Sex Differences in Non-strangulated Postoperative Adhesive Small Bowel Obstruction: A Retrospective Cohort Study

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Abstract

Background: Adhesive small bowel obstruction (ASBO) is one of the major causes of postoperative morbidity. Conservative treatment is generally applied to non-strangulated ASBO. Several factors have been reported to affect the response to conservative treatment in patients with ASBO. However, the association between sex differences and non-strangulated ASBO remains unclear. This study aimed to elucidate the effect of sex differences in non-strangulated postoperative ASBO.

Methods: We divided 192 admissions of 99 patients with non-strangulated postoperative ASBO into two groups: the male group ($n = 137$) and female group ($n = 55$). Clinical features and prognosis were compared between the two groups.

Results: Female patients had significantly poorer performance status ($p < 0.001$) and lower proportions of esophageal/gastric malignancies ($p = 0.002$), colorectal malignancies ($p = 0.034$), and history of ASBO ($p = 0.028$) than male patients. More female patients failed conservative treatment ($p = 0.036$) than male patients. Hospital length of stay (LOS) was longer ($p = 0.002$) in the female group than in the male group. Multiple logistic regression analysis showed that female sex was associated with increased odds of requiring elective surgery (odds ratio 2.381, $p = 0.040$). The Cox proportional hazards regression model revealed that female sex was an independent predictor of hospital discharge (hazard ratio 0.651, $p = 0.015$).

Conclusion: Female sex adversely affected the response to conservative treatment and LOS in patients with non-strangulated postoperative ASBO.

Background

Adhesive small bowel obstruction (ASBO) is one of the major causes of postoperative morbidity. Regarding the treatment of ASBO, when computed tomography (CT) suggests strangulation, which indicates intestinal ischemia, including decreased bowel wall enhancement, mesenteric edema, and a closed loop sign, emergency surgery is recommended (1–3). Although most patients with ASBO without strangulation (non-strangulated ASBO) respond to gastrointestinal decompression (4), some of them fail and develop persistent bowel obstruction, resulting in prolonged hospital length of stay (LOS). Based on CT imaging findings, we have previously reported that the feces sign (FS) in the transitional zone (TZ) is a good prognostic marker in non-strangulated postoperative ASBO, whereas male sex shows a tendency to be associated with an increased odds for hospital discharge (odds ratio 1.682, 95% confidence interval [CI] 0.972–2.911, $p = 0.063$) (5). In that study, we limited the study cohort to patients whose TZ was visible on CT.

Several diseases have been reported to be associated with sex differences. For example, women are associated with a better prognosis than men are in colorectal cancer (6, 7). The incidence of gallstones was significantly higher in women than in men, and the sex differences decreased with increasing age

(8). However, the relationship between ASBO and sex differences remains unclear. In this study, we aimed to evaluate the effect of sex differences in non-strangulated postoperative ASBO.

Methods

Ethics statements

This study was conducted in accordance with the ethical guidelines of the 1975 Declaration of Helsinki and approved by the Ethical Committee of Shinshu University Hospital (approval number: 4864). Informed consent was obtained from each patient included in this study by using the opt-out method. The opt-out method was approved by the Ethical Committee of Shinshu University Hospital.

Patients and study design

This retrospective cohort study aimed to evaluate the effect of sex differences in non-strangulated postoperative ASBO and included patients with postoperative ASBO who were admitted to Shinshu University Hospital between November 2007 and June 2020. ASBO was diagnosed based on clinical symptoms, including nausea, emesis, and abdominal pain as well as radiological imaging that demonstrated a dilated small intestine with a diameter > 2.5 cm. During that period, 130 patients (228 admissions) with postoperative ASBO were admitted to our department. We excluded 36 admissions of 36 patients who required emergency surgery due to intestinal ischemia caused by strangulation and confirmed by CT imaging. Our final study group consisted of 192 admissions of 99 patients with non-strangulated postoperative ASBO. They were divided into the following two groups: the male group (n = 137) and female group (n = 55) (Fig. 1).

We compared and examined the clinical backgrounds, findings on admission, and prognosis between the two groups. With regard to the management of ASBO, intravenous fluids were administered to all patients. Initially, we assessed the CT findings of strangulation of the small intestine, which requires emergency surgery. When strangulation was excluded, the patients were judged to be candidates for conservative management to treat non-strangulated ASBO. Regarding general treatment strategies for non-strangulated ASBO, patients with active symptoms, such as abdominal pain and nausea, were treated with gastrointestinal decompression, including nasogastric tube placement, hyperbaric oxygen therapy, and long tube placement. Patients with improving symptoms on admission were initially managed with fasting in the first 24–48 hours. When the obstruction persisted, the patients underwent gastrointestinal decompression. When their obstructions continued for more than 1 week or recurred after diet resumption, they were considered to have failed conservative treatment and underwent elective surgery.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences version 23.0 (IBM Corp., Armonk, NY, USA). Demographic data are presented with descriptive statistics. Non-parametric data are presented as medians with interquartile ranges. The Mann-Whitney test was used to compare

non-parametric data. Comparisons between qualitative variables were conducted using the chi-square test. LOS was evaluated using the Kaplan-Meier estimator. Multiple logistic regression analysis (forward selection method using a likelihood ratio test) was conducted to identify the patient factors associated with failure of conservative treatment for ASBO using variables that reached $p < 0.25$ in univariate analysis. The results of multiple logistic regression analysis are described as odds ratios (ORs) with 95% confidence intervals (CIs). Cox proportional hazards regression model (forward selection method using the likelihood ratio test) was conducted to assess the effect of patient factors on LOS using variables that reached $p < 0.25$ in univariate analysis. The results of Cox proportional hazards regression analysis are described as hazard ratios (HRs) with 95% confidence intervals (CIs). All tests were two-tailed, and differences with a p value of < 0.05 were considered statistically significant.

Results

The baseline characteristics of all patients are shown in Table 1. The 192 admissions included 137 men and 55 women. Most patients had visceral malignancies as the primary disease for previous abdominal surgery (74.0%). In addition, 175 of 192 admissions (91.1%) had good performance status (PS) (Eastern Cooperative Oncology Group PS 0 or 1). Regarding the treatment of ASBO, 163 of 192 admissions (84.9%) responded to conservative treatment.

Table 1
Patient characteristics

Variable	Total (n = 192)
Sex	
Male (%)	137 (71.4)
Female (%)	55 (28.6)
Age (years)	71.0 (62.0–79.0)
BMI (kg/m ²)	19.6 (18.2–22.1)
Primary disease	
Malignancy (%)	142 (74.0)
Esophagus/Stomach (%)	51 (26.6)
Colon/Rectum (%)	56 (29.2)
Uterus/Ovary (%)	26 (13.5)
Bladder/Urinary tract (%)	4 (2.1)
Other (%)	5 (2.6)
Benign (%)	50 (26.0)
Performance Status	
0 (%)	144 (75.0)
1 (%)	31 (16.1)
2 (%)	12 (6.3)
3 (%)	3 (1.6)
4 (%)	2 (1.0)
Treatment of ASBO	
Fasting (%)	54 (28.1)
Nasogastric tube placement (%)	25 (13.0)
HBO (%)	14 (7.3)
Long tube placement (%)	70 (36.5)
Elective surgery (%)	29 (15.1)
Continuous variables are presented as median (interquartile range).	
BMI, body mass index; ASBO, adhesive small bowel obstruction; HBO, hyperbaric oxygen therapy.	

Compared to male patients, female patients had a significantly lower proportion of good PS (96.4% vs. 78.2%, $p < 0.001$) and esophageal/gastric malignancies (32.8% vs. 10.9%, $p = 0.002$), colorectal malignancies (33.6% vs. 18.2%, $p = 0.034$), and history of ASBO (67.9% vs. 50.9%, $p = 0.028$). More female patients failed conservative treatment and required elective surgery than did male patients (11.7% vs. 23.6%, $p = 0.036$). LOS was longer than in the female group in the male group (12.0 days vs. 15.0 days, $p = 0.002$) (Table 2).

Table 2
Comparison of patient demographic characteristics between the male and female groups

Demographic Characteristic	Male group (n = 137)	Female group (n = 55)	<i>p</i> value
Age (years)			
Median (IQR)	72.0 (67.0–78.0)	64.0 (54.0–82.0)	0.086
Body mass index (kg/m ²)			
Median (IQR)	19.9 (18.2–22.0)	19.4 (17.2–23.6)	0.623
Performance status			
0, 1	132 (96.4)	43 (78.2)	< 0.001*
2, 3, 4	5 (3.6)	12 (21.8)	
Primary disease			
Benign (%)	39 (28.4)	11 (20.0)	0.227
Esophageal/Gastric malignancy (%)	45 (32.8)	6 (10.9)	0.002*
Colorectal malignancy (%)	46 (33.6)	10 (18.2)	0.034*
Uterine/Ovarian malignancy (%)	0 (0.0)	26 (47.3)	< 0.001*
Other malignancy (%)	7 (5.1)	2 (1.5)	0.497
Surgical approach for primary disease			
Laparotomy (%)	130 (94.9)	53 (96.4)	0.497
Laparoscopy (%)	7 (5.1)	2 (1.5)	
Postoperative period (> 5 years)			
Yes (%)	66 (48.2)	23 (41.8)	0.425
No (%)	71 (51.8)	32 (58.2)	
History of ASBO			
Yes (%)	93 (67.9)	28 (50.9)	0.028*
No (%)	44 (32.1)	27 (49.1)	
History of chemotherapy (%)			
Yes (%)	33 (24.1)	14 (25.5)	0.842
No (%)	104 (75.9)	41 (74.5)	
History of radiotherapy (%)			

Demographic Characteristic	Male group (n = 137)	Female group (n = 55)	<i>p</i> value
Yes (%)	9 (6.6)	1 (1.8)	0.164
No (%)	128 (93.4)	54 (98.2)	
White blood cell count (/μl)			
Median (IQR)	8470 (6770-10 780)	8420 (6895-11 465)	0.935
Feces sign (%)			
Yes (%)	42 (30.7)	17 (30.9)	0.973
No (%)	95 (69.3)	38 (69.1)	
Closed loop sign (%)			
Yes (%)	1 (0.7)	0 (0.0)	0.714
No (%)	136 (99.3)	55 (100.0)	
Treatment of ASBO			
Fasting (%)	35 (25.5)	19 (34.5)	0.210
Gastrointestinal decompression (%)	86 (62.8)	23 (41.8)	0.008*
Elective surgery (%)	16 (11.7)	13 (23.6)	0.036*
Gastrografen administration			
Yes (%)	76 (55.5)	27 (49.1)	0.423
No (%)	61 (44.5)	28 (50.9)	
Hospital length of stay (days)			
Median (IQR)	12.0 (8.0–17.0)	15.0 (11.0–25.0)	0.002*
Asterisk indicates a statistical significance ($p < 0.05$). IQR, interquartile range; ASBO, adhesive small bowel obstruction.			

Next, we examined the effect of sex differences on the requirement for elective surgery to treat non-strangulated ASBO. As a result of multiple logistic regression analysis of the clinical background and findings upon admission, female sex was associated with an increased odds for the requirement for elective surgery (OR 2.381, 95% CI 1.042–5.440, $p = 0.040$), whereas body mass index was associated with a decreased odds (OR 0.875, 95% CI 0.769–0.996, $p = 0.043$) (Table 3).

Table 3
Multiple logistic regression analysis of the requirement for elective surgery

Variable	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value
Sex (Female)	2.341	1.040–5.271	0.040*	2.381	1.042–5.440	0.040*
Age (year)	0.988	0.963–1.015	0.377			
Body mass index	0.868	0.757–0.995	0.043*	0.875	0.769–0.996	0.043*
Performance status	1.216	0.763–1.938	0.411			
Primary disease (benign)	1.618	0.695–3.767	0.264			
Primary disease (esophageal/gastric malignancy)	0.861	0.344–2.155	0.748			
Primary disease (colorectal malignancy)	0.590	0.226–1.537	0.280			
Primary disease (uterine/ovarian malignancy)	0.702	0.196–2.511	0.587			
Primary disease (other malignancy)	3.019	0.711–12.829	0.134	-	-	0.210
Surgical approach for primary disease (laparotomy)	0.000	0.000–0.000	0.999			
Postoperative period (> 5 years)	0.788	0.354–1.755	0.560			
History of adhesive small bowel obstruction	0.488	0.220–1.084	0.078	-	-	0.218
History of chemotherapy	0.600	0.215–1.674	0.329			
History of radiotherapy	0.611	0.074–5.015	0.647			
White blood cell count	1.000	1.000–1.000	0.974			
Feces sign	0.421	0.152–1.163	0.095	-	-	0.173
Asterisk indicates a statistical significance ($p < 0.05$). CI, confidence interval.						

Finally, we assessed the effect of sex differences on LOS. The Kaplan-Meier estimator revealed that the female group had a significantly longer LOS than the male group ($p = 0.002$) (Fig. 2). As a result of Cox proportional hazards regression model of the clinical background and findings upon admission, female sex (HR 0.651, 95% CI 0.461–0.918, $p = 0.015$), PS (HR 0.697, 95% CI 0.560–0.866, $p = 0.001$), history of ASBO (HR 1.438, 95% CI 1.062–1.947, $p = 0.019$), and FS (HR 1.525, 95% CI 1.111–2.094, $p = 0.009$) were observed as independent predictors of hospital discharge (Table 4).

Table 4
Cox proportional hazard regression analysis of hospital discharge

Variable	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	p value	Hazard ratio	95% CI	p value
Sex (Female)	0.540	0.385–0.759	< 0.001*	0.651	0.461–0.918	0.015*
Age (year)	0.993	0.984–1.002	0.111	-	-	0.722
Body mass index	1.050	1.010–1.091	0.013*	-	-	0.056
Performance status	0.648	0.522–0.805	< 0.001*	0.697	0.560–0.866	0.001*
Primary disease (benign)	1.155	0.834–1.601	0.385			
Primary disease (esophageal/gastric malignancy)	1.163	0.840–1.609	0.363			
Primary disease (colorectal malignancy)	1.202	0.877–1.650	0.253			
Primary disease (uterine/ovarian malignancy)	0.649	0.425–0.990	0.045*	-	-	0.510
Primary disease (other malignancy)	0.527	0.257–1.080	0.080	-	-	0.117
Surgical approach for primary disease (laparotomy)	1.438	0.734–2.817	0.290			
Postoperative period (> 5 years)	0.951	0.712–1.271	0.735			
History of adhesive small bowel obstruction	1.444	1.069–1.952	0.017*	1.438	1.062–1.947	0.019*
History of chemotherapy	1.294	0.927–1.806	0.130	-	-	0.554
History of radiotherapy	1.632	0.860–3.095	0.134	-	-	0.220
White blood cell count	1.000	1.000–1.000	0.943			
Feces sign	1.514	1.105–2.074	0.010*	1.525	1.111–2.094	0.009*
Asterisk indicates a statistical significance ($p < 0.05$). CI, confidence interval.						

Discussion

In the present study, we found that female sex was associated with an increased odds of requiring elective surgery to treat non-strangulated postoperative ASBO and prolonged LOS.

We have previously reported that FS is associated with good prognosis in patients with non-strangulated postoperative ASBO, on the condition that the patients who required emergency surgery and whose TZ was invisible on CT were excluded (5). In line with our previous report, this study showed that FS and PS as well as sex differences were significantly associated with LOS. Several factors affect prognosis in patients with ASBO. For example, FS (9, 10), number of TZs (11), number of beak signs (12), anterior adhesion (13, 14), and water-soluble contrast agent administration (13–15) have been reported to be associated with successful non-operative treatment in patients with ASBO. It has been reported that male sex was not associated with the need for operative exploration in univariate analysis (OR 0.61, 95% CI 0.28–1.35, $p = 0.224$) (10) and successful non-operative management in multivariate analysis (OR 1.60, 95% CI 0.90–3.10) (15). Even though these studies did not reach statistical significance, they showed that female sex was associated with poorer prognosis in ASBO than male sex. The cohort in this study did not include patients who underwent emergency surgery, resulting in only one patient presenting with a closed loop sign on CT on admission (Table 2). This may explain why female sex has not been reported to inversely affect the prognosis of postoperative ASBO.

The main etiology of sex differences in several diseases is sex hormones, in particular, estrogen. It has been reported to be associated with increased risks of coronary heart disease, breast cancer, stroke, and pulmonary embolism, and conversely a decreased risk of colorectal cancer, endometrial cancer, and hip fracture (16). In the present study, female sex was associated with failure of conservative treatment and prolonged LOS, whereas primary diseases including uterine and ovarian malignancy did not affect failure of conservative treatment or prolonged LOS, according to the results of multiple logistic regression analysis of the requirement for elective surgery (Table 3) and Cox proportional hazard regression of hospital discharge (Table 4). This finding suggests that the cause of poor prognosis in the female group is derived from female intrinsic factors, such as physiological and anatomical differences. However, there have been no previous reports on the association of sex differences with response to the treatment of ASBO.

Some limitations exist in the present study. First, it was a retrospective single-center study with a small sample size, and therefore, it may be subject to selection bias. Second, there is no unified protocol for the treatment of ASBO in our institute. Generally, the obstruction continued for more than 1 week despite gastrointestinal decompression, or if it recurred after diet resumption, we performed elective surgery. However, some patients with a high risk for surgery (e.g., old age and poor PS) were treated conservatively for longer than 1 week. Third, at our institute, patients with the closed loop sign on CT imaging generally underwent emergency surgery, even though it did not represent bowel ischemia. Therefore, as aforementioned, the poor prognosis in female patients, which was revealed in this study, may not fit ASBO with a closed loop sign.

Perspectives and significance

When considering the difficulty of predicting the response to gastrointestinal decompression and LOS in ASBO, this result is of significant importance because it suggests that sex differences are possible surrogate markers to predict the prognosis of patients with non-strangulated ASBO. Further multicenter studies incorporating a larger number of patients are needed to definitively confirm whether sex differences are associated with the prognosis of postoperative ASBO.

Conclusion

In conclusion, we found that female sex was associated with an increased odds of requiring elective surgery and prolonged LOS in patients with non-strangulated postoperative ASBO.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethical Committee of Shinshu University Hospital (approval number: 4864). Informed consent was obtained from each patient included in this study by using the opt-out method. The opt-out method was approved by the Ethical Committee of Shinshu University Hospital.

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YY designed the study, acquired the data, performed the research, and drafted the manuscript. All authors were responsible for the integrity of the data and the accuracy of the data analysis. YM and YS revised the manuscript. All authors have read and approved the final manuscript.

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Figures

Figure 1

Flow chart of the selection of study groups. ASBO, adhesive small bowel obstruction.

Figure 2

Proportion of hospital discharges among male patients (dotted line) and female patients (solid line). The cross and plus marks represent censoring in male and female patients, respectively.