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Prognostic factor of patients with short bowel syndrome due to nonCrohn disease

A single institution observational study

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Abstract

Short bowel syndrome (SBS) is a severely disabling and potentially life-threatening condition. Survival data for patients with SBS are limited. This study aimed to investigate prognostic factors in patients with SBS undergoing surgery. We reviewed the medical records of 27 consecutive patients with SBS who were treated at our hospital between January 2018 and December 2022. SBS was defined as a remaining small bowel length <200 cm, excluding patients with Crohn disease. Of the 27 patients identified, 17 were males and 10 were females, with a median age of 77 (46–90) years and a total observation time of 137 (2–1628) days. All patients underwent surgery and received parenteral nutrition (PN) and follow-up in our hospital. Superior mesenteric artery stenosis (44.4%) and nonocclusive mesenteric ischemia (25.9%) most commonly caused SBS. The median residual small bowel length and postoperative hospital stay were 50 (5–150) cm and 48 (2–104) days, respectively. Jejunostomy was performed in 17 (62.9%) patients, and 4 (14.8%) patients were weaned off their PN. Death occurred in 14 (51.8%), and the median survival time was 209 days. The survival outcome was compared between the survival (n = 13) and the death groups (n = 14). Jejunostomy and PN rates were significantly higher in the death group ($P < .01$, $P = .03$, respectively). SBS is associated with significantly higher mortality rates. Jejunostomy and long PN duration are significantly associated with death in patients with SBS.

Abbreviations: BE = base excess, HPN = home parenteral nutrition, IF = intestinal failure, NOMI = nonocclusive mesenteric ischemia, OS = overall survival, PN = parenteral nutrition, QoL = quality of life, SBS = Short bowel syndrome, SBS-IF = short bowel syndrome with intestinal failure.

Keywords: intestinal failure, jejunostomy, parenteral nutrition, short bowel syndrome

1. Introduction

The average adult male small intestine measures approximately 550 cm from the ligament of Treitz to the ileocecal valve, with a range of 350–700 cm, whereas the small intestine in average females is usually shorter.[1] The small intestine's residual length as measured postoperatively should be considered after extensive small intestinal resection, rather than the amount removed. Generally, nutritional and/or liquid supplemental support is expected to be necessary if <200 cm of the small bowel remains.[2] Short bowel syndrome (SBS) occurs when <200 cm of small intestinal continuity is left. SBS is the most common cause of intestinal failure (IF), affecting approximately 75% of adults and 50% of children on home parenteral nutrition (HPN) in Europe.[3,4] IF was first defined in 1981 as the inability of the intestine to absorb water, electrolytes, and macronutrients (protein, carbohydrate, and fat) required for survival, thereby mandating their intravenous supplementation.[5,6] A total of 14,311 articles were retrieved using "intestinal failure" as a general term for searching PubMed on October 7, 2023, and this number has rapidly grown recently. However, the frequency of IF is much lower than any other organ failure (e.g., kidney, heart, liver, respiratory).[3] Low IF frequency might explain why IF recognition remains low. A previous study reported that SBS accounts for 64% of patients and represents the most common pathophysiological mechanism for chronic IF. It is followed by gastrointestinal dysmotility (18%), intestinal fistula (7%), mechanical obstruction (4%), and severe mucosal disease (7%).[3,7] SBS with IF (SBS-IF) necessitates long-term parenteral nutrition (PN).

SBS-IF is caused by different underlying conditions, with Crohn disease as the most common reason. However, new biological therapies have contributed to better outcomes in patients with Crohn disease. A recent study from the United Kingdom revealed a decreased proportion of patients with Crohn disease. However, surgical complications and malignancies are increasing.[7] Additionally, a real-world observational study in Japan revealed that the most frequent causative disease of SBS-IF is ileus (31.8%), followed by Crohn disease (20.1%)

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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and intestinal ischemia (16.0%).[8] The main causes of SBS in adults in Italy are surgical complications (29–50%), intestinal infarction (venous or arterial thrombosis) (25–30%), neoplasm (20%), and Crohn disease (10–20%).[9] Thus, SBS has various etiologies according to their order of frequency from country to country.

SBS has many complications, either its consequence, its cause, or PN complications. These complications include diarrhea, IF-associated liver disease, catheter-related bloodstream infections, cholesterol stones, bone metabolic disorders, and iron deficiency anemia.[7] The quality of life (QoL) of patients receiving HPN treatment is significantly affected due to the restrictive nature of nighttime HPN, which might cause limited mobility, fatigue, social isolation, and sleep and psychological disorders due to the highly impacted lifestyle.[10]

SBS-IF is associated with poor outcomes and prognosis. Data on SBS with nonCrohn disease were lacking although Crohn disease has been considered a poor prognostic factor. This study aimed to investigate the prognostic factor in patients of SBS with nonCrohn disease.

2. Materials and methods

2.1. Study design

This single-center observational retrospective case series study was conducted at Kawasaki Saiwai Hospital (Kanagawa, Japan), which is an emergency medical center to which many patients are transferred from other hospitals for acute-care surgery. The study comprised consecutive patients who underwent emergency or elective surgery for several diseases from January 2018 to December 2022. We reviewed the medical records of 27 adult patients with SBS treated at our institution. Patients with Crohn disease were excluded.

The study is conducted following Helsinki standards and STROBE criteria for observational studies and was approved by the Institutional Review Board of our hospital (R5-1).

2.2. Data collection and definitions

The following data were collected: age at initial diagnosis, sex, causative disease, body mass index (kg/m^2), base excess (BE), and lactic acid at initial surgery, postcardiovascular surgery, shock vital, residual small bowel length, jejunostomy, postoperative hospital stay, PN episode, and prognosis. Overall survival (OS) in patients was defined as the time from surgery to the time of death or to January 2023 when data were collected.

2.3. Inclusion criteria

This study included patients who are clinically diagnosed with SBS, which is indicated by a remaining small bowel length of <200 cm after undergoing surgical resection. IF was diagnosed according to the European Society for Clinical Nutrition and Metabolism criteria.[3]

2.4. Statistical analysis

Qualitative data were represented as frequencies and percentages and described as proportions, whereas quantitative continuous data were described as mean ± standard deviations or median (interquartile range and range). Fisher exact test was used for correlations of categorical variables among groups. Kaplan–Meier curves were used for survival analysis and, the Log-Rank test was used for differences between groups. The R software program (The R Foundation for Statistical Computing, Vienna, Austria) with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) was used for statistical analysis. *P*-values of <0.05 were considered significantly different.

3. Results

3.1. Patient characteristics

Out of 6000 surgery cases performed at the Gastrointestinal Surgery Department in our hospital during the observation period, 27 (17 males and 10 females) patients were eligible for inclusion in this study (Table 1). The median follow-up period was 137 days (2–1628 days). The median age was 77 years (46–90 years). The mean body mass index was 20.2 ± 3.7 kg/m^2 for males and 19.7 ± 3.6 kg/m^2 for females. SBS was caused by superior mesenteric artery stenosis (n = 12, 44.4%), nonocclusive mesenteric ischemia (NOMI) (n = 7, 25.9%), small bowel volvulus (n = 2, 7.4%), surgical complications (n = 2, 7.4%), strangulated bowel obstruction (n = 2, 7.4%), radiation enteritis (n = 1), and mesenteric ischemia caused by severe constipation (n = 1). The median lactic acid was 5 mg/dL (1.36–12.9 mg/dL) and BE was – 3.25 mmol/dL (–22.4 to 2.6 mmol/dL). A total of 7 (25.9%) cases suffered shock during surgery and 7 (25.9%) cases had cardiovascular surgery, of which 3 were coronary artery bypass graft surgery, 2 were valve surgery, and 2 were thoracic aortic surgery. The median residual small bowel length was 50 cm (5–150 cm). Jejunostomy was performed on 17 (62.9%) cases. The median postoperative hospital stay was 48 days (2–104 days), and a total of 4 (14.8%) patients were weaned off PN.

3.2. Survival analysis

A total of 14 (51.8%) patients died within 1 year. The median survival time was 209 days (Fig. 1). Of the 14 patients, 8 (57.1%) died before discharge within 1 year, with 4 (28.6%) dying at home and 2 (14.3%) transferred to and dying in the hospital. Rates of jejunostomy and PN dependence were significantly higher in the death group than in the surviving group (Table 2 and Fig. 2). Out of 14 patients during the study period, 5 (35.7%) had multiple organ failure caused by NOMI, 3 (21.4%) had dehydration or electrolyte imbalance caused by SBS, 2 (14.3%) had a respiratory

Table 1

Patient demographics and clinical characteristics.

Characteristic	Total (n = 27)
Median age, years (range)	77 (46–90)
Sex	
Male/Female	17/10
Mean BMI, kg/m^2 (SD)	
Male	20.2 (3.7)
Female	19.7 (3.6)
Causative disease, n (%)	
Superior mesenteric artery stenosis	12 (44.4)
NOMI	7 (25.9)
Small bowel volvulus	2 (7.4)
Surgical complication	2 (7.4)
Strangulated bowel obstruction	2 (7.4)
Radiation enteritis	1
Mesenteric ischemia due to severe constipation	1
Lactic acid, mg/dL (range)	5 (1.36–12.9)
BE, mmol/dL (range)	–3.25 (–22.4 to 2.6)
Postcardiovascular surgery, n (%)	7 (25.9)
Shock vital, n (%)	7 (25.9)
Residual small bowel length, cm (range)	50 (5–150)
Jejunostomy, n (%)	17 (62.9)
Postoperative hospital stay, day (range)	48 (2–104)
PN, n (%)	Weaned 4 (14.8)
	Not weaned 23 (85.2)

Categorical data are shown as n (%); continuous data are expressed as median (interquartile range).

BE = base excess, BMI = body mass index, NOMI = nonocclusive mesenteric ischemia, PN = parenteral nutrition, SD = standard deviation.

infection, 2 (14.3%) had cancer (esophageal and uterine, respectively), 1 had IF-associated liver disease, and 1 had radiation enteritis (Table 3). PN- and SBS-related complications occurred in 4 (28.5%) patients. The most common cause of death was cardiovascular disease (5 cases, 35.7%).

4. Discussion

This single-center study reported on the outcome of patients with SBS after excluding those with Crohn disease-associated SBS. Mesenteric ischemia, such as superior mesenteric artery stenosis and NOMI, occupied the greater part of the causative diseases in our data although a recent study from Japan reported that the most frequent causative diseases for SBS-IF were ileus and Crohn disease.[8] Intestinal ischemia occurs either due to stenosis or celiac or superior mesenteric artery dissection with a complication rate of 2% to 7%.[11,12] A nationwide survey from Germany reported that 34 per million people were estimated to have SBS from 2011 to 2012.[13] Thus, SBS is an extremely rare disease.

Several studies have reported on the long-term prognosis of IF.[7,10,13] A recent study revealed 54.3%, 29.8%, and 16.7% probability of survival in patients with nonmalignant IF at 10, 20, and 30 years, respectively.[7] The overall mortality rates were higher among patients with IF when compared with the general population with a standardized mortality ratio.[7] Another study reported a 64% 5-year survival rate of IF among those who remained on HPN. Survival probability was higher in patients with Crohn disease and chronic intestinal pseudo-obstruction than other causative diseases.[14] Most of the eligible patients were in their 30s to 50s according to the previously published reports to date. This could explain why many cases of Crohn disease were included. Age at the onset of mesenteric ischemia is significantly higher than age at the onset of other diseases that cause SBS. The older age and presence of mesenteric ischemia were recognized as synergistic poor prognostic factors.[14] SBS prognosis depends significantly on the underlying disease. Our study revealed worse OS because we included many older patients with cardiovascular diseases. Furthermore, aging is closely associated with increased morbidity and mortality. We may have more elderly patients with SBS in the future because life expectancy in Japan is rapidly increasing.

The length of the remaining intestinal tract is also an important prognostic factor. Intestinal lengths are measured from the duodenojejunal flexure to the terminal ileum and are usually measured at the surgery using an opisiometer.[15,16] Surgical rulers are commonly used in our country. HPN dependence was reported to significantly increase with a remnant small bowel length of <75 cm. The intestines are shortened progressively after successive and repeated surgeries in the case of Crohn disease. Careful systemic management, including hemodynamic stability, infection control, and fluid and electrolyte management, is required in cases of mesenteric ischemia because massive bowel resection is usually required and abruptly performed at the initial surgery. HPN-dependent rates are associated with prognosis, and the intestinal tract should be preserved as much as possible. Long-term survival is significantly worse in patients with HPN dependence compared with those independent of HPN.[17]

The current study revealed that NOMI included 7 (25.9%) cases out of 27 patients. NOMI was first reported by Ende in 1958.[18] It is a rare disease after cardiovascular surgery and its rate was reported to be approximately 0.4% to 9.0%.[19] NOMI is defined as discontinuous or segmental intestinal ischemia and/or necrosis in the absence of an organic obstruction within the main trunk of the mesenteric artery or vein.[20] A

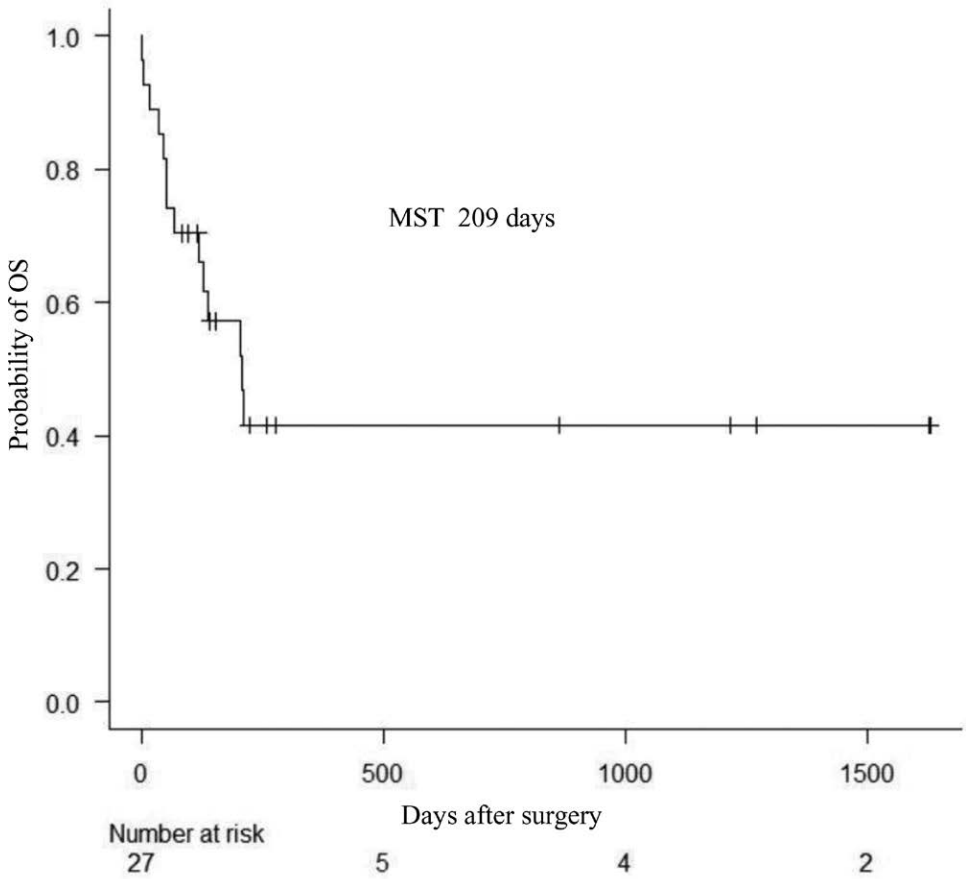

Figure 1. Survival curve of overall survival.

Table 2

Comparison of discharge outcomes in 27 patients with short bowel syndrome.

Characteristic	Survival (n = 13)	Death (n = 14)	*P*-value
Median age, years (range)	77 (60–90)	76 (46–87)	.18
Sex			.91
Male/Female	7/6	10/4	
Mean BMI, kg/m^2 (SD)	19.9 (3.0)	20.1 (4.0)	.89
Causative disease			
Superior mesenteric artery stenosis	8	4	
NOMI	2	5	
Small bowel volvulus	1	1	
Surgical complication	0	2	
Strangulated bowel obstruction	1	1	
Radiation enteritis	0	1	
Mesenteric ischemia due to severe constipation	1	0	
Lactic acid, mg/dL (range)	6.15 (1.36–12.9)	4.75 (2.11–10.06)	.36
BE, mmol/dL (range)	−6.9 (−22.4 to 2.6)	−2.75 (−9.1 to 3.2)	.08
Post cardiovascular surgery	2	5	.28
Shock vital	3	4	.84
Residual small bowel length, cm (range)	70 (5–150)	50 (10–100)	.14
Jejunostomy, n (%)	4 (30.7)	13 (92.8)	<.01
Postoperative hospital stay, day (range)	50 (32–102)	47 (2–104)	.13
PN, n (%)	Weaned 4 (14.8)	Weaned 0 (0)	.03

Categorical data are shown as n (%); continuous data are expressed as median (interquartile range).

BE = base excess, BMI = body mass index, NOMI = nonocclusive mesenteric ischemia, PN = parenteral nutrition.

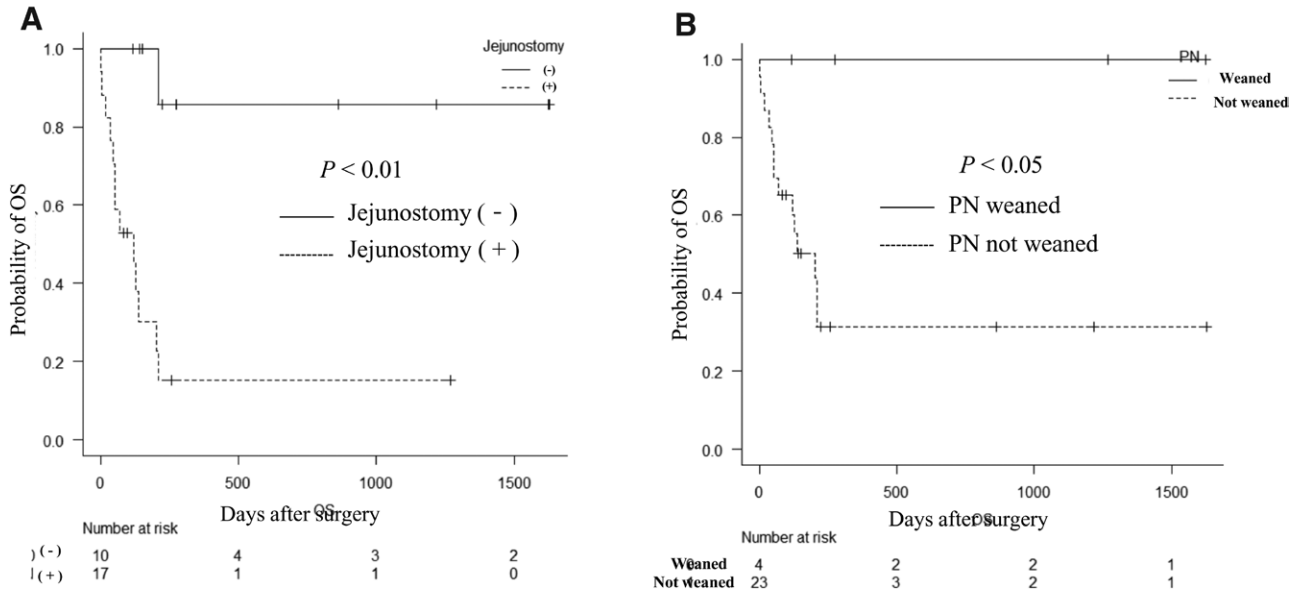

Figure 2. Survival curve of overall survival based on jejunostomy (a) and parenteral nutrition (PN) (b).

Table 3

Cause of death.

MOF	5
Dehydration/electrolyte imbalance	3
Respiratory infection	2
Cancer (esophagus: 1, Uterine: 1)	2
IFALD	1
Radiation enteritis	1

IFALD = intestinal-failure associated liver disease, MOF = multiple organ failure.

multicenter survey in Japan reported a 52.2% overall mortality rate for NOMI. This survey revealed that a multivariate regression analysis demonstrated low average blood pressure and BE as independent prognostic factors in patients with NOMI. Moreover, among patients undergoing surgery, those with long bowel resections had a worse prognosis than those with short resections.[21] SBS is also a prognostic factor in patients with NOMI. Our study revealed that most of the death cases were not attributed to SBS but to coexisting vascular disorders.

Our study indicated that jejunostomy was associated with a worse OS. We had recognized previous papers with reports on jejunostomy and HPN dependence rates,[17] but no reports indicated jejunostomy as a poor prognostic factor. Patients with jejunostomy lose much salt and water from the stoma and have many other problems, including dehydration, electrolyte imbalance, drug absorption disturbance, and gall stones. The patients' organization, patients on intravenous or nasogastric nutritional therapy, in the United Kingdom guide the management of a high-output jejunostomy or ileostomy.[2] Careful management in such cases is necessary because excess fluid and/or electrolyte imbalance can occur if the infusion is not properly administered.[22,23] SBS prognosis depends on multiple factors. However,

the presence of jejunostomy itself was the poor prognostic factor in our study. This might be attributed to the extremely short residual bowel lengths. PN withdrawal rates were significantly lower in death cases. This was thought to be caused by the shorter residual bowel tract and high jejunostomy rates. This is following the previous report, which revealed that the PN dependence rate correlates with prognosis.[17] The effect of HPN dependence on the daily lives of patients is substantial and has generated an increasing interest in evaluating QoL in such patients.[24,25] Many issues affect QoL in these patients, including the restrictive nature of overnight HPN that is associated with limited mobility, fatigue, social isolation, sleep interference, infection, and psychological problems associated with the highly regulated lifestyle required for intravenous feeding.[25–27] Teduglutide is a stable recombinant analog of glucagon-like peptide 2, which is a trophic hormone secreted by intestinal L cells.[28–30] It has been approved in Japan since 2021 for use in adult patients with SBS who are dependent on PN. Phase III trials revealed that teduglutide enhanced bowel-absorptive function and reduced PN requirements in patients with SBS-IF.[31,32] Hence, teduglutide might improve long-term prognosis due to the reduction of PN dependence.

Previously published real-world observational studies reported the most common clinical department attended by patients with SBS-IF is the surgery department (47.6%).[8] Patients are seen continuously by their primary physician in Japan; however, SBS requires multifaceted and careful management because SBS is a complex condition. We think it is advisable to deal with SBS in a multidisciplinary bowel-rehabilitation team as much as possible.

The major limitation of our study is its retrospective design and single-center experience together with the small number of included participants due to this rare disease.

5. Conclusion

To our knowledge, this is the first study to investigate the detailed prognosis of SBS with causes other than Crohn disease. Prognostic data on SBS without Crohn disease were also extremely poor. PN dependence and jejunostomy are significantly associated with poor outcomes and survival. Early jejunostomy closure as soon as possible is thought to improve the prognosis and survival of patients with SBS. Multicenter large sample size prospective studies are needed to further assess prognostic factors associated with SBS.

Author contributions

Investigation: Yasuhiro Ishiyama, Manabu Amiki.
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