

## Impact of Resuming Oral Intake after Palliative Surgery in Patients with Malignant Bowel Obstruction

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### Abstract

**Objective:** Malignant bowel obstruction (MBO) is serious problem in patients with advanced cancer, often results in poor quality of life and prolonged hospitalization at the end of life. The important role of surgical treatment in these patients is symptom palliation and restoration of the ability to eat rather than cure. The purpose of this study was to evaluate the postoperative outcomes of patients with MBO and to assess the benefit of palliative operation.

**Methods:** Medical records of patients with stage IV cancer with bowel obstruction underwent laparotomy by a single experienced surgeon at Seoul National University Hospital between 1998 and 2012 were collected retrospectively. A total of 747 patients underwent laparotomy for MBO was identified and 517 patients who underwent curative intent operation were excluded. Overall survival and tolerable feeding duration was evaluated using the Kaplan-Meier method and log-rank test. The primary outcome was defined as the restoration of ability to intake oral feeding.

**Results:** Two-hundred thirty patients underwent palliative operation. The origin of malignancies was colorectal in 114 patients, gynaecological in 37, gastric in 35 and other sites in 44 patients. 171 patients had large bowel obstruction and 59 had small bowel obstruction. 110 patients underwent palliative primary tumour resection, 103 had only stoma formation or bypass surgery. Mean length of stay after operation was 17.1 days. The complication rate was 26.5% and postoperative 30-day mortality was 7.8%. 205 patients (89.1%) were able to restore oral feeding and it lasted for median duration of 5.7 months. The median overall survival was 7.1 months. Palliative primary tumour resection showed superior overall survival to stoma formation or bypass surgery ( $p < 0.001$ ). Resume oral intake, length of oral nutrition, wound complication, re-operation for obstruction and postoperative chemotherapy were associated with overall survival on multivariate analysis.

**Conclusions:** Palliative resection of primary cancer in patients with MBO had survival benefit. Especially resume oral intake is a good predictor of survival outcome for most patients. Patients with advanced cancer with MBO need a highly individualized approach and aggressive procedure for restoration of oral feeding could be one of important goal of care.

**Keywords:** Malignant bowel obstruction; Seeding obstruction; Cancer obstruction; Palliative surgery; Palliative care; Stage IV; Advanced cancer

### Introduction

At an international consensus conference, Anthony et al. [1] proposed the diagnostic criteria of malignant bowel obstruction (MBO) as 'clinical evidence of bowel obstruction beyond the ligament of Treitz in the context of intra-abdominal primary cancer with incurable disease or extra-abdominal primary cancer with clear evidence of intraperitoneal disease'. MBO frequently occurs in patients with advanced cancer, especially of gastrointestinal or gynaecological origin [2-4]. Bowel obstruction signifies any mechanical or functional obstruction of the intestine, and it might lead to significant morbidity and symptom development [4]. Nausea, vomiting and abdominal pain are the most common symptoms of bowel obstruction [5] and have a significant negative impact on oral intake, subsequently deteriorating the general condition of the patient. Bowel obstruction may present as an initial symptom but occurs more frequently with recurrent or advanced disease.

The basic aim of management for patients with MBO is to reduce symptoms by providing an individualised approach depending on the type of obstruction, the extent of the cancer, the prognosis, and the preferences of the patient [6]. Palliative surgery, defined as an operative procedure for non-curative relief of symptoms caused by advanced cancer, should always be considered [7]. When surgical approaches are not possible, a devastating clinical picture develops, which leads to intense symptoms, rapid deterioration of the patient's

general status, and a short life expectancy. Moreover, palliative surgical management has high morbidity and mortality [8, 9]. A number of previous studies have investigated the effects and outcomes of palliative surgery for MBO, and there are several prognostic criteria to select patients who are likely to benefit from surgery [2]; however, the role of surgical treatment for these terminal-stage patients is controversial [10]. Therefore, in this study, we investigated the outcome of palliative surgery in MBO patients. The primary objective of this study was to evaluate the outcomes of palliative surgery indirectly by resuming oral food intake.

### Methods

#### Study design and population

Prospectively collected medical records of patients who underwent operations for MBO in our institution between 1998 and 2015 were analysed retrospectively. All included patients had bowel obstruction

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diagnosed by symptoms such as nausea, vomiting, abdominal pain or bowel distension, physical examination or radiologic findings and were not able to eat pre-operatively. All patients were followed until death or the last visit. Patient data, including age, sex, initial symptoms, primary origins of malignancy, body mass index (BMI), American Society of Anaesthesiologists (ASA) physical status classification, location and number of bowel obstructions, pre-operative chemotherapy regimen, peritoneal cancer index (PCI) score, operative methods, post-operative length of hospital stay, duration of post-operative oral intake, and 30-day morbidity and mortality, were retrieved through retrospective electronic medical records and database reviews.

### Definition and measurements

The primary outcome was resuming oral food intake, which was defined as the ability to tolerate regular oral feeding after palliative surgery to evaluate the operative outcomes indirectly. The secondary outcomes were tolerable feeding duration, survival impact of resuming oral intake, and overall survival after palliative surgery. Tolerable feeding duration was defined as the period from the first day to the last day of enteral feeding post-operatively. Adverse outcomes were defined as one of the following: re-obstruction symptoms after oral feeding, reoperation or death within 30 days post-operatively.

### Ethics statement

The Institutional Review Board of Seoul National University Hospital approved the study protocol (IRB number 1910-081-1070), and the study was conducted in accordance with the Helsinki Declaration. Informed consent was waived by the board.

### Data analysis

All continuous variables are expressed as the mean ± standard deviation, and follow-up duration is described as the mean and range. Categorical variables were compared with Fisher's exact test and the chi-square test, and continuous variables were compared using Student's t test. Survival was calculated with the Kaplan-Meier method. Groups were compared by log-rank tests. Variables with p values less than 0.1 were entered into a Cox proportional hazards regression model for multivariable analysis. All statistical analyses were performed using SPSS version 23.0 (IBM Corporation, Armonk, NY). The results were considered statistically significant at P values of 0.05 or less.

## Results

### Baseline characteristics of the study population

A total of 747 patients with stage IV cancers underwent operations for MBO during the study period. After excluding 517 patients in whom curative resection was possible, 230 patients underwent operation with palliative intent, and a retrospective analysis was performed.

Patient demographics and clinical parameters are described in Table 1. The mean patient age was 59.29 ± 13.62 years (range, 20-

92 years), and 118 (51.3%) patients were male. The mean BMI at the time of surgery was 20.78 ± 3.47 kg/m<sup>2</sup> (range, 12.78-34.42 kg/m<sup>2</sup>). The ASA score distribution at the time of the operation included 25 class I patients (10.9%), 115 class II patients (50.0%), 60 class III tumours (26.1%) and 2 class IV tumours (8.7%), and 28 patients were not assessed pre-operatively. The primary origins of malignancy were colorectal cancer (n=128, 55.7%), gynaecologic cancer (n=38, 16.5%), gastric cancer (n=35, 15.2%), pancreatic cancer (n=7, 3.0%), bladder cancer (n=5, 2.2%), lymphoma (n=4, 1.7%), gastrointestinal stromal tumour (n=3, 1.3%), prostate cancer (n=2, 0.8%) and other cancers (n=8, 3.5%). Fifty-four patients (23.5%) were on chemotherapy at the time of operation.

### Intraoperative findings

Thirty-five (15.2%) patients underwent emergency surgery. Fifty-nine (25.7%) patients had small bowel obstruction, and 171 (74.3%) had large bowel obstruction. The number of bowel obstruction sites was single in 164 (71.3%) patients and multiple in 66 (28.7%) patients. The mean PCI score at the time of surgery was 6.00±3.99 (range, 2-25). The mean intraoperative blood loss was 435.74±1047.64 ml, and the mean operative time was 123.61±67.93 minutes (range, 25-430). One hundred ten (47.8%) patients underwent palliative resection of obstructing primary tumours, 103 (44.8%) underwent stoma formation without primary tumour resection, and 13(5.7%) underwent bypass surgery without primary tumour resection. Four (1.7%) patients underwent exploration only without any palliative procedure since the tumour was extensive and there were no viable bowels for stoma formation or bypass surgery (Table 1 and Figure 1a-e). The type of palliative procedures according to the bowel obstruction site was also evaluated (Table 2).

### Operative outcome

The mean length of stay after the operation was 17.09 days (range, 1-216 days). Two hundred and five (89.1%) patients were able to resume oral intake after the operation regardless of the type of operation, and the mean duration of post-operative tolerable feeding was 13.54 months (range 0.1-197.5 months). Post-operative chemotherapy was administered to 155 (67.4%) patients. The post-operative 30-day morbidity and mortality rates were 27.4% and 7.8%, respectively. Post-operative re-obstruction occurred in 38 (16.5%) patients, and 17 (7.4%) underwent reoperation. The mean overall survival time of all patients was 15.51 months (range 0.1-197.5 months), whereas the mean overall survival time of patients who resumed oral intake was 16.82 months (range 0.4-197.5 months) (Figure 2). In the univariate analysis, resumed oral nutrition (p<0.001) and duration of oral nutrition (p<0.001) were significantly associated with overall survival, and in the multivariate analysis, resumed oral nutrition (HR 2.207, 95% CI, 1.379~3.532, p=0.001) and duration of oral nutrition (HR 0.866, 95% CI, 0.846~0.885, p<0.001) was significantly associated with overall survival (Table 3).

Clinical characteristics (N=230)	
<i>Baseline Characteristics</i>	
Age, years (Mean ± SD, range)	59.29±13.62 (20-92)
Gender, n (%)	
Male	118 (51.3)
Female	112 (48.7)
BMI, kg/m <sup>2</sup> (Mean±SD, range)	20.78 ± 3.47 (12.78-34.42)
ASA Class, n (%) (n=202)	

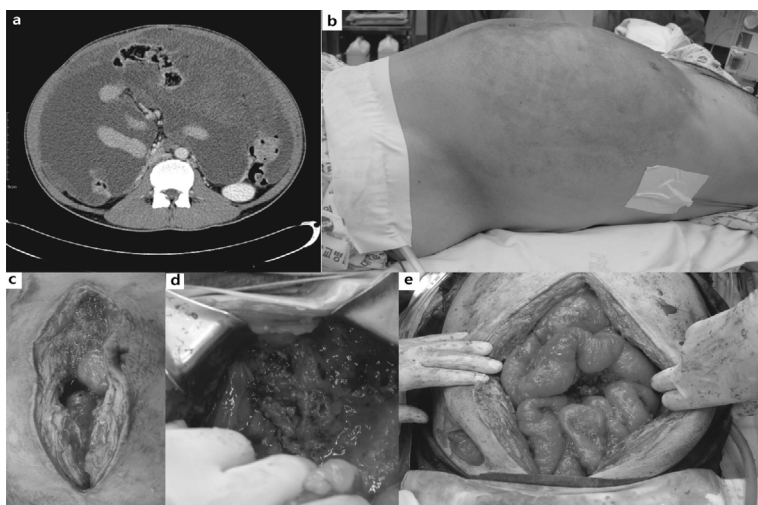
I	25 (10.9)
II	115 (50.0)
III	60 (26.4)
IV	2 (8.7)
Primary origin of malignancy, n (%)	
Colorectal cancer	128 (55.7)
Gynecologic cancer	38 (16.5)
Gastric cancer	35 (15.2)
Pancreatic cancer	7 (3.0)
Bladder cancer	5 (2.2)
Lymphoma	4 (1.7)
Gastrointestinal stromal tumor	3 (1.3)
Prostate cancer	2 (0.8)
Other cancers	8 (3.5)
Preoperative chemotherapy, n (%)	54 (23.5)
<i>Intraoperative Findings</i>	
Emergency surgery, n (%)	35 (15.2)
Obstruction level	
Small bowel	59 (25.7)
Large bowel	171 (74.3)
Number of obstruction sites	
Single	164 (71.3)
Multiple	66 (28.7)
PCI score (Mean ± SD, range)	6.00±3.99 (2-25)
Type of palliative surgery	
Palliative resection	110 (47.8%)
Stoma formation	103 (44.8%)
Bypass surgery	13 (5.7%)
Exploration only	4 (1.7%)
EBL, ml (Mean ± SD, range)	435.74±1047.64 (0-11800)
Duration of operation, min (Mean ± SD, range)	123.61±67.93 (25-430)
<i>Postoperative Findings</i>	
Length of postoperative stay, days (Mean ± SD, range)	17.09±23.65 (1-216)
Resume oral intake, n (%)	205 (89.1)
Length of postoperative oral nutrition, months (Mean ± SD, range) (n=205)	13.54±25.70 (0.1-197.5)
Postoperative chemotherapy, n (%)	155 (67.4%)
30-day morbidity, n (%)	63 (27.4)
Wound	31 (13.5)
Infectious	3 (1.3)
Noninfectious	29 (12.6)
Adverse outcome, n (%)	55 (23.9)
Reobstruction	38 (16.5)
Reoperation	17 (7.4)
30-day mortality	18 (7.8)
Overall survival, months (Mean ± SD, range)	15.51±24.69 (0.1-197.5)

Abbreviations: BMI: Body Mass Index; ASA score: American Society of Anesthesiologists (ASA) physical status classification; PCI score: Peritoneal Cancer Index score; EBL: Estimated Blood Loss.

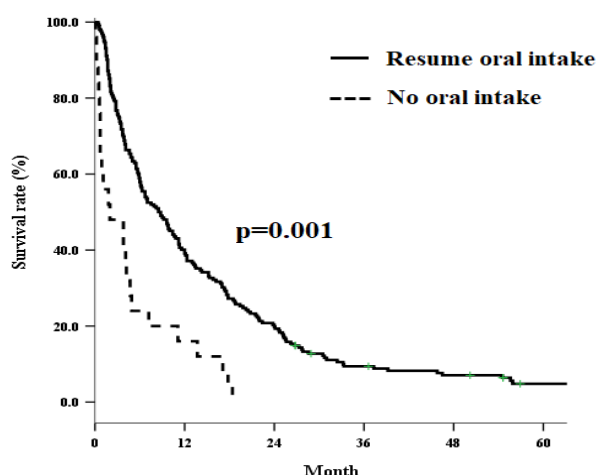
**Table 1:** Baseline characteristics of the patients.

Procedure, n(%)	Overall (n=230)	Small bowel obstruction (n=59)	Large bowel obstruction (n=171)
Palliative resection	110 (47.8%)	13 (22.0%)	97 (56.7%)
Stoma formation	103 (44.8%)	35 (59.3%)	68 (39.8%)
Bypass surgery	13 (5.7%)	8 (13.6%)	5 (2.9%)
Exploration only	4 (1.7%)	3 (5.1%)	1 (0.6%)

**Table 2:** Type of palliative procedures according to bowel obstruction site.



**Figure 1:** Patient with pseudomyxoma peritonei. (a-b) A 39-year-old male patient with pseudomyxoma peritonei replacing whole abdominal cavity. This patient presented with symptoms of colon obstruction. (c-d) Intraoperative finding of the same patient. (e) Debulking surgery with total colectomy was performed.



**Figure 2:** Overall survival according to resume oral intake.

	Univariate	Multivariable		
		HR	95% CI	P-Value
Age, years	0.997			
Gender	0.959			
ASA Class	0.994			
Primary origin of cancer	0.992			
PCI score	0.999			
Obstruction level	0.473			
Obstruction site	0.999			
Preoperative chemotherapy	0.999			
Palliative resection of primary tumor	0.999			
Duration of operative	0.993			
EBL	0.999			
Resume oral nutrition	<0.001	2.207	1.379~3.532	0.001
Duration of oral nutrition	<0.001	0.846	0.825~0.868	<0.001
Postoperative chemotherapy	0.888			
Postoperative length of stay	0.922			
Postoperative complication	0.999			
Adverse outcome	0.999			

**Abbreviations:** ASA score: American Society of Anesthesiologists (ASA) physical status classification; PCI score: Peritoneal Cancer Index score; EBL: Estimated Blood Loss.

**Table 3:** Univariate and multivariate cox regression analysis of overall survival.

## Discussion

Symptom palliation is one of the most important aspects of managing incurable cancer [11]. However, the best management for patients with MBO is controversial, and various clinical situations make it difficult to develop an optimal management strategy. Choices for the management of patients with bowel obstruction due to progressive advanced malignancy have both pros and cons [12,13]. Palliative surgery can relieve obstructive symptoms, but the operative mortality rate is 21-40%, and the complication rates vary from 20-40% [9]. A report in the United Kingdom from the National Confidential Enquiry into Perioperative Deaths (NCEPOD) stated that surgeons are performing too many 'inappropriate and aggressive' operations on patients who are frail or terminally ill, and it is explicit from the report that surgeons need to be clear about the aims of each operation [14]. On the other hand, although supportive care has less risk than palliative surgery, it also has the risks of rapid deterioration of the general condition of the patient and obstructive symptoms. Although there are several prognostic criteria to help select patients who are likely to benefit from palliative surgery [15-18], the definition of MBO and patient characteristics vary between reports, so the criteria simply cannot be applied.

In this study, we evaluated the impact of palliative surgery on overall survival indirectly by resuming oral food intake regardless of the type of operation. Additionally, our study demonstrated intraoperative findings and post-operative clinical courses in patients who underwent palliative surgery for MBO. We expect the results of this study to provide a better understanding of palliative surgery and to choose the best management strategy for patients with MBO.

Surgical techniques and perioperative patient management have evolved over the past decades; however, morbidities and mortalities after operations for MBO remain high. Studies have shown a 30-day mortality rate of 25% (9-40%), a post-operative morbidity rate of 50% (9-90%), a re-obstruction rate of 48% (39-57%), and median survival time of 7 months (2-12 months) [9,19-22]. In this study, the post-operative 30-day morbidity rate was 27.4%, the 30-day mortality rate was 7.8%, and the re-obstruction rate was 16.5%, which were much lower than those reported in the literature. We had to perform reoperation in 17 patients (7.4%).

In this study, the overall survival rate was higher in patients who were able to resume oral intake after palliative surgery regardless of the primary origins of malignancy and severity, including the obstruction level, number of obstruction sites and PCI score, compared to patients who were unable to resume oral intake after palliative surgery. A prospective randomised study by Hurwitz et al. [23] evaluated the survival benefit of bevacizumab plus irinotecan, fluorouracil, and leucovorin (IFL) in patients with metastatic colorectal cancer. The median duration of survival was 20.3 months in patients given IFL plus bevacizumab. In our study, the median duration of survival was 16.8 months in patients who resumed oral nutrition after palliative surgery and the median duration of survival was 18.8 months in colorectal cancer patients who resumed oral nutrition after palliative surgery. These results cannot be directly compared, but they imply that resuming oral intake after palliative surgery has a weak but certain survival benefit as a biologic, in contrast to existing data in the literature.

The results of this study showed high success rates of resuming oral intake (89.1%) after palliative surgery regardless of the type of operation. The duration of oral intake after palliative surgery was significantly associated with overall survival ( $p < 0.001$ ) in patients with

MBO. Our study also demonstrated the impact of palliative surgery on resuming oral intake and introduced clinical risk factors associated with overall survival in patients with MBO who underwent palliative surgery. Therefore, our results support aggressive palliative surgery in patients with stage IV cancers with MBO. The general condition would have been better in patients who were able to resume oral intake after palliative surgery, but there were no significant differences in their baseline characteristics.

However, our study had a number of limitations that need to be considered. First, this was a retrospective study, and potential selection bias may have influenced the results. Second, our sample size was small, and there was no control group for comparison. All of our patients underwent palliative surgery, and patients who received supportive care, such as stent insertion, percutaneous endoscopic gastrostomy or chemotherapy/pharmacological, were not included. Third, detailed data on chemotherapy regimens and tumour response before and after palliative surgery were lacking. Finally, similar to many other studies, this study lacked data on quality of life after palliative surgery. This is a meaningful outcome for patients and their family members since obstructive symptoms, pain relief or improvements in quality of life are major concerns in incurable patients. Quality of life after palliative surgery is rarely measured or is measured with invalidated tools in the majority of studies. Further larger studies are warranted to confirm the results of this study and to establish more strengthened treatment strategies for stage IV cancer patients with MBO.

## Conclusion

In conclusion, palliative surgery for stage IV cancer patients with MBO was beneficial for resuming oral intake for most individuals (89.1%). Our data indicate that the longer the duration of oral intake is, the longer the overall survival of these incurable patients.

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