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Long-term outcomes of colorectal cancer patients with and without malignant large-bowel obstruction

Shinya Munakata^{*1}, Yuta Murai¹, Akihiro Koizumi¹, Hisaki Kato¹, Riku Yamamoto¹, Shuhei Ueda¹, Satoshi Tokuda¹, Shunsuke Sakuraba¹, Tomoyuki Kushida¹, Hajime Orita¹, Mutsumi Sakurada¹, Hiroshi Maekawa¹ & Koichi Sato¹

¹Department of Surgery, Juntendo Shizuoka Hospital, Juntendo University School of Medicine, Shizuoka, Japan

^{*}Author for correspondence: Tel.: +81 5 5948 3111; Fax: +81 5 5946 0514; smunaka@juntendo.ac.jp

Aim: Colorectal cancer patients with malignant large-bowel obstruction (MLBO) require emergency treatment. Here we evaluated the long-term outcomes of recurrence and prognosis (not short-term mortality or nonocclusive cancer T1–T2) in colorectal cancer patients with and without an MLBO. **Methods:** We retrospectively analyzed the cases of the consecutive patients who underwent curative resection for colon cancer. We compared the groups regarding patients' age and gender, the tumor location, T and N factor, tumor stage, disease-free survival and overall survival. **Results:** The nonobstruction group had a significantly longer disease-free survival and overall survival compared with the MLBO group. **Conclusion:** MLBO was associated with cancer recurrence and poorer overall survival regardless of the staging and adjuvant chemotherapy.

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Many patients with colon cancer exhibit locally advanced or metastatic disease at the time of presentation. An estimated 8–29% of colorectal cancer patients who present with an acute malignant large-bowel obstruction (MLBO) require emergency management, a stoma, self-expandable metallic stenting (SEMS) and a transanal decompression tube (TDT) [1]. These patients, who often are in poor physical condition due to several days of reduced intake, vomiting and weight loss, have operative risk leading to high mortality rates. The reported postoperative mortality following acute resection is 12–35% [2].

Initial colonic decompression using a minimally invasive procedure as a bridge to surgery might be an appropriate alternative to emergency operation. This approach creates time to optimize the patient's condition and prevents the stoma creation [3–5]. In addition, if a SEMS or TDT is not technically feasible, a decompressing stoma may be necessary to achieve a symptom-free condition for the patient. Although the mortality rate of these patients in the short term is high, little is known about the long-term outcomes of recurrence and prognosis [6,7]. In the present study, we analyzed the specific prognosis (except for short-term mortality such as progression of disease and postoperative complications) in colon cancer patients with and without an MLBO.

Methods

We reviewed cases of 256 consecutive patients who underwent curative resection for the treatment of their colorectal cancer at Juntendo University Shizuoka Hospital (Shizuoka, Japan) between January 2011 and December 2015. All cases of stage 0–I, IV, double cancers and rectal cancer were excluded from the analysis. Regarding stage 3 cancers, T1–2 cases were excluded because the tumor sizes were less than the colon obstruction group. The cases of the patients who died within 30 days postoperatively, classified as short-term mortalities, were also excluded from the analysis. All patients had histologically confirmed colon adenocarcinoma. Patients operated on by the authors

Table 1. Baseline characteristics of the 148 patients who underwent surgical curative resection for colon cancer.	
Characteristic	n = 148
Age	75
Sex (M/F)	76/72
T3/T4a/T4b	133/9/6
N0/N1/N2	88/45/15
Stage II	85
Stage III	63
Location (Cecum/Ascending/Transverse/ Descending/Sigmoid)	16/36/16/14/66
Laparoscopic/open	75/73
Adjuvant chemotherapy	80

were given the option of open/laparoscopic surgery and the final decision depended on the surgeon’s discretion. All patients were confirmed by pathology to have had a successful R0 resection.

We divided the patients into two groups: the MLBO group, with obstructive colon cancer (n = 21) and the non-MLBO group, with nonobstructive colon cancer (n = 127). The staging of all cancers is described according to the TNM Classification of Malignant Tumors, seventh edition (TNM 7th). We compared the following factors between the MLBO and non-MLBO groups: the patient’s age, gender, the tumor location, T and N factor, tumor stage, the surgical approach (open vs laparoscopic-assisted colectomy), disease-free survival and overall survival. The surveillance protocol for the postoperative follow-up schedule was as follows: physical examination, serum carcinoembryonic antigen analysis, serum carbohydrate antigen 19–9 analysis, chest radiography and spiral abdominal computed tomography were performed every 6 months for 3 years and annually thereafter. Other procedures, such as colonoscopy and gastrofiberscope, were performed every 6–12 months depending on the status of the patient.

Definitions

The patients with a colon obstruction were identified based on clinical, radiological, endoscopic and intraoperative findings (complete obstruction) with oral perforation by tumor obstruction, which was confirmed using images, pathological findings and operative records. Cases of iatrogenic perforations and distant perforation sites were excluded.

Local recurrence was defined as recurrent tumors in the original tumor bed. Distant recurrence was defined as recurrent tumors outside the peritoneal cavity. Overall survival was defined as the duration from surgery to death or the last follow-up. Disease-free survival was defined as the duration from surgery to cancer recurrence. Colostomies were constructed on the transverse colon. After colostomy construction or TDT, patients received enteral feeding as soon as possible. Elective resection was performed within approximately 4 weeks.

Statistical analyses

The comparison of categorical variables was performed using the chi-square test or Fisher’s exact test where appropriate. Continuous variables are presented as median values and were compared using the Mann-Whitney U-test. The length of time before the recurrence of colorectal cancer and death measured from the date of surgery were referenced against disease-free survival and overall survival time. Survival duration was calculated by the Kaplan-Meier method. The log-rank test was used for the comparison of the cumulative survival rate and disease-free survival in each patient group.

Results

Patient characteristics

Table 1 summarizes the clinicopathologic characteristics of the 148 patients who underwent surgical curative resection for colon cancer. The study group comprised 86 males and 72 females aged 35–92 years (median 75 years). Tumor location was the cecum (C) in 16 patients (10.8%), followed by the ascending colon (A) in 36 patients (24.3%), the transverse colon (T) in 16 patients (10.8%), the descending colon (D) in 14 patients (9.4%) and the sigmoid colon in 66 patients (44.6%). The laparoscopic approach was performed in 75 patients (50.6%). Others were operated by the open approach.

Figure 1. Flowchart of the management of patients with colon obstruction.

Table 2. The malignant large-bowel obstruction cases.

Characteristic	MLBO (n = 21)	Non-MLBO (n = 127)	p-value
Age	72	76	0.46
Sex (M/F)	12/9	64/63	0.56
T3/T4a/T4b	18/1/2	115/8/4	0.38
N0/N1/N2	14/6/1	74/39/14	0.62
Stage II	14	71	0.35
Stage III	7	56	
Location (Cecum/Ascending/ Transverse/Descending/Sigmoid)	0/0/2/7/12	16/36/14/7/54	< 0.001
Laparoscopic/open	0/21	75/52	< 0.001
Adjuvant chemotherapy	12	68	0.75

MLBO: Malignant large-bowel obstruction.

The TNM-7th T categories were T3 in 133 patients (89.8%), T4a in nine patients (6.0%), T4b in six patients (4.1%) and N0 in 88 patients (59.4%), N1 in 45 patients (30.4%), and N2 in 15 patients (10.1%). Regarding TNM staging, 85 patients (57.4%) were stage II and 63 patients (42.6%) were stage III. The median follow-up duration was 38 months (range 2–76 months).

The MLBO group's characteristics

The flowchart of the colon obstruction management is depicted in [Figure 1](#). [Table 2](#) summarizes the details of the MLBO group. The patients in whom a temporary stoma creation was performed without primary resection (n = 6) proceeded to elective resection within approximately 4 weeks and stoma creation with primary resection (n = 6). The other patients (n = 3) decompressed by TDT proceed to elective resection. In the rest of the patients (n = 7), the perforation was caused, only to primary resection with stoma creation (n = 6) and with anastomosis (n = 1). Unfortunately, SEMS could not be performed due to health insurance circumstances in this periods.

MLBO is revealed to be a prognostic factor

In the comparison of the MLBO and non-MLBO groups, laparoscopic surgery was not performed in any patients in the MLBO group ($p < 0.001$). The tumor locations were partial between the two groups ($p < 0.001$). No significant difference in adjuvant chemotherapy was noted between the groups ([Table 3](#)). As shown in [Figure 2](#), the univariate log-rank analysis showed that the non-MLBO group had a significantly longer disease-free survival ($p < 0.0001$).

Table 3. Characteristics of the patients with and without malignant large-bowel obstruction.	
Characteristic	n = 21
Stoma creation without primary resection	6
Stoma creation with primary resection	6
Decompressed by transanal decompression tube proceed to elective resection	3
Perforation with primary resection and stoma creation	5
Perforation with anastomosis	1

Figure 2. Survival curves of stage II–III colon cancer with or without malignant large-bowel obstruction. (A) Disease-free survival. (B) Overall survival. MLBO: Malignant large-bowel obstruction.

and overall survival ($p < 0.003$) compared with the MLBO group, indicating that MLBO was associated with the cancer recurrence and poorer overall survival regardless of the staging and adjuvant chemotherapy.

Discussion

The most common procedure for MLBO was traditionally emergency surgery without preoperative decompression. Preoperative decompression of colon distension has recently become the main treatment for MLBO. We had not performed SEMs in the present study period because Kim *et al.* showed that SEMs was associated with peritoneal seeding after perforation [8]. However, it was shown that the technical success rates were 100% for SEMs and 78.9% for TDT and significantly greater resolution of histopathological edema was achieved after the placement of SEMs than after the placement of TDTs [9]. No significant difference in postoperative mortality was reported between SEMs and TDT [2]. Thus, although it is a controversial way to decompress the colon for obstructed

colorectal cancer treatment, it is a possible option for decompression for an MLBO as a bridge to surgery. Future research is required to test the validity, reliability, reproducibility and clinical usefulness of SEMS.

Laparoscopy was considered to be difficult to perform for patients with colon obstruction within the limited working space, and there is a higher risk of causing inadvertent injury to the dilated bowel. In the present study period, we could not perform the laparoscopic surgery for patients with MLBO even if decompression succeeded. As recent studies showed that laparoscopic resection was completed in 74.2% patients in the SEMS group [10], this decompression therapy enables us to operate by the laparoscopic approach, but this should be confirmed by obtaining data regarding long-term outcomes for MLBO patients in randomized clinical trials the future.

Generally, there is a lack of evidence-based literature concerning laparoscopic surgery for locally advanced colon cancer. Indeed, cases of T3–T4 tumors, perforated tumors and acute bowel obstructions were excluded in large randomized, controlled trials comparing the laparoscopic approach with the open approach for colorectal cancer [11]. Here we observed that laparoscopic surgery did not compromise oncological outcomes in T3–T4 colon cancer patients compared with the open approach ($p = 0.67$, data not shown). Therefore, at our institute, patients who will be treated with a SEMS benefit from a one-stage operation, without stoma creation and a safe primary anastomosis.

Despite the lack of robust data, the American Society of Clinical Oncology, the US National Comprehensive Cancer Network and the European Society for Medical Oncology guidelines recommend that adjuvant treatment be considered in patients with stage II colon cancer if specific high-risk features are present. These include perforation, T4 tumor, suboptimal lymph node sampling, poor differentiation, colonic obstruction, lymphovascular or perineural invasion, and positive resection margins. Kumor *et al.* indicated that adjuvant chemotherapy in patients with T4 disease only was associated with significantly improved recurrence-free survival, disease-specific survival, and overall survival. As for patients with MLBO, the advantage of adjuvant chemotherapy in overall survival only was observed in the overall high-risk stage II patients [12]. This may contribute to the worse short-term outcomes of MLBO patients. Therefore, our analysis of outcomes other than short-term mortality and nonocclusive cancer T1–T2 is necessary.

Petrelli *et al.* recently reported that right-sided cancers had a higher risk of mortality than left-sided cancers across all stages. The reasons for the inconsistent relationship between mortality and tumor location by stage are not clear. However, right-colon tumors are more likely to have V-raf murine sarcoma viral oncogene homolog B (BRAF) mutations, microsatellite instability (MSI), and the CpG island methylator phenotype [13]. On the other hand, as far as MSI is concerned, multiple studies have found that patients with MSI-positive tumors have a better overall prognosis, and it was reported that MSI status is an independent favorable predictor of survival [14]. Therefore, adjuvant chemotherapy is needed for patients with low-frequency MSI or microsatellite stable stage II or stage III colon cancer [14]. In Japan, MSI could not be measured due to health insurance requirements, but there were no significant differences between the right- and left-side colon cancers in the present study ($p = 0.29$, data not shown).

This study is limited by its retrospective design and the small number of patients, which was due to our strict inclusion and exclusion criteria. More data are required regarding the prognoses of MLBO patients, and thus further studies are warranted.

Summary points

- Colorectal cancer patients with malignant large-bowel obstruction (MLBO) are frequently excluded from survival analyses.
- We retrospectively analyzed the cases of 148 consecutive patients who underwent curative resection for colon cancer.
- The 21 colon cancer patients with MLBO had worse disease-free survival and overall survival compared with the 127 non-MLBO patients, even when we excluded short-term mortality and nonocclusive T1–T2 cancer cases.

Authors' contributions

S Munakata and K Sato studied concept and design. S Munakata performed data acquisition. S Munakata, Y Murai, A Koizumi, H Kato, R Yamamoto, S Ueda, S Tokuda, S Sakuraba, T Kushida, H Orita, M Sakurada, H Maekawa performed analysis and interpretation of data. S Munakata performed drafting of the manuscript. K Satocritical performed revision of the manuscript.

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No writing assistance was utilized in the production of this manuscript.

Ethical approval

This study was performed in accordance with the ethical standards of the Committee on Human Experimentation of our institution (Institutional Review Board No. 539 29.336).

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