain unclear, with mortality rates ranging from 5 to 40% [2, 3, 6, 9–11, 17, 20, 44, 51]. Kriwanek et al. [11] compared 130 patients with benign colonic perforations to 35 patients with colon cancer perforation. Although the degree of peritonitis was not markedly different between the groups, the patients with cancer perforation presented with more severe sepsis and developed organ failure more often than those with benign perforation. The incidence of surgical complications was roughly the same in both groups, but the mortality rate in the cancer perforation group was 40%, which was significantly higher than that in the benign perforation group (13.8%). The influence of perforation on the long-term survival rate is still controversial. The high postsurgical mortality rate in perforated cancer patients has been attributed to the cumulative effect of the increasing age and debility of patients, sepsis, more advanced malignancy at presentation, preexisting comorbidities and lower rates of curative resection. Some investigators believe that perforation may be responsible for the spillage of cancer cells into the peritoneal cavity, resulting in peritoneal dissemination and a negative influence on the survival. Malignant perforation has been shown to be associated with an increased risk of local recurrence and decreased survival rates [3, 52–54] and is an independent poor prognostic factor of the survival after adjustment for the tumor stage [10, 55, 56].

However, other studies have found that the negative effect of colon cancer perforation may be limited to the perioperative period, with the long-term survival depending on the tumor stage rather than on the emergency presentation [5, 11, 13, 19, 44, 57–59]. Chen et al. [6] reported that the perioperative mortality was much greater in cases of perforation proximal to the cancer than cancer site perforation. However, the site of perforation did not appear to influence the 5-year survival (Table 1). Indeed, perforation itself was not a predictor of a poor prognosis, and the effects on the short- and long-term survival were found to be due to the associated sepsis and advanced disease stage. Perforation was associated with a reduced overall survival due to a higher immediate postoperative mortality, but perforation itself was not shown to have a significant impact on the disease-free survival. Abdelrazeq et al. [58] showed that, after controlling for the 30-day operative mortality and stage IV disease at presentation, the disease-free survival rates were similar in the perforated and non-perforated T4 cancers. They also found a statistically significant association between the mortality and morbidity rates and the ASA grade, as well as the acute physiology component

of the Acute Physiology and Chronic Health Evaluation II (APACHE II) score of the patients with colon cancer perforation. These findings are supported by those of others [6, 11, 16, 44, 60, 61]. Tan et al. [7] showed that the short-term outcome was determined by the ASA grade and severity of peritonitis, while the long-term outcome was determined only by the stage of the cancer (Table 2).

Mandava et al. [5] reported that the overall operative mortality rate of perforated colorectal cancers was 12%, and the overall 5-year survival rate was 32%. After excluding patients with stage IV disease at the diagnosis and operative mortalities, the 5-year survival rate was 58%. The prognosis after curative resection of patients with perforated colon cancer is not poor compared with that of patients with uncomplicated colon cancer. This finding suggests that aggressive treatment rather than palliative treatment may be warranted for perforated colon cancer to improve the long-term prognosis.

Adjuvant chemotherapy affects the long-term prognosis of perforated colorectal cancer [54]. For stage III and

Table 2 The prognosis of colon cancer with perforation and its factors

Author	Ref.	Year	n	Perioperative mortality	5-year survival	Short-term prognostic factor	Long-term prognostic factor	Others
Welch	20	1974	118	29.7%	15.6%			The 5-year survival after curative resection: 35.7%
Kelley	3	1981	27	30%	–			
Umpleby	13	1984	22	52%	18%	Perforation	Curative resection, tumor site, tumor stage, tumor differentiation	
Willet	52	1985	34	–	44%			
Steinberg	55	1986	14	–	–		Perforation	
Griffin	57	1987	40	5%	50%			Perforation is associated with the risk of recurrence but not with the survival
Runkel	10	1991	20	30%	15% (4-year survival)		Emergent surgery	
Kriwanek	11	1996	35	40%	38%			
Mandava	5	1996	51	12%	32%			The 5-year survival rate excluding stage IV and perioperative death: 58%
Carraro	17	1998	83	31.5%	38.4%			The 5-year survival rate excluding perioperative death: 60.9%
Chen	6	2000	48	14.6%	---			
Khan	18	2001	48	14%	14% (5-year DFS[a])		Perforation proximal to cancer	
Alvarez	19	2005	24	29.2%	---	Older age, high APACHE II score		
Anwar	16	2006	42	40.5	35.7% (2-year survival)	ASA grade, POSSUM score		
Lee	44	2007	26	11%	30.8%		Perforation proximal to cancer, number of the metastatic lymph nodes	The 5-yaer survival rate excluding perioperative death: 57.8%
Abdelrazeq	58	2008	52	17%	28%		Emergency surgery, age > 75 years	
Biondo	51	2008	38	13.2%	74.3%			
Tan	7	2010	45	17.8%	–	ASA grade, severity of peritonitis	Staging of the cancer	

DFS disease-free survival, *APACHE II score* Acute Physiology and Chronic Health Evaluation II score, *ASA grade* American Society of Anesthesiologists grade, *POSSUM score* Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity Score

high-risk stage II colon cancer, adjuvant chemotherapy is recommended and perforation is a high-risk factor of stage II [62]. Chen et al. evaluated the outcomes of colon cancer with perforation or obstruction. They showed that the tumor stage was a risk factor, while receiving adjuvant chemotherapy or radiotherapy was a protective factor in their multivariate analysis of the overall survival [63].

Conclusion

While emergent surgery for colon cancer with perforation is associated with a high mortality and morbidity, the long-term prognosis seems to be independent of the existence of perforation. Oncologically curative operation should be performed when possible, and laparoscopic surgery can be attempted under certain conditions.

Compliance with ethical standards

Conflict of interest None of the authors have any conflicts of interest to declare in association with this work.

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