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Original Article

Palliative surgery as a bridge to systemic treatment for malignant bowel obstruction due to peritoneal metastases: A retrospective, case-control study

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SUMMARY

Background: High-quality data on palliative surgery in patients with malignant bowel obstruction (MBO) caused by peritoneal metastases (PM) are lacking. We aimed to determine the utility of palliative surgery for such patients.

Methods: We retrospectively analyzed patients considered for surgery for MBO, caused by PM, in our department from January 2019 to October 2020. None of them could tolerate a diet, despite conservative treatment. We investigated the clinical characteristics and perioperative outcomes and calculated overall survival (OS). Kaplan–Meier survival analysis was performed, with the log-rank test to evaluate differences in OS rates. Multivariate Cox regression was performed to determine prognostic factors.

Results: Sixty (67%) patients underwent surgery, whereas, 30 (33%) received the best supportive care (BSC) treatment. A better ($p = 0.002$) median OS was observed in patients undergoing surgery (3.9 months) than in those receiving BSC (2.6 months). Severe complications were observed in 12 (20%) patients, including 30-day mortality (7 patients). Forty-eight (80%) patients in the surgery group could tolerate a diet and the hospital stay (mean ± standard deviation) was 20.0 ± 23.1 days. Re-obstruction was observed in five (8.3%) patients after 78.6 ± 63.3 days. Patients in the postoperative chemotherapy group exhibited a better ($p < 0.001$) median OS (12.3 months) than did those in the no-postoperative chemotherapy group (3.5 months). Only postoperative chemotherapy (hazard ratio 0.264, 95% confidence interval 0.143–0.487, $p < 0.001$) was identified as an independent prognostic factor.

Conclusions: Compared with BSC, surgery is associated with a better OS in patients with MBO due to PM. Surgery should be considered as a bridge to systemic treatment for such patients.

1. Introduction

Peritoneal metastases (PM) originating from any type of cancer are usually resistant to systemic therapy. They cause malignant bowel obstruction (MBO), which often leads to considerable patient discomfort.[1] The prognosis for MBO is very poor; patients with MBO have an average survival of 3–8 months and 4–5 weeks in operable and inoperable cases, respectively.[2]

Patients with MBO and their families experience considerable distress. Patients suffer from symptoms such as intractable nausea, vomiting, and peristaltic pain, and commonly require long-term maintenance using a Levin tube. However, one of the important problems is that they cannot undergo further systemic treatment for malignancy. A patient's general condition is important while ongoing systemic treatment, but without a tolerable diet, it cannot be maintained. Furthermore, the above-mentioned symptoms are to be managed with priority before systemic disease management.

Abbreviations: PM, Pertoneal metastasis; MBO, Malignant bowel obstruction; OS, Overall survival; BSC, Best supportive care.

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There are several modes of supportive care for MBO. Supportive medications, used especially for inoperable patients, include antiemetics, antisecretory medications, and corticosteroids.[3] An endoscopic stent can be inserted to treat colonic obstruction instead of surgery.[4,5] However, there is currently no established, evidence-based medical guideline for its treatment.[1] In addition, there has been limited evidence on the role of surgery in affected patients. Palliative operations can be an effective treatment for patients with MBO due to intraluminal or localized tumors but are less successful for patients with MBO associated with carcinomatosis.[3,6,7]

Surgeons often find it difficult to determine whether to operate in patients with MBO due to PM. Firstly, surgery does not guarantee relief of symptoms. For instance, bowel function may not be improved even after a successful operation. Secondly, adverse events are reportedly prevalent, because of malnutrition and underlying disease.[3,6] The scope of surgery may be extensive, as most patients have already undergone surgery for the primary carcinoma and adhesions due to malignant tumors. Third, even if the surgery is completed successfully, patients may only have weeks or months left to live.[1,8] Patients with a terminal illness may prefer to avoid burdensome treatments.[9–11] Fourth, there is currently a lack of high-quality data on surgery for patients with MBO due to PM.[12–14]

In recent years, systemic treatment for malignancy and perioperative management have improved in patients' care. Various systemic agents, used for the treatment of terminally ill patients have improved and are being tested in clinical trials. Therefore, we hypothesized that patients who, following surgery, recover to such an extent that they can tolerate a diet would be more likely to tolerate systemic chemotherapy, which would improve their survival. If surgery can serve as a bridge to systemic treatment, it warrants consideration. Therefore, we included only patients with MBO due to PM, as the effectiveness of surgery was more questionable in those patients. Hence, the aim of the present study was to determine the utility of surgery as a bridge to systemic therapy for patients who have MBO due to PM.

2. Methods

2.1. Study design

We retrospectively analyzed patients who were consulted to our department for surgery to treat MBO caused by PM (regardless of the origin of cancer) from January 2019 to October 2020 at Severance Hospital. None of these patients could tolerate a diet for at least one week, despite conservative treatments such as Levin tube insertion and fluid therapy. All patients were evaluated with abdominopelvic CT within one month prior to consultation. We excluded patients with MBO complicated by ischemia or perforation; those who recovered from MBO after stenting or conservative management; and those who had unstable vital signs before the consultation. This study was approved by the Institutional Review Board of Severance Hospital (4-2020-1318).

Detailed information was obtained on patient age, gender, primary cancer origin, the date of diagnosis, and the history of previous treatment (surgery and chemotherapy). We investigated the extent of metastases and the obstruction site using the preoperative CT images.

Perioperative outcomes were investigated. The decision whether to operate, the type of surgery, and surgical methods were determined according to each doctor's (seven doctors) judgment. All operations were performed only to relieve the bowel obstruction, prevent vomiting, and attempt to re-establish enteral nutrition. Operative findings were investigated using operative records. Clavien-Dindo classification was used to evaluate complications, and the 30-day mortality was investigated. The rate of being able to tolerate a diet after the surgery was also investigated, defined as a patient's ability to ingest a liquid diet without symptoms such as vomiting. Hospital stay was defined from surgery to discharge, including the period that was required for treatment such as chemotherapy. Reobstruction was defined as Levin tube reinsertion due to bowel obstruction. The decision for postoperative chemotherapy was decided by medical oncologists or gynecologists, depending on the origin of primary cancer.

Long-term outcomes were analyzed in terms of overall survival (OS). OS was defined as the time from surgery to death from any cause. In patients receiving best supportive care (BSC), OS was defined as the time from consultation to death from any cause.

2.2. Statistical analysis

Summary statistics for continuous variables were reported as the mean ± standard deviation, while categorical variables were reported as frequency (percentage). A two-tailed Student's t-test was employed for comparing continuous variables, and the chi-square and two-tailed Fisher's exact tests were employed for comparing categorical variables. The Kaplan–Meier method was utilized for univariate analyses of survival, and the log-rank test was utilized for statistical evaluation of differences in survival rates. Multivariate Cox regression models were implemented to assess the association between OS and clinical factors. All data were analyzed with IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Treatment for MBO

We identified 90 patients who met the criteria for inclusion. Among them, 60 patients had undergone surgery for palliation, whereas 30 patients were treated conservatively. In patients receiving BSC, 17 patients had been judged inoperable and 13 patients had refused surgery despite the surgeon's recommendation. Of the surgeries that were performed, five were open-and-close surgeries due to severe PM. In 42 patients, only palliative stoma formation was performed. Other patients needed further procedures such as bypass or bowel resection and anastomosis. Among patients in whom it was possible to remove the Levin tube after the surgery, 22 patients were approved for systemic treatment (Fig. 1).

3.2. Patient characteristics

Patients' baseline demographics, except the obstruction site, did not differ between the surgery and BSC groups. The colon and rectum were more commonly the sites of obstruction in the surgery group than in the BSC group (35% vs. 10%, $p = 0.011$). The origin of primary cancer did not differ between the groups ($p = 0.271$). Among 90 patients, 81 patients had already undergone surgery for primary cancer; 40/90 (44%) had undergone abdominal surgery more than one time for malignancy. In total, 42 patients (47%) had been diagnosed with primary cancer at least two years before the MBO-related consultation, and 87 (97%) had received systemic chemotherapy. By the time of the consultation, 52/90 patients (58%) exhibited metastases to intra- or extraperitoneal organs (Table 1).

3.3. Perioperative outcomes

The operative approach was laparoscopy in 26 (43%) patients,

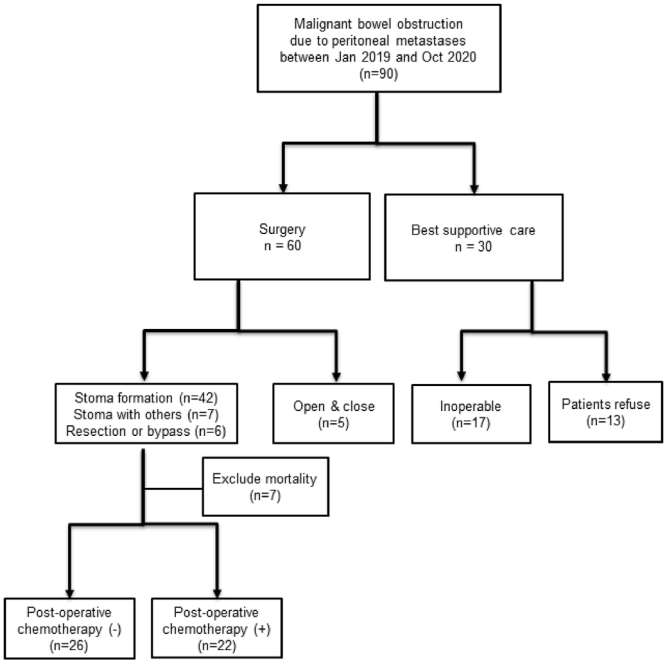

Fig. 1. Flow diagram of patients in this study.

primarily for stoma formation. There was a wide range of operative times and blood loss due to unexpected operative findings.

Perioperative complications were observed in 20 (33%) patients. Severe complications (those with a Clavien-Dindo grade of 3 or above) were observed in 12 (20%) patients; among them, 7 (12%) died within 30 days after surgery. In total, 48 (80%) patients were discharged as they could tolerate a diet, and the mean hospital stay was 20 days. Reobstruction was observed in five (8%) patients, on average 79 days after surgery (Table 2).

3.4. Long-term survival according to treatment for MBO and prognostic factors for survival

Kaplan–Meier analysis revealed a better OS among patients who underwent surgery than among those who received BSC (median OS: surgery, 3.9 months vs. BSC, 2.6 months; $p = 0.002$) (Fig. 2).

Using univariate analysis, BSC (hazard ratio [HR] 2.168, 95% confidence interval [CI] 1.321–3.558, $p = 0.002$), metastasis to intraperitoneal organs (HR 1.991, 95% CI 1.146–3.460, $p = 0.015$), and postoperative chemotherapy (HR 0.264, 95% CI 0.143–0.487, $p < 0.001$) were identified as prognostic factors. Using multivariate analysis, only postoperative chemotherapy (HR 0.264, 95% CI 0.143–0.487, $p < 0.001$) was identified as an independent prognostic factor (Table 3).

3.5. Long-term survival according to postoperative chemotherapy

Among patients who underwent surgery, after excluding those who underwent open-and-close surgery and those who died shortly after surgery, 22 (46%) were deemed eligible for systemic chemotherapy. The only clinical factor that differed between the two groups was the extent of metastases detected in the preoperative CT scan ($p = 0.008$) (Table 4).

Using Kaplan–Meier analysis, we discovered that patients who received post-operative chemotherapy exhibited a better OS than did patients who did not receive it (median OS: chemotherapy, 12.3 months vs. no chemotherapy, 3.5 months; $p < 0.001$; Fig. 3).

4. Discussion

In this study, we determined the utility of palliative surgery for MBO due to PM. Patients who underwent palliative surgery exhibited better OS compared with those receiving BSC. However, palliative surgery for MBO in patients with PM is controversial. Bateni et al[15] reported the potential benefit of medical management for MBO patients at the end of life compared with surgical management in a population-based study. Cousins et al[13] identified 43 studies (the vast majority of which were retrospective) examining 4265 participants in a Cochrane review. However, the studies were generally of low quality, and outcomes were measured differently. In one systematic review, most of the 17 related studies had a single-arm design, revealing outcomes after palliative surgery; only five were outcomes compared between palliative surgery and BSC.[12] Of the latter, better survival outcomes following surgery compared to BSC were demonstrated in only two studies.[16,17] Olson et al[12] concluded that, despite its benefits, palliative surgery comes at the

Table 1
Patient characteristics according to treatment.

Variable	Surgery (n = 60)	Best supportive care (n = 30)	*p*
Age	59.2 ± 14.4	61.7 ± 11.2	0.393
Gender			0.361
Male	26 (43)	10 (33)	
Female	34 (57)	20 (67)	
Primary cancer			0.271
Gynecologic	17 (28)	14 (47)	
Colorectal	16 (27)	9 (30)	
Gastric	12 (20)	1 (3)	
Hepato-biliary-pancreatic	7 (12)	2 (7)	
Small bowel	4 (7)	2 (7)	
Urological	4 (7)	2 (7)	
History of past surgery (number)	1.6 ± 1.2	1.6 ± 0.9	0.844
Duration from diagnosis with primary cancer (months)	38.8 ± 36.2	30.0 ± 23.7	0.172
History of chemotherapy	58 (97)	29 (97)	1.000
Metastases (preoperative radiology)			0.222
Only peritoneal	28 (47)	10 (33)	
Intraperitoneal organs	17 (28)	14 (47)	
Extraperitoneal organs	15 (25)	6 (20)	
Obstruction site (preoperative radiology)			0.011
Small bowel	39 (65)	27 (90)	
Colon & rectum	21 (35)	3 (10)	

Continuous variables are reported as the mean ± standard deviation, while categorical variables are reported as frequency (percentage).

Table 2
Perioperative outcomes.

Variable	Surgery (n = 60)
Operation	
Stoma formation	42 (70)
Stoma formation + resection or bypass	7 (12)
Resection or bypass	6 (10)
Open & close	5 (8)
American Society of Anesthesiologists physical status	
2	16 (27)
3	41 (68)
4	3 (5)
Operative approach	
Open	31 (52)
Laparoscopic	26 (43)
Conversion to open	3 (5)
Ascites	23 (38)
Operative time (min)	99.9 ± 91.4 [20–512]
Blood loss (ml)	85.3 ± 200.3 [0–1000]
Perioperative complications	20 (33)
30-day mortality	7 (12)
Clavien-Dindo classification	
1	4 (7)
2	4 (7)
3a	5 (8)
5	7 (12)
Toleration of diet upon discharge	48 (80)
Hospital stay (days)	20.0 ± 23.1 [3–134]
Reobstruction	5 (8)
Days to reobstruction	78.6 ± 63.3 [19–182]

Continuous variables are reported as the mean ± standard deviation [range], while categorical variables are reported as frequency (percentage).

cost of high mortality and substantial hospitalization relative to the remainder of the patient's life.

However, data on palliative surgery in those patients still are lacking. Most of the studies cited in systematic reviews were published long ago. In addition, we are aware of only one prospective study on surgical versus non-surgical management of patients with MBO (NCT02270450).[18] The recent trend for study focuses on hyperthermic intraperitoneal chemotherapy (HIPEC) or systemic therapy in patients with PM. In terms of palliation, medications such as octreotide have been studied in inoperable patients with MBO.[19,20] Kars et al[21] reported that the fear of placing a burden on vulnerable patients is an important reason why prospective studies in this field are rare. Other reasons include the difficulty in disclosing to such patients their health status, a fear of burdening their families, doubts about the importance or quality of the study,

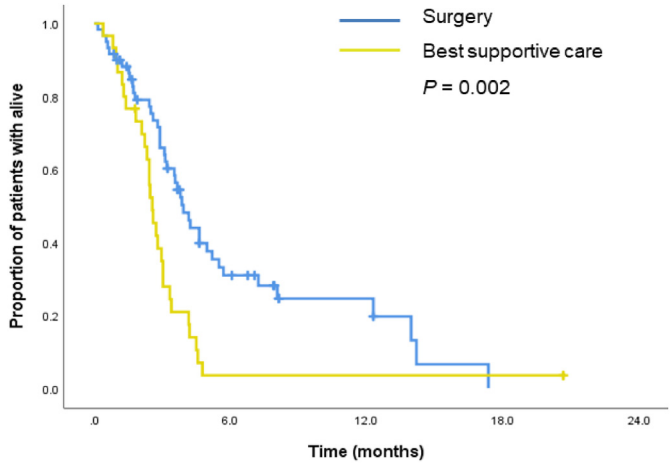

Fig. 2. Comparison of overall survival between patients undergoing surgery and those receiving best supportive care (median overall survival: surgery, 3.9 months vs. best supportive care, 2.6 months; $p = 0.002$).

general attitudes toward research, and overall logistic challenges. It was therefore not possible to conclude whether surgery was of more benefit or harm to patients with MBO due to PM.

With recent progress in systemic treatment and perioperative management of patients with MBO, we hypothesized that patients who, following surgery, recover to such an extent that they can tolerate a diet would be more likely to tolerate systemic treatment, which would improve their survival without deterioration in perioperative outcomes. To date, there have been few studies, which include the relation between systemic chemotherapy after surgery and survival in such patients. Our data revealed survival benefits from systemic chemotherapy after surgery. In the multivariate analysis, using a Cox proportional-hazards model, postoperative chemotherapy was identified as a prognostic factor (HR 0.264, 95% CI 0.143–0.487, $p < 0.001$). Moreover, patients who received postoperative chemotherapy exhibited a dramatically longer OS compared to those who did not (median OS: chemotherapy, 12.3 months vs. no chemotherapy, 3.5 months; $p < 0.001$). Even though the surgery was also identified as a prognostic factor in the univariate analysis (HR 2.168, 95% CI 1.321–3.558, $p = 0.002$) and yielded a slightly better survival outcome than did BSC (median OS: surgery, 3.9 months vs. BSC, 2.6 months; $p = 0.002$), the data suggests that the goal of surgery should be to enable postoperative chemotherapy. In our study, 46% of patients who recovered from surgery could receive systemic chemotherapy. Although surgery does not guarantee that systemic chemotherapy will be viable, it should be considered as the primary treatment for MBO due to PM.

In our study, we enrolled patients with PM regardless of the origin of primary cancer. Although the origin of primary cancer may alter the survival rate of patients with PM, it has less of an effect on patients with MBO due to PM. Unfortunately, the degree of PM could not be described in detail in this study, as most of the patients had already undergone more than one surgery as well as systemic chemotherapy by the time of consultation. These clinical features are an indication that patients in our study had severe metastasis and a poor response to chemotherapy. To date, there is no consensus on the indications for performing surgery for MBO due to PM in patients with an advanced terminal illness; therefore, the decision to perform surgery varies between surgeons. Further research of detailed indications for such a surgery is necessary. The peritoneal cancer index has been used to describe the severity of PM in patients undergoing HIPEC; however, it is inaccurate on a preoperative CT scan.[22]

The perioperative outcomes in our study were comparable with those of previous studies. In their systematic review, Olson et al[12] reported pooled rates of palliation for obstructive symptoms (32%-100%), reobstruction (6%-47%), 30-day postoperative mortality (6%–32%), postoperative complications (7%–44%), and hospital stay (12–25 days), although the definitions of these parameters were unclear and/or varied between studies. We reported the rates of toleration of diet and subsequent discharge (80%), reobstruction (8.3%), 30-day postoperative mortality (12%), postoperative complications (33%, including mortality), and hospital stay (mean: 20.0 days). Although the preoperative patient status and operative findings could not be compared in detail with those of previous studies, advanced perioperative management is necessary for patients to recover from surgery.

Once the decision to operate is made, the operative type and approach should be carefully considered. In our study, 43% of patients underwent surgery via a laparoscopic approach. Where possible, laparoscopy should be considered as the first approach, as conversion to open surgery can be done at any time. Operative findings are usually more severe than the findings detected using a preoperative CT scan in patients with PM. However, the laparoscopic approach has several problems. First, severe adhesion can be

Table 3
Univariate and multivariate analyses for overall survival.

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*	HR (95% CI)	*p*
Treatment (surgery)	2.168 (1.321–3.558)	0.002	1.270 (0.744–2.167)	0.380
Age (≤60 years)	0.851 (0.532–1.362)	0.502		
Gender (male)	0.977 (0.607–1.573)	1.924		
Primary cancer (gynecologic)	1			
Colorectal	1.035 (0.567–1.889)	0.911		
Gastric	0.728 (0.345–1.540)	0.407		
Other	0.654 (0.344–1.242)	0.194		
Duration from diagnosis (≤24 months)	1.303 (0.812–2.093)	0.273		
Metastases (only peritoneum)				
Intraperitoneal organs	1.991 (1.146–3.460)	0.015	1.312 (0.738–2.331)	0.355
Extraperitoneal organs	1.205 (0.646–2.249)	0.558	1.362 (0.721–2.573)	0.341
History of past surgery (≤1)	0.915 (0.566–1.478)	0.716		
Obstruction site (colon & rectum)	1.022 (0.606–1.723)	0.936		
History of chemotherapy (No)	1.658 (0.517–5.320)	0.395		
Postoperative chemotherapy (No)	0.264 (0.143–0.487)	<0.001	0.264 (0.143–0.487)	<0.001

HR hazard ratio, *CI* confidence interval.

Table 4
Patient characteristics according to postoperative chemotherapy.

Variable	Postoperative chemotherapy (−) (n = 26)	Postoperative chemotherapy (+) (n = 22)	*p*
Age	60.8 ± 15.3	57.4 ± 14.9	0.442
Gender			0.265
Male	10 (38)	12 (55)	
Female	16 (62)	10 (45)	
Primary cancer			0.356
Gynecologic	6 (23)	7 (32)	
Colorectal	8 (31)	4 (18)	
Gastric	3 (12)	6 (27)	
Other	9 (35)	5 (23)	
History of past surgery (number)	1.4 ± 0.9	1.5 ± 1.2	0.804
Duration from diagnosis with primary cancer (months)	35.2 ± 37.6	36.2 ± 28.6	0.917
History of chemotherapy	25 (96)	21 (95)	1.000
Metastases (preoperative radiology)			0.008
Only peritoneal	8 (31)	14 (64)	
Intraperitoneal organs	11 (42)	1 (5)	
Extraperitoneal organs	7 (27)	7 (32)	
Obstruction site (preoperative radiology)			0.881
Small bowel	16 (62)	14 (64)	
Colon & rectum	10 (38)	8 (36)	
Operation			0.209
Stoma formation	19 (73)	17 (77)	
Stoma formation + resection or bypass	5 (19)	1 (5)	
Resection or bypass	2 (8)	4 (18)	
American Society of Anesthesiologists physical status			0.504
2	8 (31)	5 (23)	
3	17 (65)	17 (77)	
4	1 (4)	0	
Operative approach			0.961
Open (including convulsion)	14 (54)	12 (55)	
Laparoscopic	12 (46)	10 (45)	
Ascites	12 (46)	6 (27)	0.178
Operative time (min)	108.8 ± 99.9	102.1 ± 102.2	0.820
Blood loss (ml)	113.5 ± 256.0	82.3 ± 175.4	0.631
Perioperative complications	7 (27)	6 (27)	0.978
Toleration of diet upon discharge	24 (92)	22 (100)	0.493
Hospital stays (days)	17.7 ± 12.8	17.1 ± 27.0	0.914

Continuous variables are reported as the mean ± standard deviation, while categorical variables are reported as frequency (percentage).

expected due to PM and previous surgeries. This complicates trocar insertion and increases the risk of damage to the intestines. The location of the camera trocar must be carefully determined. Second, the operative field may be too narrow due to bowel dilatation, complicating the evaluation of the orientation of the bowel. If the stoma is formed in the proximal small bowel, a high output is inevitable, and the patient's condition will deteriorate. Although the plan may change depending on the operative findings, the type of surgical relief for MBO should be determined before surgery. Occasionally, more extensive surgery is required than was expected. Surgery should be minimized to only that which is necessary for relieving MBO, to reduce the possibility of adverse events. Moreover, minimizing surgery increases the probability that the patient will be eligible for systemic therapy soon thereafter. In our study, 70% of patients underwent only stoma formation.

There were several limitations to our study. First, it was subject to the bias inherent in a retrospective analysis. Second, a major limitation was the lack of a standardized indication for surgery.

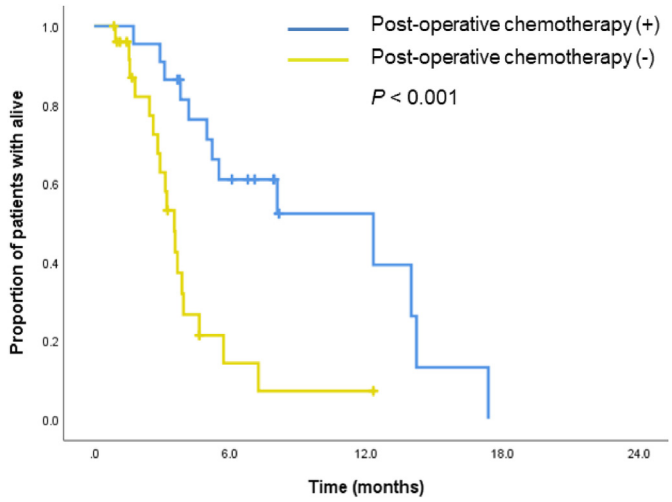

Fig. 3. Overall survival according to postoperative chemotherapy (median overall survival: chemotherapy, 12.3 months vs. no chemotherapy, 3.5 months; $p < 0.001$).

Therefore, the decision to operate was left at the discretion of each surgeon, based on factors that are not always clear. Similarly, the method and extent of surgery were left to the discretion of each surgeon. Standardization of surgery is difficult due to patients' unique patterns of disease. Moreover, the severity of PM cannot be accurately quantified preoperatively. Third, the sample size was small in the present study. Nonetheless, to our knowledge, we enrolled more patients than in previous studies where surgery and BSC groups were compared. Fourth, the study population was heterogeneous, as the underlying etiology of MBO was PM, regardless of the cancer of origin. However, as discussed earlier, the data suggested that patient survival was not affected substantially by the origin of primary cancer. Fifth, no quality-of-life measures were assessed as they were in previous studies. However, the role of chemotherapy in combination with surgery was suggested by the improved survival of patients receiving postoperative chemotherapy compared with those who did not, which, to our knowledge, was not investigated in previous studies.

In conclusion, we have demonstrated that, compared with BSC, surgery is associated with a better OS in patients with MBO due to PM. Patient survival was statistically significantly longer in patients who underwent systemic treatment after surgery, compared with that in those who did not. Perioperative outcomes were comparable with those in previous studies. We have provided evidence in favor of our hypothesis that survival outcomes will improve if patients are enabled to tolerate a diet after surgery, as subsequent systemic therapy is more likely to be viable for such patients. As there have been few studies about the role of palliative surgery in patients with MBO due to PM, further research is necessary.

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5. Synopsis

Palliative surgery as a bridge to systemic treatment revealed a better OS in patients with MBO due to PM.

Declaration of competing interest

There are no conflicts of interest to declare.

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